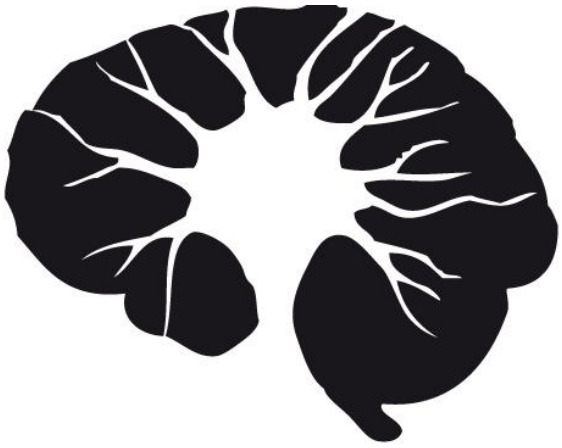

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APRIL 25, 2014 (Friday)

12.30	Registration opens	
13.30 - 14.30	- Large Aula A - Lecture and interactive presentation: **Guilherme A. Zimeo Morais** ***fNIRS: a cost-effective and robust technique for measuring neuroactivation*** (NIRx Instrumentation and Application Engineer)	
14.45	- Large Aula A - Opening Ceremony	
15.00 – 16.00	- Large Aula A - Opening Lecture: **David Colquhoun** ***Inference of mechanisms from single ion channel observations. New light on the mechanism of partial agonism*** (University College London, UK)	
16.15 – 17.45	- Large Aula A - Session I **<u>Basic Neuroscience</u>** chaired by: **Laura Cancedda** (Italian Institute of Technology, Genova, Italy) 1. **Laura Cancedda**: Modulation of intracellular chloride to regulate synaptic plasticity and rescue cognitive functions in Down Syndrome	- Medium Aula - Session I **<u>Neural Correlates of Language Processing</u>** chaired by: **Marcin Szwed** (Jagiellonian University, Poland) 1. **Marcin Szwed:** Understanding learning to read through fMRI of rapid letter detection in skilled adult readers and dyslexic 10-year old children

	2. **Joanna Szczurkowska**: Negr1 is required for transition of migrating pyramidal neurons from layer V to layer II/III of the mouse cerebral cortex 3. **Magdalena Kisiel**: Mutations of a position alpha1F64 in GABAA receptor binding site differently influence modulation GABA-ergic currents by basic and acidic pH 4. **Urszula Górska**: Cholesterol determines fusion pore properties	2. **Anna Beres:** Translanguaging: a way to facilitate new knowledge acquisition 3. **Szymon Biduła:** Modulations within the right temporal lobe differentiate between typically and atypically organized language 4. **Katarzyna Siuda:** Reading with eyes closed: the preliminary effects of tactile Braille reading course for sighted measured with fMRI 5. **Łukasz Bola:** When the sighted brain goes tactile: neuroplasticity in sighted Braille learners
17.45 – 18.15	Coffee Break	
18.15 – 19.15	- Large Aula A - Plenary lecture: **Nikos Logothetis** ***Hippocampal–cortical interactions during periods of subcortical silence*** (Max Planck Institute for Biological Cybernetics, Tübingen, Germany)	
19.15 - 20.15	- Large Aula A - 'Meet Your Speaker' with special lecture by **David Colquhoun** ***The crisis of reproducibility. Why is so much published science wrong?***	
20.15	Welcome Reception	

APRIL 26, 2014 (Saturday)

8.30	Registration opens	
9.00 - 10.30	- Large Aula A - Session II **Neuropathology** chaired by: **Gilles van Luijtelaar** (Radboud University Nijmegen, the Netherlands) 1. **Gilles van Luijtelaar**: New outlooks on absence epilepsy 2. **Valerio D'Amore**: Effects of chronic treatment with the mGluR5 (VU0360172) and the mGluR1 (RO0711401) enhancers on absence seizures 3. **Dragan Hrncic**: Modulation of NO signaling pathways in an experimental model of epilepsy: focus on ictal EEG 4. **Bálint Péter Kerekes**: Simultaneous Electrophysiology and Ca-imaging of human cortical sinchronous population activity in vitro	- Medium Aula - Session II **Affective Neuroscience** chaired by: **Hadas Okon-Singer** (University of Haifa, Israel) 1. **Hadas Okon-Singer:** Are we able to ignore emotional distractors? The influence of attention, personality, and neural architecture 2. **Wojciech Zajkowski:** Frustrated brain – introduction to a novel fMRI stress induction procedure 3. **Marta Jaśkiewicz:** The affective aspect of music aesthetic. An ERP study 4. **Mirosław Wyczesany:** EEG connectivity reveals effects of emotional state on visual and attentional systems
10.30 – 11.00	Coffee Break	
11.00 - 12.30	- Large Aula A - Session III **Neurophysiology** chaired by: **Fabian Kloosterman** (Neuro-Electronics Research Flanders, Leuven, Belgium)	- Medium Aula - Session III **Visual Processing** chaired by: **Gilles Pourtois** (Ghent University, Belgium)

	1. **Fabian Kloosterman***:* Reliving your experiences: memory replay in the hippocampus 2. **Anna Pitas**: Neuronal tuning to instantaneous stimulation interval in the barrel cortex 3. **Yaneri A. Ayala**: Stimulus specific adaptation and its modulation by inhibition and acetylcholine in the auditory brain 4. **Jarosław Motylewski**: Pimary cortical neuronal cultures on graphene oxide and reduced graphene oxide	1. **Gilles Pourtois:** Modulation of the earliest stimulus-driven wave of activation in human primary visual cortex through competition with endogenous attention 2. **Ewa Beldzik:** Dissociating EEG sources associated to stimulus and response evaluation in numerical Stroop task using Independent Component Analysis 3. **Michał Bola**: Functional connectivity network breakdown in blindness 4. **Rob van der Lubbe:** The influence of Mindfulness training on EEG indices for attentional orienting
12.45 - 13.45	- Large Aula A – Plenary lecture: **Rafael Malach** ***Letting go in human brain research*** (Weizmann Institute of Science, Israel)		
13.45 - 15.00	Lunch		
15.00 - 16.30	- Large Aula A - Session IV **Neurogenetics** chaired by: **Paul Franken** (University of Lausanne, Switzerland)	- Medium Aula - Session IV **Neural Correlates of Pain and Somatosensory Stimulation** chaired by: **Tineke van Rijn** (Radboud University Nijmegen, the Netherlands)	- Conference Room - **Interactive Session on Medical Case Reports** chaired by: **Krzysztof Banaszkiewicz** (John Paul's Hospital in Krakow, Poland)

	1. **Paul Franken**- IBRO Alumni Lecture: Genetic dissection of rhythmic brain activity during sleep 2. **Urszula Skupio**: Chronic activation of the glucocorticoid receptor induces behavioural and molecular markers of depression in mice 3. **Katarzyna Lepeta:** Untranslated region polymorphisms of matrix metalloproteinase 9 and their role in schizophrenia. The role in the local translation 4. **Stefano Espinoza**: Frontostriatal dysfunction in mice lacking TAAR1	1. **Emanuel van der Broeke:** Characterizing secondary hyperalgesia induced by high frequency electrical stimulation 2. **Joukje Oosterman:** Cognitive correlates of pain report in the elderly 3. **Diana Torta:** Visuo-proprioceptive conflicts and nociception 4. **Dagmar van Rijckevorsel**: Altered neuronal pain processing in anterior cutaneous nerve entrapment syndrome	1. **Michał Błaż**: An encephalitic patient with psychiatric symptoms at onset 2. **Carmen Góralski**: Recovery of a Patient with Miller-Fisher Syndrome, a Variant of Guillain-Barre Syndrome 3. **Mark-Victor Siwoski**: Insidious progression of hereditary vascular dementia in a patient with migraines and stroke 4. **Natalia Pawełczyk**: Pelizaeus-Merzbacher Disease - a case report 5. **Katarzyna Siuda**: Emotional disorders in patients with cerebellar lesions 6. **Piotr Śliwiński**: Tethered spinal cord syndrome – Usability of surgical treatment in adults - case report 7. **Piravin Kumar Ramakrishnan**: Mother and son diagnosed with Tick-borne Encephalitis transmitted by consumption of unpasteurized goat milk

			8. **Grzegorz Siwek**: Obsessive Compulsive Disorder as a complication of deep brain stimulation therapy for Parkinson's Disease: a case study
16.30 - 18.15	- Exhibition Room - Poster Session I & Coffee		
18.15 - 19.15	- Large Aula A - Plenary lecture: **Philbert Tsai** ***Blood flow and the angioarchitecture of mouse cerebral cortex*** (University of California, San Diego, USA)		
21.00	Social Event: party for all participants		

APRIL 27, 2014 (Sunday)		
9.00 – 10.30	- Large Aula A - Session V **<u>Neurode(re)generation</u>** chaired by Patrik Verstreken (VIB Center for the Biology of Disease, Department of Human Genetics, KU Leuven, Belgium) 1. **Patrik Verstreken**: Targeting mitochondrial dysfunction in Parkinson's disease 2. **Henrike Kristen**: Herpes simplex virus type 2 induces the apprearance of Alzheimer´s disease-like neurodegenrative markers	- Medium Aula - Session V **<u>Psychopathology in Neuroscientific Research</u>** chaired by: **Adrianna Mendrek** (Bishop's University, Canada) 1. **Adrianna Mendrek:** Sex, drugs and the brain 2. **Sven Müller:** Incidental threat during visuo-spatial working memory in adolescent anxiety: An emotional memory-guided saccade task

	3. **Mayank Chaturvedi**: TIMP-1 loaded nanoparticles: a therapeutic strategy for neuroprotection 4. **Maciej Sułkowski**: Distinct neuronal differentiation of induced Pluripotent Stem Cells (iPS) into dopamine and neuromelanin producing cells	3. **Ingrida Antonova:** Schizophrenic patients show abnormal early brain activation during lateralized visual stimulation 4. **Ingar Zielinski:** Developmental Disregard in children with unilateral Cerebral Palsy - A spatial attention deficit?
10.30 – 11.00	Coffee Break	
11.00 – 12.00	- Large Aula A - Plenary lecture: **Angela Roberts** ***Neurobiological mechanisms underlying the regulation of negative emotion*** (University of Cambridge, UK)	
12.00 – 13.00	Lunch	
13.00 – 14.30	- Exhibition Room - Poster Session II	
14.30 – 16.00	- Large Aula A - Session VI **<u>Learning and Memory</u>** chaired by Ewelina Knapska (Nencki Institute of Experimental Biology, Warsaw, Poland) 1. **Ewelina Knapska**: A cure for fear: apart or together? 2. **Alicja Puścian**: Diverse patterns of behavioral deficits in subjects being genetic mouse model of Fragile X syndrome	- Medium Aula - Session VI **<u>SSVEP Frequency Responses in Human EEG Studies</u>** chaired by: **Jarosław Żygierewicz** (University of Warsaw, Poland) 1. **Jarosław Żygierewicz:** Quantification of SSVEP Frequency Responses in Human EEG related to BCI 2. **Anna Chabuda:** SSVEP-BCI based on the phase relationship of the stimulus and response

	3. **Jeffrey Martin**: Delay discounting behaviour in dopamine D1 mutant and wild type rats 4. **Dominika Drulis-Fajdasz**: Inhibition of glycogen metabolism in astrocytes positively influence on the synaptic plasticity in old rats	3. **Maciej Łabęcki:** Habituation of Steady State Visual Evoked Potentials 4. **Maria Nowicka:** Time evolution of Steady State Visual Evoked Potentials for different stimulation frequencies 5. **Aleksandra Pidde:** Comparison of LDA and SVM classifiers in classification of motor imagery based on EEG 6. **Paweł Kordowski:** Spatio-Temporal Dictionaries for Multivariate Matching Pursuit Decompositions of Evoked Brain Responses in MEG
16.15 - 17.15	- Large Aula A - Closing lecture: **Carles Escera** ***Neural mechanisms of auditory perception: regularity encoding and deviance detection from brainstem to cortex*** (University of Barcelona, Spain)	
17.15 - 17.30	Closing remarks (with awards for the best oral and poster presentations)	

April 25, 2014 (Friday)

LECTURE & INTERACTIVE PRESENTATION:
13.30 – 14.30

fNIRS: a cost-effective and robust technique for measuring neuroactivation

Guilherme A. Zimeo Morais

NIRx Instrumentation and Application Engineer

In recent years, functional Near-Infrared Spectroscopy (fNIRS) has increasingly become a valuable tool in the neurosciences as a robust imaging method to retrieve hemodynamic states (Hb, HbO) information from the brain. It consists of a safe and minimally invasive technique relying on small and relatively inexpensive, easy-to-handle technology. fNIRS applications embrace a wide range of research areas, such as Brain-Computer Interface (BCI), attention, language, learning, child development and neonatal studies. Furthermore, the technology may be easily integrated and synchronized with other neuroscience modalities such as EEG, brain stimulation (TMS and tDCS) and Eye-tracking, adding physiological information to these methods. As one of the world-leading fNIRS providers, NIRx offers scalable systems from portable to high-density whole head measurements. In this one-hour talk, we will present the fNIRS foundations, examples of active areas of research and solutions provided by NIRx.

OPENING LECTURE:
15.00 – 16.00

Inference of mechanisms from single ion channel observations. New light on the mechanism of partial agonism

David Colquhoun

University College London, UK

Receptor mechanisms are described as transitions between discrete states if the receptor. If the rate constants for each of the transitions can be measured we can predict the behaviour of the receptor under any experimental conditions. In particular we can predict its behaviour in synapses. Single ion channel records allow estimation of up to 18 free parameters (rate constants), far more than can be estimated by any other method. Use of such methods allowed us to postulate a new view of partial agonism.

Basic Neuroscience

16.15 – 17.45
chaired by: Laura Cancedda (Italian Institute of Technology, Genova, Italy)

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1. ***Modulation of Intracellular Chloride to Regulate Synaptic Plasticity and Rescue Cognitive Functions in Down Syndrome***

Laura Cancedda

Italian Institute of Technology, Genova, Italy

Down syndrome (DS) is the most frequent genetic cause of mental retardation, with DS patients displaying low intelligence quotient, learning deficits, and memory impairment particularly in hippocampus-related functions. Trisomic mouse models of DS reproduce the main cognitive disabilities of the human syndrome. In particular, Ts65Dn mice show impaired synaptic plasticity (i.e., long-term potentiation, LTP) as well as learning and memory deficits. Increased GABAergic transmission through Cl- permeable GABAA receptors (GABAAR) largely determines these deficits in DS mice. Indeed, LTP and cognitive impairment can be rescued reducing the magnitude of GABA-mediated signaling by treatment with GABAAR antagonists. Nevertheless, the efficacy of GABAergic transmission has never been directly assessed in DS. Here, we show that GABAergic signaling is excitatory rather than inhibitory and the reversal potential for GABAA-driven Cl- currents (ECl) is depolarized in hippocampi from adult DS mice. Accordingly, expression of cation/Cl- importer NKCC1 is increased in the hippocampus of trisomic mice and DS patients. Notably, NKCC1

inhibition by the FDA-approved drug bumetanide restores EcI, synaptic plasticity and hippocampus-dependent learning and memory in DS mice. Our findings demonstrate that GABA is excitatory in DS adult mice, and identify a new and safe therapeutic approach to rescue cognitive disabilities of DS patients.

2. *Negr1 is required for transition of migrating pyramidal neurons from layer V to layer II/III of the mouse cerebral cortex*

Joanna Szczurkowska [a], F. Pischedda[b], F. Manago[a], C. Haas[c], F. Papaleo[a], M. Schäfer [d], G. Piccoli [b]*, L. Cancedda[a]*

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[b] CNR Institute of Neuroscience and Department of Pharmacology, University of Milan, Italy
[c]University of Freiburg, Germany
[d]Department of Anesthesiology, University Medical Center of Mainz, Germany
*: equal contribution

Newborn pyramidal neurons migrate along radial glia fibers, to create the six-layered structure of the neocortex. Disruption in neural migration can lead to brain malformations and neurodevelopmental disorders such as Autism Spectrum Disorders (ASD). Common knowledge indicates cell-adhesion molecules (CAMs) as essential for neural migration. Neuronal growth regulator 1 (Negr1) is a CAM, and NEGR1-gene mutations have been recently associated to ASD. By in utero electroporation coupled with RNA interference (siRNA), we downregulated Negr1 in late-born pyramidal neurons migrating to layers 2/3 of the neocortex. We found that Negr1 siRNA caused ectopic positioning of neurons concentrated at the border between layer 5 and layer 4 of the somatosensory cortex but did not cause migration defects in the motor or prefrontal cortices. We found that FGFR2 (also associated to ASD) and its partner NCAM physically and functionally interact with Negr1and downregulation of NCAM in utero resulted in a strikingly similar phenotype on neuronal migration as found for Negr1. Interestingly, downregulation of Negr1 in the embryonic somatosensory cortex resulted in decreased number of ultrasound vocalizations in pups. Thus, Negr1/FGFR2/NCAM complex is necessary for proper neuronal migration of pyramidal neurons in the somatosensory cortex, indicating a possible role for this complex in autism.

3. *Mutations of a position alpha1F64 in GABAA receptor binding site differently influence modulation GABA-ergic currents by basic and acidic pH*

Magdalena Kisiel, Magdalena Jatczak, Marta M. Czyżewska, Jerzy W. Mozrzymas

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Laboratory of Neuroscience, Department of Biophysics, Wrocław Medical University, Poland

GABAAR plays a crucial role in a neuroinhibition. It was previously found that GABAARs are sensitive to changes of the local pH which may be connected to physiological and pathological processes. Proposed mechanisms of pH action on GABAARs included modulation of agonist binding and desensitization. Our recent results (Szczot et al. 2014) have shown that alpha1F64 residue at the receptor binding site affects receptor's preactivation transition preceding channel opening. The same residue has been shown to affect GABAARs sensitivity to modulation by protons. Therefore, we decided to use GABAARs (alpha1 beta2 gamma2) with alpha1F64 mutations to investigate whether pH may module preactivated transitions (which were not considered in previous studies). We used a patch clamp technique with ultrafast exchange of solutions to address this problem.We found that alpha1F64 mutations weaken the upregulation of GABA-ergic currents by acidification, and enhance the downregulation of GABA-ergic currents at alkaline pH. Our observations for mutated receptors (at basic pH: large amplitude reduction, slower deactivation after long pulse, accelerated desensitization; at acidic pH: small amplitude increase, slower desensitization) are difficult to explain by changes solely in preactivation kinetics, indicating thus that other gating characteristics are affected by protons.

4. *Cholesterol determines fusion pore properties*

Urszula Górska [a], Boštjan Rituper, PhD[b], Prof. Robert Zorec, PhD[b]

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[a]Jagiellonian University, Krakow, Poland
[b]Institute of Pathophysiology, Faculty of Medicine, University of Ljubljana, Slovenia

Regulated exocytosis is a process in which secretory vesicles merge with plasma membrane and release their content into extracellular space. During membrane merging a channel-like structure termed fusion pore is created. Many proteins and lipids are involved in the regulation of membrane fusion, but among them cholesterol seems to play a special role. We tested how manipulation of cellular cholesterol content affects critical part of regulated exocytosis,

membrane fusion. To monitor and measure membrane fusion, we have performed electrophysiologic high-resolution patch-clamp cell-attached membrane capacitance measurements. All experiments were done on primary pituitary lactotroph cultures prepared up to three days before the experiments. Membrane fusion parameters were recorded and analysed for control cells and cholesterol depleted cells (to 71% of control value). Cholesterol was depleted with 10 mM methyl-β-cyclodextrin (MβCD) solution. The manipulation of cellular cholesterol content did not affect cellular viability. We showed that cholesterol depletion strongly attenuates unitary transient exocytic event frequency. At the same time, depletion also prolongs open fusion pore time. The increase in normalized fusion pore conductance (to vesicle size, i.e. Gp/Cv ratio) suggests that cholesterol depleted cells favour the formation of wider, less stable fusion pores. These experiments demonstrate that cholesterol is involved in regulation of transient fusion pore stability as well as dynamics of membrane fusion.

Neural Correlates of Language Processing

16.15 – 17.45

chaired by: Marcin Szwed (Jagiellonian University, Poland)

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1. *Understanding learning to read through fMRI of rapid letter detection in skilled adult readers and dyslexic 10-year old children*

Marcin Szwed

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Psychophysiology Laboratory, Jagiellonian University, Krakow, Poland

The study of neural bases of reading offers an opportunity to ask general questions on the nature of learning and expertise. Learning to read results in the development of the Visual Word Form Area (VWFA), a high-level visual reading area. Most fMRI of reading used word-stimuli, which engage top-down linguistic influences. Here, we examine children and adults in a rapid detection task with letters, digit, symbol and false-font strings that do not engage such feedback. We ask: 1) will we replicate the underactivation of the VWFA commonly found in children with dyslexia? 2) Can we substantiate reports of expertise-dependent engagement of retinotopic visual areas in reading (Szwed et al., 2011, 2014)? Relative to control subjects, 18 10-year old dyslexic children showed the largest underactivation not in the VWFA but in the dorsal visual stream. In contrast, during rapid letter detection task in adults, we found that retinotopic visual areas were activated more for correct vs. incorrect trials for (over-practiced) letters, but not for (novel) false fonts. Learning to read thus involves 1) changes in dorsal stream brain regions that seem different from regions involved in skilled reading in adults, 2) leads to expertise-dependent recruitment of early retinotopic areas in adults.

2. *Translanguaging: a way to facilitate new knowledge acquisition*

Anna Beres, Manon Jones, Nick Davis, Bastien Boutonnet, Guillaume Thierry

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Bangor University, UK

Bilingual education has witnessed a major shift towards mixing two languages in the classroom. Garcia (2009) argues that children engage in 'translanguaging' - the production of an output of their learning in a language different to that of instruction. So far, insights into the potential benefits of this method have been qualitative; here we aim at quantifying the benefits of translanguaging for semantic integration. We tested Welsh-English bilinguals on a novel-object learning task and manipulated the learning context. Information about the novel objects was presented in English and participants named familiar, related picture from an array of four objects, either in English (monolingual) or Welsh (translanguaging). After completing a staircase learning procedure, the efficiency of semantic integration was measured using a picture-picture priming paradigm and ERPs. As expected, we found a semantic priming effect indexed by amplitude reduction of the N400 component when novel objects were followed by related rather than unrelated picture. Moreover, novel objects learnt through translanguaging induced more N400 amplitude reduction than those learnt in a monolingual context, suggesting that translanguaging successfully heightens the level of engagement of the conceptual system. Such results provide neuroscientific evidence of the benefit of using language alternation in learning new concepts.

3. *Modulations within the right temporal lobe differentiate between typically and atypically organized language*

Szymon Biduła[a], Łukasz Przybylski[a], Mikołaj Pawlak[a,b], Grzegorz Króliczak[a]

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[b]Department of Neurology and Cerebrovascular Disorders, Poznan University of Medical Sciences, Poland

It is commonly assumed that the left hemisphere is critical for language processing. Although the engagement of its right counterpart might be also essential, it is poorly understood because of the exclusion of atypical cases, and the focus on brain activation (increases of signal above the resting baseline). Using functional magnetic resonance imaging (fMRI) during verbal fluency test (VFT) we evaluated language lateralization in 39 healthy subjects, including left-handers. 13 participants showed bilateral or more rightward activity in the Broca's area, a greater engagement of the angular gyrus and the whole right hemisphere. This group was compared with the remaining subjects. We confirmed that atypical lateralization of language is associated with increased activity in the right inferior frontal gyrus. Notably, we found the that the most critical difference between individuals with typical and atypical language laterality might be the modulation within the posterior-to-mid right inferior and middle temporal gyri, and the superior temporal sulcus. Namely, people with typical language organization show significant suppression of neuronal activity in this cortical region. Yet, atypical group still shows some weak inhibition in this area. These results have theoretical implications for understanding the role of the right hemisphere in language processing.

4. *Reading with eyes closed: the preliminary effects of tactile Braille reading course for sighted measured with fMRI*

Katarzyna Siuda, Łukasz Bola, Małgorzata Paplińska, Ewa Sumera, Katarzyna Jednoróg, Artur Marchewka, Marcin Szwed

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Psychophysiology Laboratory, Jagiellonian University, Krakow, Poland

Reading Braille in blind subjects activates the visual cortex, which challenges the brain's sensory-based division-of-labour. Below we present brain regions activated by Braille reading in sighted readers, who lack the large-scale brain reorganization characteristic of blind individuals. 34 sighted, Tactile-Braille naive subjects underwent an fMRI experiment involving reading in Latin, Visual-Braille and Tactile-Braille contrasted with suitable controls, plus touching objects. Subjects then enrolled in a 9-month Tactile-Braille course. Here we describe the results of the first scan and 9 subjects' scans taken in the middle of the course. In the first session Visual-Braille and Latin-reading activated typical reading and language networks. Visual-Braille also strongly activated the Inferior-Parietal Lobules suggesting an important attentional component in this process. The Lateral-Occipital-Tactile-Visual area was activated by touching objects vs.imaging objects, which replicates the results of Amedi, 2001 confirming the multimodal character of this region. Very preliminary assessments of Braille learning effects (second vs. first session) for the Tactile-Braille vs. control revealed activations in the lingual and parahyppocampal gyri - associated with amodal conceptual knowledge; left and medial supplementary-motor-area and medial cerebellum - linked to motor components of reading. This suggests that tactile-reading in sighted might be achieved by different brain mechanisms than in blind.

5. *When the sighted brain goes tactile: neuroplasticity in sighted Braille learners tracked by resting-state fMRI and structural MRI*

Łukasz Bola[a,b], Katarzyna Siuda[d], Małgorzata Paplińska[d], Ewa Sumera[e], Katarzyna Jednoróg[f], Artur Marchewka[b], Marcin Szwed[c]

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Several studies suggest that tactile reading in congenitally blind subjects can recruit the visual cortex. This finding challenges the canonical view of sensory processing. Here we wanted to resolve whether tactile reading course can induce neuroplasticity in the visual system of sighted subjects, whose brains did not undergo large-scale reorganization caused by loss of sight. 34 sighted subjects underwent resting-state functional magnetic resonance imaging (rsfMRI).

Additionally, T1 weighted and diffusion weighted images were acquired for Voxel-Based Morphometry (VBM) and Diffusion Tensor Imaging (DTI) analyses. After the first scans, subjects were enrolled in 9-month Braille course. Here we describe preliminary results of 8 subjects\' scans in the middle of the course. Subjects' reading rate at that time was 8+/-1 Braille words-per-minute, which demonstrates that tactile Braille can be mastered by sighted adults. rsfMRI revealed that left inferior frontal gyrus and left middle/superior temporal gyrus increased functional connectivity with left higher-level visual cortices – V4, V5 and lateral occipital complex (LOC). VBM showed extensive grey matter increase in the right cerebellum lobules VI and VII. These results suggest that tactile reading course can trigger plastic changes in the visual cortex of the sighted. Moreover, Braille learning seems to alter classic cortico-cerebellar language network.

PLENARY LECTURE:
18.15 – 19.15

Hippocampal–Cortical Interactions During Periods of Subcortical Silence

Nikos Logothetis

Department Physiology of Cognitive Processes, Max Planck Institute for Biological Cybernetics, Tübingen, Germany

Hippocampal ripples, episodic high-frequency field-potential oscillations primarily occurring during sleep and calmness, have been described in mice, rats, rabbits, monkeys and humans, and so far they have been associated with retention of previously acquired awake experience. Although hippocampal ripples have been studied in detail using neurophysiological methods, the global effects of ripples on the entire brain remain elusive, primarily owing to a lack of methodologies permitting concurrent hippocampal recordings and whole-brain activity mapping. By combining electrophysiological recordings in hippocampus with ripple-triggered functional magnetic resonance imaging, here we show that most of the cerebral cortex is selectively activated during the ripples, whereas most diencephalic, midbrain and brainstem regions are strongly and consistently inhibited. Analysis of regional temporal response patterns indicates that thalamic activity suppression precedes the hippocampal population burst, which itself is temporally bounded by massive activations of association and primary cortical areas. These findings suggest that during off-line memory consolidation, synergistic thalamocortical activity may be orchestrating a privileged interaction state between hippocampus and cortex by silencing the output of subcortical centers involved in sensory processing or potentially mediating procedural learning. Several clinical studies, have demonstrated the phase-dependent synergistic or antagonistic relationship between the neural structures related to declarative and non-declarative (e.g. procedural) memory; Yet our observation demonstrates for the first time that such antagonistic relationship may exist during the "consolidation phase of long-term memory. The down regulation evidently generates conditions of minimal interference between subsystems, enabling consolidation of hippocampus-dependent memory. Importantly, neither the activation maps nor the sequences of up and down-regulation should be thought of indicating a causal relationship between the trigger event and the network activity changes. The state of widespread networks probably depends on a large number of variables (for example, activity changes in individual structures, or changes in inter-structure correlations), a subset of which may be eventually characterized following intensive future experimentation. The outcome of each experimental session may be conceived as a partially ordered sequence of system states, and such a sequence may indeed provide information related to memory. However, events in isolation are likely to be indicators rather than effectors of any cognitive capacity.

April 26, 2014 (Saturday)

Neuropathology

9.00 - 10.30

chaired by: Gilles van Luijtelaar (Radboud University Nijmegen, the Netherlands)

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1. ***New outlooks on absence epilepsy***

Gilles van Luijtelaar

Radboud University Nijmegen, the Netherlands

The concepts on the origin of the for absence epilepsy archetypical spike-wave discharges, that can be seen in the EEG in children with absence epilepsy and in other patient groups are evolving since the middle of the last century. It has been widely assumed, that absence epilepsy is classical type of the generalized epilepsies with a subcortical origin. Outcomes of advanced non-linear signal analyses of multiside cortical and thalamic local field potentials in WAG/Rij rats (rats of this strain are commonly used as a genetic model of absence epilepsy, Depaulis and van Luijtelaar, 2006) and outcomes of various types of electrical cortical stimulation studies, have shown that SWDs originate from a small hyperexcitable region in the somatosensory cortex and involve primarily a cortico-thalamo-cortical network, that consists of the posterior nucleus of the thalamus, the ventro-posterior medial thalamic nucleus, and the rostral pole of the reticular thalamus, while the caudal part of the reticular thalamus acts as a break on their occurrence. Microinfusions and lesion studies in cortex and thalamus confirm that absence epilepsy can be considered as a focal type of epilepsy, and that this cortical focal region recruits rapidly and dynamically other cortical and thalamic regions and networks. The discovery of focal initiation sites facilitates both new research targets and new treatment possibilities, such as focal electrical stimulation. Recent MEG data from children with absence seizures confirm a preferential role for some cortical prefrontal and parietal regions in the onset and propagation of absence seizures, consistent with a focal cortical origin in initiating absence seizures as found in genetic absence models.

2. ***Effects of chronic treatment with the mGluR5 (VU0360172) and the mGluR1 (RO0711401) enhancers on absence seizures***

V. D'Amore[a,b], C.M. van Rijn[b], I. Santolini[a], F. Nicoletti[a,c], R.T. Ngomba[a], G. van Luijtelaar[b]

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Spike-wave discharges (SWDs), the electroclinical hallmark of clinical absences, are generated within cortico-thalamo-cortical circuits. mGluRs located within this network are potential targets for SWD modulatory drugs. Symptomatic WAG/Rij rats endowed with spontaneous occurring absence seizures showed that the acute administration of the mGlu1 (RO0711401) and the mGlu5 (VU0360172) receptor agonists reduced the incidence of SWDs dose dependently without affecting motor behaviour. The purpose of this study was to examine the effects of chronic treatment of both compounds on SWDs and behaviour in order to establish whether tolerance occurred and whether the sensitivity for the drugs changed after 2 withdrawal days. The mGlu5 receptor agonist reduced the incidence of SWDs without signs of tolerance and without affecting motor behaviour during chronic administration. In contrast, the mGlu1 receptor agonist developed signs of tolerance. Pharmacokinetic data showed that the brain concentration of mGlu1 agonist decreased from day 3 until day 8, while the brain concentration of mGlu5 agonist remained unchanged over the days. These data suggest that a possible pharmacokinetic tolerance occurs for RO0711401, while no tolerance is present for VU0360172. These findings confirm that mGlu5 agonist could be developed for the treatment of absence epilepsy.

3. ***Modulation of NO signaling pathways in an experimental model of epilepsy: focus on ictal EEG***

Dragan Hrncic, Aleskandra Rasic - Markovic, Nikola Sutulovic, Zeljko Grubac, Marko Vorkapic,Veselinka Susic, Dragan Djuric, Olivera Stanojlovic

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Homocysteine and its reactive thioester homocysteine thiolactone (HcT) is recognized as potent excitatory agent in the

CNS. One of the EEG hallmarks of HcT-induced epilepsy is spike-and-wave discharges (SWD). Nitric oxide (NO) is gasotransmitter produced by neuronal, endothelial and inducible NO synthesis (NOS) Contribution of NO-mediated signaling in epileptogenesis is unclear. The aim of this study was to examine the effects of non-selective (L-NAME) and selective (7-nitroindazole for neuronal and aminoguanidine for inducible) NOS inhibitors on ictal EEG phenomena in a model of HcT-induced epilepsy in rats.Male Wistar rats with implanted EEG-recording electrodes were intraperitoneally treated with HcT (5.5 mmol/kg) and EEG activity was recorded during next 90 min. L-NAME (700 mg/kg), 7-nitroindazole (75 mg/kg), aminoguanidine (100 mg/kg) or saline were injected 30 min prior to homocysteine administration. Visual inspection of EEG and analysis of number and duration of SWDs was performed offline. L-NAME significantly increased the number of SWDs per rat induced by HcT, but didn't affect its duration. 7-nitroindazole increased duration, but not the number of SWDs in this model. Aminoguanidine increased both paremeters significantly. These results indicates that modulation of NO-singaling pathways could affect EEG manifestations of HcT epilepsy showing contribution of this gasotransmitter in epileptogenesis.

4. ***Simultaneous Electrophysiology and Ca-imaging of human cortical sinchronous population activity in vitro***

Bálint Péter Kerekes, Kinga Tóth, Attila Kaszás, Balázs Chiovini, Gergely Szalai, Zoltán Szadai, Dénes Pálfi, Klaudia Spitzer, Balázs Rózsa, István Ulbert, Lucia Wittner

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Institute of Cognitive Neuroscience and Psychology, Research Center for Natural Sciences, Hungarian Academy of Sciences, Budapest, Hungary

From the cortical slices of epileptic and non-epileptic tumor patients maintained in physiological medium in vitro spontaneous synchronous population activity (SPA) emerges. SPA was recorded until now by our group using sharp intracellular and laminar extracellular methods to analyze the neural mechanisms giving rise to population synaptic/trans-membrane and spiking activity. We introduced the two-photon line scan Ca-imaging technique on human in vitro slice preparations to gain additional information about the network mechanisms involved in the SPA generation. The excellent spatial coverage and resolution of this technique supplements the laminar extracellular, sharp intracellular and whole cell patch techniques. Human slices were maintained in a dual superfusion chamber of high flow rate physiological incubation medium and otherwise conventional submerged technique to elicit SPA in a two-photon microscope. The population activity was recorded by laminar extracellular electrodes and an extracellular patch electrode. Bolus loading of OGB-1 and SR101 was applied on the tissue. The neuronal and glial cells took up these dies, thus we were able to image the SPA related Ca-transients in pyramidal or interneuron cells with two-photon technique, simultaneously with extracellular and whole cell patch measurements. Combining high spatial resolution two-photon Ca-imaging technique and high temporal resolution extra- and intracellular electrophysiology techniques may permit a deeper understanding about the network properties of SPA in the human cortex.

Affective Neuroscience

9.00 – 10.30

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

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1. ***Are we able to ignore emotional distractors? The influence of attention, personality, and neural architecture***

Hadas Okon-Singer

Department of Psychology, University of Haifa, Israel

The classic view regards reactions to aversive stimuli as automatic, pre-attentive, and sub-conscious. Recent evidence, however, shows that the processing of aversive stimuli depends on several modulating factors. In our studies, we focus on the impact of attention mechanisms, personality traits, and anxiety disorders, on the behavioral, neural, and blood pressure reactions to highly-negative emotional distractors. Our findings demonstrate that in healthy individuals, attention modulates behavioral and neural reactions to highly-negative material. Reactions to emotional information are further modulated by personality traits, and are reflected in enural connectivity patterns. In healthy individuals, manipulation of attention also impacts action-related blood pressure reactions to emotional distractors. In line with this data, we demonstrated that attention training leads to reduced emotional reactions, as well as to plasticity in the underlying neural network. In contrast to these findings in healthy individuals, we demonstrated biased attention, and inability to ignore emotional distractors, in participants with anxiety disorders and in depressed patients. Taken together, these studies suggest that attention, personality and neural architecture modulate emotional reactions in

health and disease. These findings may have clinical implications for individuals with anxiety disorders, as well as individuals that show enhanced blood pressure reactivity to emotional stimuli.

2. *Frustrated brain – introduction to a novel fMRI stress induction procedure*

Wojciech Zajkowski[a], Sobczak Pamela[a], Marchewka Artur[b], Bielecki Maksymilian[a], Bierzyńska Maria[a,b], Kossut Małgorzata[a,b]

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Currently there are very few fMRI applicable procedures where stress induction is embedded in the experimental task. Our new procedure allows for comparative analysis of performance on the same task prior to and after the stress induction in an fMRI setting. Effectiveness of this design had been previously confirmed in a pilot study using GSR and heart rate measures. We examined 28 university students in the Laboratory of Brain Imaging of Nencki Institute. Prior to the scan, they attended two weeks Braille training. During the experiment they were asked to distinguish whether the signs appearing under their fingers are identical. The procedure consisted of two runs of braille signs discrimination separated by a stress and frustration-inducing condition, where participants were exposed to recurring negative feedback about their performance. We contrasted the second and first run. Second level contrasts from single subjects were entered into full factorial design placing the task on two levels: after and before stress induction. The results revealed increased activity in bilateral insula, anterior cingulate cortex and thalamus during the run following frustration induction, confirming the effectiveness of the proposed stress manipulation and identifying neural substrates of frustration.

3. *The affective aspect of music aesthetic. An ERP study*

Marta Jaśkiewicz, Piotr Francuz

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The John Paul II Catholic University of Lublin, Lublin, Poland

The aim of our study was investigating the influence of harmonic violation and music expertise on aesthetic judgment of music. Music experts (14 subjects) and music laypersons (13 subjects) took part in experiment. Subjects were asked to listen the excerpt of Bach's chorales and judge its beauty or correctness. Each of the excerpt was modified to obtain three versions of one excerpt: version with chord sounded: congruous, ambiguous or incongruous to harmonic context of the piece. The findings of our study showed that the affective aspect of music processing is reflected by LPP – Late Positive Potential. This effect differ in respect of degree of harmonic violation indicating that the incongruous chords enhanced the higher amplitudes. What is more, there was significant difference between two judgments (aesthetic and correctness) showing that the LPP is sensitive on task manipulation. Higher amplitudes for beauty judgment task than for correctness judgment task indicted that aesthetic evaluation is perceived as an affective task. However, our study did not confirm the influence of music expertise on affective aspect of music aesthetic processing. All our findings are discussed in the context of previous studies.

4. *EEG connectivity reveals effects of emotional state on visual and attentional systems*

Mirek Wyczesany

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Psychophysiology Laboratory, Jagiellonian University, Krakow, Poland

Our limited cognitive resources require selection of incoming visual information in order for this information to be properly processed. This selection is achieved through collaboration between collaboration of the bottom-up and top-down attentional systems, which remain in constant interaction while modulating the perceptual systems. However, the characteristics of this selection process vary with time and depend on numerous external and internal conditions. The study was aimed at determining how the ongoing emotional state affects functional connectivity between visual and attentional brain areas during perception of affective visual stimuli. Directed Transfer Function was applied on a 32-electrode EEG recording to quantify the direction and intensity of information flow between electrodes during two sessions, positive and negative. These data were correlated with a self-report on the emotional state. Both dorsal and ventral systems were specifically involved in mood-related changes in connectivity patterns. A massive increase in prefrontal top-down control of attentional as well as visual areas was also revealed in a state of tension. It was accompanied by increased transfer from the occipital area to the dorsal attentional network and the prefrontal control centre. The functional significance of the revealed effect is discussed.

Neurophysiology

11.00 – 12.30

chaired by: Fabian Kloosterman (Neuro-Electronics Research Flanders, Leuven, Belgium)

1. *Reliving your experiences: memory replay in the hippocampus*

Fabian Kloosterman

Neuro-Electronics Research Flanders, Leuven, Belgium

Memory is the capacity to store information about past experiences. The important benefit of memory is that the knowledge derived from prior experiences can be used to guide behaviour in the future. A key brain structure for memory and in particular for remembering specific events and locations ("episodic memory") is the hippocampus. In both humans and animal models damage to the hippocampus leads to profound deficits in the acquisition of new knowledge and the retrieval of old memories. The hippocampal memory system is not only involved in storing and retrieving memories of past experiences, but is implicated in connecting past, present and future. For example, patients with hippocampal damage are unable to imagine new experiences. In rodents the hippocampus is studied mainly in the context of spatial memory and navigation. As animals explore their environment, principal cells in the hippocampus ("place cells") are preferentially active in specific locations ("place fields"). As a consequence of the spatial firing properties of hippocampal place cells, the experience of walking along a trajectory in the environment is associated with a unique population activity pattern. Under certain circumstances, these specific activity patterns can be replayed outside the context of the original experience during periods of immobility or slow-wave sleep ("idle moments"). The hippocampal memory replay events are expressed at high speed during short-lasting bursts of activity. The functional role of hippocampal replay events in learning, task execution and decision making is subject of intense research. In this talk I will present an overview of our work in characterizing hippocampal replay events and understanding their contribution to memory processing.

2. *Neuronal tuning to instantaneous stimulation interval in the barrel cortex*

Anna Pitas, A.L. Albarracín, M. Molano, M. Maravall

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Instituto de Neurociencias de Alicante, Spain

Making sense of the world requires the ability to integrate sensory patterns and sequences over time. Here we measured whether neurons in the barrel cortex (BC) can perform temporal integration of sequences of whisker movements. It is known that rodents can carry out sensory discrimination tasks involving integration and that BC neurons can adjust their responses over long timescales as a function of changes in stimulation context; whether this implies that individual neurons convey information about temporally integrated properties of a sequence remains unknown. To address this, we performed juxtacellular recordings from BC in anesthetized mice. Stimulation was applied with a piezoelectric wafer and consisted of sequences of stimuli applied at periodic and random intervals. We compared the information carried by individual neurons about single intervals (reflecting sensitivity to instantaneous frequency) and about sets of successive intervals (reflecting integration over time). We found that neurons throughout BC layers carry overwhelmingly more information about the latest single intervals than about earlier ones or interval sequences, with layer 4 neurons carrying the lowest amount of integrated information. Our results support the notion that primary sensory cortex is principally an encoder of current stimulation values.

3. *Stimulus specific adaptation and its modulation by inhibition and acetylcholine in the auditory brain*

Yaneri A. Ayala, Manuel S. Malmerca

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Auditory Neurophysiology Laboratory, Instituto de Neurociencias de Castilla y León, Universidad de Salamanca, Spain

Stimulus-specific adaptation (SSA) in neural excitability that does not generalize to another stimulus is exhibited by neurons across different sensory modalities (Grill-Spector et al., 2006). This feature of the neural response may be

implicated in novelty processing observed at larger spatial and temporal scales (Ranganath and Rainer, 2003). In the auditory brain, SSA is elicited under an oddball paradigm consisting in a sequentially repeated tone (standard) which is occasionally replaced by a deviant or novel sound (Carles and Malmierca, 2014, Ayala and Malmierca, 2013). We explored the neuromodulatory influences of inhibition and of acetylcholine on the SSA exhibited by neurons in the inferior colliculus of the anesthetized rat. We recorded the extracellular responses of single neurons under the oddball paradigm before, during and after the microintophoretic application of acetylcholine (n=69), as well as, of blockers of the GABAergic and glycinergic receptors (n=20). We found that the blockade of inhibitory receptors decreased the SSA by increasing the overall excitability of all the recorded cells. On the other hand, acetylcholine affected only those neurons with moderate levels of SSA. Our data suggest the inhibitory neurotransmitters and neuromodulators affect the response to deviant and to standard stimulus in a different manner.

4. ***Primary cortical neuronal cultures on graphene oxide and reduced graphene oxide***

Jarosław Motylewski, Andrew M. H. Ng[b], Milos Nesladek[c], Loh Kian Ping [d], Michele Giugliano[a,e,f]

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One of the goals of neural tissue engineering is to investigate and design novel nanostructured materials, providing biocompatible scaffolding and active cues for neuronal network formation and nerve regeneration. Graphene has been recently suggested for several biological applications, given its unique mechanical, chemical, and electrical properties, such as elasticity, ease of surface functionalization, and high conductivity. While these, make graphene an ideal candidate for neuronal interfacing, too little is known on the interaction between graphene and the nerve tissue. In this study we explored the use of graphene as a substrate for ex vivo primary neuronal networks culturing. Two kinds of substrates were considered, graphene oxide (GO) and reduced graphene oxide (rGo). Firstly, biocompatibility was examined by conventional cell viability assays, revealing that rGO outperforms both GO and glass control conditions. Immunostaining was next employed to dissect glial versus neuronal density and basic neuronal morphological observables, such as number of neurites per neuron. Finally, patch-clamp recordings were carried out, to reveal passive and active cellular electrical properties and the impact of nanostructured conductive substrates. All the results on cell viability, morphology, and physiology show that graphene is an excellent biocompatible material and has a strong potential for future applications in neuroprosthetics. Financial support from the European Commission (FP7-NMP MERIDIAN contract n. 280778-02), from the Research Foundation Flanders (FWO, n. G.0888.12N), and from the Belgian Science Policy Office is kindly acknowledged.

Visual Processing

11.00 – 12.30
chaired by: Gilles Pourtois (Ghent University, Belgium)

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1. ***Modulation of the earliest stimulus-driven wave of activation in human primary visual cortex through competition with endogenous attention***

Gilles Pourtois

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Psychopathology & Affective Neuroscience Laboratory, Ghent University, Belgium

Attention provides humans with a powerful filtering mechanism through which the sensory processing of irrelevant information is suppressed when task demands increase. However, whether or not attention operates in V1 during the first (feedforward) sweep of activation following stimulus onset remains debated in human neurophysiology. Scalp EEG or MEG recordings cannot ensure a locus in V1. In the current study, we recorded intracranial Local Field Potentials (iLFPs) directly from the upper bank of the calcarine fissure as well as lateral occipital cortex of a human patient (with refractory epilepsy), while she performed a standard discrimination task at fixation, being either low or high in perceptual load. Concurrently, peripheral distractors were briefly shown randomly in one out of the four visual quadrants. ILFPs results showed a retinotopically-organized visual response to the distractor, peaking at 60 ms following stimulus onset in V1. Crucially, its magnitude systematically decreased when load imposed at fixation increased. Moreover, we found that this rapid bottleneck effect in V1 was causally related to a non-overlapping task-related neural activity arising at the junction between the occipital and (inferior) parietal cortex. This report provides

evidence for a rapid modulation of the human primary visual cortex activity following stimulus onset resulting from the competition with endogenous attention control mechanisms.

2. *Dissociating EEG sources associated to stimulus and response evaluation in numerical Stroop task using Independent Component Analysis*

Ewa Beldzik

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Institute of Applied Psychology, Jagiellonian University, Krakow, Poland

Independent Component Analysis (ICA) is a powerful data-driven technique, which separates EEG data into functionally and physiologically distinct source activities. This way, artifacts can be identified and removed from the data, while remaining neural sources can be further analysed. In this study, ICA was applied to dense-array EEG data obtained from 20 participants performing numerical Stroop paradigm. Traditional ERP analysis confirmed that the amplitude of late positive complex (LPC) is conflict-sensitive. The ICA results revealed two clusters of components, which mostly contributed to the LPC variance: the mid-parietal cluster with source estimated in posterior cingulate cortex (PCC) and fronto-central cluster with source in anterior cingulate cortex (ACC). The former showed increased ('prolonged') activity with the increasing cognitive demands around 200ms before the reaction, while the latter showed negative deflection for incongruent trials at 70ms after the reaction. Moreover, PCC activity was decreased ('shortened') before erroneous responses, while ACC showed strong error-related negativity afterwards, indicating that errors are committed due to insufficient stimuli processing within PCC. The results suggest that PCC is responsible for conflict-sensitive stimulus evaluation, while ACC is responsible for evaluating the action outcome within error/conflict detection process. ICA proved to be reliable and effective method for ERP analysis.

3. *Functional connectivity network breakdown in blindness*

Michał Bola, Carolin Gall, Christian Moewes, Anton Fedorov, Hermann Hinrichs, Bernhard A Sabel

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Loss of vision after brain damage is treated as the direct consequence of missing bottom-up input. Yet, perception is not a simple bottom-up process - various brain networks act in concert to create a unified perceptual experience. We now studied whether synchronization of brain networks and brain functional connectivity are related to perceptual capabilities in patients with visual system damage. Resting state eyes-closed EEG activity was recorded in patients with partial optic nerve damage (n=15) and uninjured controls (n=13). Power density and functional connectivity (coherence, Granger Causality) were analyzed, the latter as (i) between-areal coupling strength and (ii) binary graphs characterized with graph measures. Patients had lower amplitude ($p=0.005$) and decreased short- ($p=0.015$) and long-range ($p=0.033$) coherence in the EEG high-alpha band (11-14Hz) and less densely clustered high-alpha coherence networks ($p=0.025$). Weaker alpha coherence was related to worse detection abilities ($r=-0.53$; $p=0.043$) and slower reaction time in patients ($r=0.58$, $p=0.025$). Peripheral visual system damage permanently disturbs spontaneous cortical synchronization. We argue that brain synchronization might facilitate perception and compensate for incomplete input from the retina. Therefore patients' vision might be better (or worse, if synchronization is impaired) than expected based on extent of anatomical damage.

4. *The influence of Mindfulness training on EEG indices for attentional orienting*

Rob H.J. Van der Lubbe[a,b], Elian De Kleine[a], Yuna van den Adel[a], Karlein M.G. Schreurs[a], and Ernst T. Bohlmeijer[a]

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Previous research indicated that Mindfulness Based Stress Reduction (MBSR) training reduces automatic attention effects by to-be-ignored high intensity painful stimuli. This was examined in a variant of the Posner endogenous cuing paradigm in which participants had to focus their attention at the left or right forearm, and in which the to-be-attended side varied from trial to trial. These findings suggest that MBSR training may affect the efficiency of attentional orienting, which may already be visible during the orienting phase in the cue-target interval. We explored this possibility by focusing on lateralized power spectra for different frequency bands of the electroencephalogram (EEG) in the cue-target interval of 1000 ms. Thirty-four participants participated in the aforementioned task, half of them before (the control group), and half of them after the MBSR training (the MBSR group). Results revealed increased power in the posterior α band at ipsilateral relative to contralateral sites from 750-1000 ms, being more pronounced for the MBSR group than for the controls. These findings suggest increased inhibition of to-be-ignored stimuli for the MBSR group, thereby confirming the idea that the efficiency of attentional orienting increases due to MBSR training.

PLENARY LECTURE:
12.45 – 13.45

Letting go in human brain research

Rafael Malach

Department of Neurobiology, Weizmann Institute of Science, Israel

Mapping the functional properties of human visual cortical areas has traditionally followed a stimulus-response paradigm whereby a selected set of stimuli is presented under highly controlled experimental conditions. This approach has led to a remarkable success in delineated functionally selective cortical regions- however it deemphasizes internally-driven biases and processes which play an important role in visual perception as well as in cognition in general. Here I will review a number of studies from our group- in which our attempts to deviate from such highly controlled paradigms led to interesting insights. These include using naturalistic movies as stimuli and following neuronal activity during spontaneous free recall. At the extreme end of such a trend is the complete dissociation from any stimulus or task- during resting state and sleep. Our results show that removing external controls rather than introducing variability and noise, actually allows human neuro-cognitive traits to be expressed spontaneously and can be studied in a robust and sensitive manner.

Neurogenetics
15.00 – 16.30
chaired by: Paul Franken (University of Lausanne, Switzerland)

1. IBRO Alumni Lecture: ***Genetic dissection of rhythmic brain activity during sleep***

Paul Franken

University of Lausanne, Switzerland

Early twin studies already demonstrated that genetic factors importantly contribute to the duration and architecture of sleep. With heritabilities of 0.4 to 0.6, these genetic factors account for about half of the phenotypic variance. Later twin studies, quantifying the contribution of various frequency components to the sleep EEG, reported heritabilities of 0.9 and higher, demonstrating that for these traits genetic factors importantly outweigh environmental influences. EEG traits thus qualify as the most heritable traits in humans suggesting that they are amenable to genetic dissection. Despite the numerous reports illustrating the genetic contributions to physiological sleep and the EEG, remarkable little progress has been made in identifying the underlying genes. We have used a combination of forward, reverse, and molecular genetics in the mouse to gain insight into the molecular pathways underlying sleep and rhythmic brain activity. Using Quantitative Trait Loci (QTL) analysis, we were able to successfully map the genes underlying three EEG traits. After an initial assessment of the phenotypic variance in a set of inbred mouse strains we noted large genotype differences in the dominant frequency of EEG theta (6-9Hz) oscillations during REM sleep as well as in the prevalence of EEG delta (1-4Hz) oscillations to the non-REM sleep EEG. The segregation of the first EEG trait was followed in an extensive panel of inter- and backcrosses between two strains that differed for theta peak frequency. A single QTL was identified on chromosome 5 and subsequent fine mapping and functional analysis revealed a mutation in *Acads* (short-chain acyl-coenzyme A dehydrogenase) responsible for slowing down theta oscillations during sleep. The second trait was mapped in a panel of recombinant inbred strains of mice derived from two inbred strains differing for EEG delta power. A QTL on chromosome 14 was found and through a combination of forward, molecular, and reverse genetic approaches, *Rarb* (Retinoic acid receptor beta) was identified as the underlying gene, thus implicating retinoic acid signaling in modulating cortical synchrony during non-REM sleep. A third example from our laboratories concerns the homeostatic regulation of sleep. Comparisons of the sleep-wake dependent dynamics of EEG delta power in a panel of inbred mouse strains, for the first time, demonstrated that the sleep homeostatic process is under genetic control and with it came the promise to identify molecules that modulate the rate at which sleep need increases during wakefulness. QTL analysis in a panel of RI strains yielded a significant locus on chromosome 13. Based on *in silico* and transcriptome analyses, *Homer1a* was identified as a credible candidate gene. These examples demonstrate that QTL analysis can be successful in identifying novel gene and signaling pathways underlying normal sleep and EEG traits.

2. ***Chronic activation of the glucocorticoid receptor induces behavioural and molecular markers of depression in mice***

Urszula Skupio, M. Sikora, M. Tertil , S. Golda, A. Wawrzczak-Bargiela , R. Przewlocki

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Corticosterone (CORT) administration is a well-known depression model in rodents. Because CORT affects two types of corticosteroid receptors, the mineralocorticoid (MR) and glucocorticoid (GR) receptors, the role of each specific receptor in the development of depressive symptoms remains unknown. In the present study, we used dexamethasone a selective GR agonist to determine whether its chronic administration increases behavioural and molecular signatures of depression-like symptoms in mice. C57BL/6N mice were injected once daily for 3 weeks with dexamethasone (4mg/kg i.p.) or saline. The behaviour of the animals was assessed in: the forced swimming test, the saccharin preference test, the elevated-plus maze test and the open field test. In addition, expression levels of the stress-related genes were analysed in selected brain regions. A variety of depression-like behaviours characterised dexamethasone treated mice: increased immobility time in the FST, reduced preference for saccharin consumption, severe loss of body mass and increased anxiety-like behaviour. Moreover, behavioural alterations were accompanied by significant changes in GR-dependent genes expression (such as SGK1 and Fkbp5). The study indicate that prior chronic dexamethasone exposure to mice produces a lasting depressive-like state and induction of stress-related molecular markers in mice.

3. ***3' untranslated region polymorphisms of matrix metalloproteinase 9 and their role in schizophrenia. The role in the local translation***

Katarzyna Łepeta, Magdalena Dziembowska, Leszek Kaczmarek

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Recent studies have implicated MMP-9 in schizophrenia. In particular, Domenici et al. reported highly elevated plasma levels of MMP-9 in schizophrenic patients. Rybakowski et al. demonstrated an association of MMP-9 5'UTR polymorphism -1562C/T with schizophrenia. Recent studies from our lab have shown that MMP-9 is locally translated in neurons in response to synaptic stimulation. Our collaborators from MPI in Gottingen found correlation between polymorphism in the 3'UTR of MMP-9 and schizophrenia age onset in humans. Since 3'UTR plays an essential role in mRNA transport to the dendrites and in its local translation, polymorphisms in this region may affect synaptic availability of MMP-9, which in turn can influence the development and severity of the disease. Our preliminary results from rat neuronal culture indicate that there is a difference in MMP-9 levels depending on the 3'UTR polymorphism. Currently we investigate the mechanism underlying observed difference by using MS2 system for mRNA tracking in dendrites and FRAP technique to measure efficacy of MMP-9 local translation. Studying MMP-9 genetic variants can help us understand better MMP-9 regulation and mechanism of action and hopefully thanks to this – to have a better insight into the pathogenesis of many diseases in which the protein plays a role.

4. ***Frontostriatal dysfunction in mice lacking TAAR1***

Stefano Espinoza, Gabriele Lignani, Lucia Caffino, Silvia Maggi, Ilya Sukhanov, Damiana Leo, Liudmila Mus, Valentina Ghisi, Marco Emanuele, Giuseppe Ronzitti, Lucian Medrihan , Tatiana D. Sotnikova, Evelina Chieregatti, Fabio Benfenati, Valter Tucci, Fabio Fumagalli, Raul R. Gainetdinov

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Trace Amine Associated Receptor 1 (TAAR1) is a GPCR that is expressed in the mammalian brain and is known to influence monoaminergic transmission. Monoamines, such as dopamine, play an important role within the frontostriatal circuitry, which is critically involved in cognitive processes; however, the mechanisms through which TAAR1 can affect frontostriatal system remain to be clarified. In this study, we investigated how TAAR1 modulates frontostriatal signaling by analyzing dopamine- and glutamate- mediated processes and related behaviors in the striatum and the prefrontal cortex (PFC) of TAAR1-KO mice. In the striatum, TAAR1-KO mice showed an up-regulation of D2 dopamine receptors and concomitant activation of the AKT/GSK3 pathway. In the PFC, we observed deficient NMDA receptor functionality located in the pyramidal neurons of layer V, as assessed by electrophysiology, with concomitant changes in NMDA receptor subunit expression. The dysregulated frontostriatal transmission in TAAR1-KO mice was associated with aberrant behaviors in several tests, indicating a perseverative and impulsive phenotype. Conversely, pharmacological activation of TAAR1 with selective agonists reduced premature impulsive responses observed in the fixed-interval conditioning schedule in normal mice. Our study indicates that TAAR1 plays an important role in the modulation of frontostriatal function, through changes in dopaminergic and glutamatergic transmission.

Neural Correlates of Pain and Somatosensory Stimulation

15.00 – 16.30

chaired by: Tineke van Rijn (Radboud University Nijmegen, the Netherlands)

1. *Characterizing secondary hyperalgesia induced by high frequency electrical stimulation*

Emanuel van den Broeke, Andre Mouraux

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Universite Catholique de Louvain (UCL), Belgium

High frequency electrical stimulation (HFS) of the human skin induces increased pain sensitivity in the surrounding unconditioned skin (i.e. secondary hyperalgesia). The aim of this talk is to discuss recently obtained findings about the relatively contribution of nociceptive and non-nociceptive fibers to secondary hyperalgesia induced by HFS. In healthy volunteers we applied HFS to the ventral forearm. In a first experiment, brief and intense CO2 laser stimuli were used to concomitantly activate heat-sensitive Aδ- and C-fiber nociceptive afferents. These stimuli were detected with reaction times compatible with the conduction velocity of Aδ-fibers. We also used vibrotactile stimuli selectively activating low-threshold mechanoreceptors. In a second experiment, temperature-controlled laser stimulation was used to activate low-threshold C-fiber afferents without concomitantly activating Aδ-fiber afferents. These stimuli were detected with reaction times compatible with the conduction velocity of C-fibers. The intensity of perception and event-related brain potentials (ERPs) elicited by the vibrotactile and two types of thermonociceptive stimuli delivered to the surrounding unconditioned skin were recorded before and after HFS. Mechanical hyperalgesia following HFS was confirmed by measuring the changes in the intensity of perception elicited by mechanical punctate stimuli. HFS enhanced the perception to mechanical punctate stimuli and thermonociceptive stimuli co-activating Aδ- and C-fibers. HFS did not enhance the perception to thermonociceptive stimuli selectively activating C-fibers. The ERPs elicited by concomitantly activating Aδ-fiber and C-fibers afferents were not enhanced after HFS. Similarly, ERPs elicited by selectively activated C-fibers were also not enhanced following HFS. In contrast, vibrotactile ERPs were enhanced after HFS. Our results clearly show that HFS induces secondary heat hyperalgesia to thermonociceptive stimuli activating both Aδ- and C-fibers. However, the heat hyperalgesia was not accompanied by an enhancement of the Aδ fiber related ERPs indicating that the heat-sensitive Aδ-fiber afferents (Type II AMHs) do not contribute to this secondary heat hyperalgesia. Likewise, HFS induced heat hyperalgesia is also not mediated by the quickly adapting C-fibers. Furthermore, HFS also affects vibrotactile processing, as evidenced by the enhanced vibrotactile elicited ERPs.

2. *Cognitve correlates of pain report in the elderly*

Joukje Oosterman

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Radboud University Nijmegen, the Netherlands

Studies show that, in general, clinical pain reports decline as cognitive function declines. These results have been found in both older, non-demented people as well as in patients suffering from dementia. Little is known, however, about the precise role of cognition in pain report. For example, it is unknown whether this association is one reflecting a mere tendency to report less pain in the context of general decline, or whether specific cognitive functions are involved. And if the latter is the case, is this association then reflected by underlying reduced gray and/or white matter integrity? I will present data of how cognition is associated with both clinical and experimental pain in normal aging. Furthermore, I will present data of this association in dementia, together with underlying patterns of neuroanatomical abnormalities.

3. *Visuo-proprioceptive conflicts and nociception*

Diana Torta, Legrain V, Mouraux A

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Pain has the evolutionary function of protecting the body. It has been proposed that brain activations in response to nociceptive stimuli reflect, at least partly, the activity of a multimodal attentional system which detects potential dangers in the peripersonal space (that is, the space surrounding our body) and organizes appropriate responses. There is growing interest in understanding how the perception of pain is influenced by body and space representation and, viceversa, how pain can shape the representation of our body and the surrounding space. In this talk, evidence will be discussed about: i) how we localize somatosensory stimuli on our body and how conflicts between vision and

proprioception, induced by uncommon body postures and ii) how vision influences the perception of pain and brain responses to nociceptive stimuli.

4. ***Altered neuronal pain processing in anterior cutaneous nerve entrapment syndrome***

Dagmar van Rijckevorsel, Marjan de Vries, Oliver Wilder-Smith, Harry van Goor

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Pain and Nociception Neuroscience researchgroup, Donders center for neuroscience, Nijmegen, the Netherlands

Anterior Cutaneous Nerve Entrapment Syndrome (ACNES) is a common cause of chronic abdominal pain, refractory to treatment in about 30% of cases for yet unknown reasons. To assess, by using quantitative sensory testing (QST), whether central neuronal pain processing is altered in ACNES patients and possibly contributes to treatment failure. 35 patients treated for ACNES were compared to 210 healthy controls. ACNES patients were allocated to successful or unsuccessful after treatment based on pre- and post treatment VAS-scores. Thresholds to pressure and electric skin stimulations were determined in the ACNES dermatomes and four control areas. Conditioned pain modulation (CPM) response to a cold pressor task was determined. Results were related to three pain-related questionnaires. Duration of complaints to diagnosis was significantly longer in the unsuccessful compared to the successful group. Patients with pain relief showed significantly higher pressure pain detection thresholds than unsuccessful patients or healthy volunteers. No differences were found for electric testing or CPM response between groups. The unsuccessful group showed more signs of anxiety and depression. ACNES patients show signs of altered central pain processing. Duration of complaints before diagnosis might be a risk factor for treatment failure.

Interactive Session on Medical Case Reports

15.00 – 16.30
chaired by: Krzysztof Banaszkiewicz (John Paul's Hospital in Krakow, Poland)

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1. ***An encephalitic patient with psychiatric symptoms at onset***

Michał Błaż

Jagiellonian University Medical College, Krakow, Poland

Anti-N-methyl-D-aspartate receptor (anti-NMDAR) encephalitis is a newly described form of encephalitis associated with prominent psychiatric symptoms at onset. This case report presents a patient with NMDAR encephalitis whose early clinical picture of psychosis led to the initial misdiagnosis of this disease. A 32-year old female patient was referred to the neurology unit from the psychiatry ward with a 4 month history of progressive behavioral impairment. The disease onset was preceded by a rapid headache and a psychotic episode. On neurological examination the patient presented with catatony and very poor verbal contact. Examination revealed also right-sided primitive reflexes (glabellar, snout, palmomental), ocular myoclonus, increased muscle tone in all limbs, hyperreflexia, bilateral Jacobson reflex, Babinski sign on the right, meningeal signs were absent. In MRI no major findings despite blistering of caudate's caput were described; EEG was normal; lumbar punction revealed high protein content of CSF and presence of oligoclonal bands. Laboratory tests excluded an acute viral infection, but detected high level of IgG antibodies against HSV. After extensive diagnostics, antibodies against NMDA receptors were identified. The patient was treated with steroids and subsequently with plasmapheresis with minor clinical improvement. She was released and remains under oncological surveillance, as NMDAR encephalitis might be considered a paraneoplastic syndrome. To differentiate many causes of acute psychotic disorders it is important to be aware of neurological mimics of psychosis. One of them is a rare form of encephalitis: anti-NMDAR encephalitis.

2. ***Recovery of a Patient with Miller-Fisher Syndrome, a Variant of Guillain-Barre Syndrome***

Carmen Góralski, Saad Mumtaz, Peter Kuszta, Kossi Tete, Akshita Khetarpal

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Medical University of Lublin, Lublin, Poland

Miller-Fisher Syndrome (MFS) is the rarest variant (about 5%) of Guillain-Barre Syndrome, an acute inflammatory demyelinating polyneuropathy. It is characterized by the presence of a triad of symptoms that are ophthalmoplegia, areflexia and ataxia. Differential diagnosis includes Botulism Toxin. Characteristic feature is the presence of antiganglioside anti-GQ1B IgG antibody. A 68-years old male farmer presented in February 2013 with a chief complaint

of a sore throat and was prescribed empiric antibiotics. After 10 days he then presented to Bilgoraj Hospital with an acute onset of diplopia, dysphagia and ptosis due to consumption of a sausage two days prior. Botulinum infection was suspected, and he was transferred to the Infectious Diseases Department. Antibody test against Botulinum proved to be negative, however there was no clinical improvement. The consultant neurologist suspected MFS. The patient was further transferred to the Neurology Department, and the diagnosis was confirmed with neurophysiological studies. The patient recovered after repeated courses of plasma exchange. MFS overall has generally an indolent course and good prognosis. Only in less than 5% of cases the outcome is fatal. Because of an autoimmune characteristic of the disease, the treatment of choice is plasma exchange and intravenous immunoglobulins (IVIG).

3. *Insidious progression of hereditary vascular dementia in a patient with migraines and stroke*

Mark-Victor Siwoski

Jagiellonian University Medical College, Krakow, Poland

Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is characterized by migraine, dementia, transient ischemic attacks (TIA) and stroke. CADASIL is a rare and devastating hereditary disease that should be diagnosed quickly and treated rigorously to slow rate of progression. This case report presents a 57 year old female patient with severe and recurrent migraines associated with left-sided weakness since 2004 after admission and treatment for right hemisphere ischemic stroke. Magnetic resonance imaging (MRI) showed characteristic findings of diffuse vascular changes involving the frontal and temporal lobes, periventricular white matter, and the body of the corpus callosum. Genetic testing performed in 2008 confirmed a mutation in the NOTCH3 gene and the diagnosis of CADASIL. A discussion of diagnostic methods, differential diagnosis, progression, and treatment of patients with CADASIL is presented.

4. *Pelizaeus-Merzbacher Disease - a case report*

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Pelizaeus-Merzbacher Disease (PMD) is a rare leukodystrophy, the estimated prevalence is 1:400 000. It is inherited in an X-linked pattern and caused by inability to form myelin in the central nervous system due to mutation of the PLP1 gene (major myelin protein gene). Depending on the age of onset and severity there are three sub-forms: congenital, classical and transitional. The clinical spectrum of the disease is broad, though there are some common symptoms such as: developmental delay, pyramidal and cerebellar syndrome, variable intellectual deficit. Typical finding in Magnetic Resonance Imaging is diffuse lack of myelination. The authors present a 20-month-old boy with impaired motor and physical development, axial hypotonia, limb spasticity and horizontal nystagmus. Magnetic Resonance Imaging revealed hypomyelination characteristic for PMD. Additionally it showed abnormal size of spinal cord on C1 level, asymetrical venous sinuses of the dura mater and thyroglossal cyst in radix linguae. Genetic testing confirmed mutation within the PLP1 gene: Ext_7 dup (duplication of all exons). PMD is a rare neurodegenerative disease. The correct diagnosis depends on correlation of clinical presentation and neuroimaging findings with confirmation of the diagnosis by genetic testing.

5. *Emotional disorders in patients with cerebellar lesions*

Katarzyna Siuda, Adrian Andrzej Chrobak, Anna Starowicz-Filip, Anna Tereszko, Dominika Dudek

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Research shows that cerebellum takes part in affect. Cerebellar lesions can lead to emotional disregulation, a component of the Cerebellar Cognitive Affective Syndrome. Below, we present two cases : one female and one male who suffered from cerebellar damage and presented post-traumatic affective and personality change. The patients' neuropsychological examination was performed with Raven's Progressive Matrices Test, Trial Making Test, Wisconsin Card Sorting Test, Łuria's Auditory Verbal Learning Test, Benton Visual Retention Test, Verbal Fluency Test, Stroop Interference Test, Attention and Perceptivity Test (Test Uwagi i Spostrzegawczości TUS), Frontal Behavioral Inventory (FBI). We observed oversensitivity, irritability, impulsivity and self-neglect in all 3 patients. The man with right-sided lesion presented symptoms like: rigidity of thought, stubbornness, lack of criticism, jocular and inappropriate behavior. The woman with left-sided cerebellar lesion was adynamic, apathic and passive, she presented emotional blunting, social isolation, lack of interests and motivation, general cognitive slowdown. The symptoms presented by described patients were most probably a consequence of damaged cerebellar projections to subcortical structures (the limbic system) and frontal areas. The recognition of the cerebellum's role in neuropsychological disorders is important for the diagnostic process and can provide basis for more adequate therapeutic interventions.

6. *Tethered spinal cord syndrome - Usability of surgical treatment in adults - case report*

Piotr Śliwiński, Mateusz Szkobel

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A patient with longstanding, undiagnosed pain of lower limbs connected with spastic paresis has been admitted to the Clinic of Neurology and Neurosurgery. After Magnetic Resonance Imaging which has been done using 3T Magnetic resonance a diagnose has been made - Tethered spinal cord syndrome (TCS). Patients with long lasting TCS are commonly not qualified to the surgery because of low effectiveness of the operation and outlasting neurological deficits. Pursuant to the article of German neurosurgeons who indicated that positive results of the operations prevailed over the inefficient ones in adults, a decision to perform an operation has been made. In our research we want to demonstrate how performing the operation, in spite of longstanding TCS altered to the neurological defects and also the medical history of the patient diagnostic methods, treatment abilities, and the differential diagnosis.

7. *Mother and son diagnosed with Tick-borne Encephalitis transmitted by consumption of unpasteurized goat milk*

Piravin Kumar Ramakrishnan, Joyeeta Roy, Brandon Henry

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Tick-borne Encephalitis (TBE) is a flavivirus infection of the CNS that typically follows a biphasic course. The first phase presents with flu-like symptoms while the second phase is characterized by CNS involvement. TBE Virus is endemic to Central and Eastern Europe and is mostly transmitted by tick-bites. Rarely, it can be transmitted by consumption of unpasteurized milk from infected livestock. We present the case of a 67 year-old female and her 36 year-old son with TBE. Both patients were seen in the emergency department with flu-like symptoms several days prior to being admitted to the Infectious Diseases Department at the University Hospital, Krakow. The patients presented with symptoms of mild meningoencephalitis including fever, nausea, vomiting, myalgia, severe headache, vertigo, and drowsiness. The son also suffered from rare non-CNS manifestations of transient hepatitis and pancreatitis. Diagnosis was confirmed by ELISA for IgG and IgM antibodies. Both patients denied tick-bites or skin changes. However, both recently consumed unpasteurized goat milk, which was identified as the source of infection. They received supportive therapy and recovered after hospitalization. Patients will be further monitored for potential neurological sequelae. Our case demonstrates the need to vaccinate high-risk communities and the importance of consuming only pasteurized milk.

8. *Obsessive Compulsive Disorder as a complication of deep brain stimulation therapy for Parkinson's Disease: a case study*

Grzegorz Siwek, Adrian Chrobak, Szymon Jeziorko, Anna Krygowska-Wajs

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Parkinson's Disease (PD) is a common neurodegenerative disorder, characterized by muscle tremor, stiffness and bradykinesia and classically treated using dopamine receptor agonists. One of the rare side effects of dopamine agonists treatment is the development of Obsessive Compulsive Disorder. Deep Brain Stimulation of Subthalamic Nucleus (DBS STN) is an established method of treatment of PD patients, however there is a growing incidence of psychiatric complications following implantation of the electrodes. The case of a 66 year old male patient with an 18-year history of PD is presented. The patient suffered from: left hand tremor, severe bradykinesia and rigidity, later followed by early morning dystonia of the feet. Wearing-off and on-off effect was observed after 7 years of levodopa therapy. No cognitive decline, autonomic dysfunction or other atypical symptoms were observed. The patient was qualified for DBS STN. Four months after surgery he developed pathological gambling, shopping, hypersexuality and aggressiveness. Despite many obvious advantages of DBS STN therapy, its long term complications and underlying mechanism of action are still not understood. Further investigation and long term follow up is required to evaluate possible risks and benefits for PD patients.

PLENARY LECTURE:
18.15 – 19.15

Blood flow and the angioarchitecture of mouse cerebral cortex

Philbert S. Tsai

University of California, San Diego, USA

How is the vascular architecture in the cortex organized to allow blood flow to meet the metabolic demands of neuronal computation? What are the microscopic details of the layout and connectivity of the microvasculature and to what degree does that topology dictate the patterns of blood flow seen in the brain? Blood flow is responsible for providing brain tissue with the oxygen, glucose, and waste removal necessary for proper physiological function, and thus represents a vital but limited resource for ongoing neuronal activity. The study of cortical blood flow and angioarchitecture is necessary for understanding the details of pathological mechanisms following ischemic stroke. Furthermore, it is critical for elucidating the mechanisms underlying techniques that utilize blood oxygenation as a surrogate for measuring neuronal activity. This includes widely-used techniques such as intrinsic optical imaging (IOS) and blood-oxygenation level dependent functional magnetic resonance imaging (BOLD fMRI). To address these issues, we use high-throughput 3D histology on a region spanning multiple cubic millimeters of vibrissa primary sensory cortex in mouse. Within this region, we reconstruct the complete cortical angioarchitecture along with the positions of all neuronal somata. We derive vectorized vascular networks from these histological reconstructions and apply graph-theoretical analyses to reveal underlying principles of neurovascular architecture. I will discuss the results of these analyses along with a body of work on *in vivo* imaging of cortical blood flow using optical techniques, both with and without optical perturbation. Through such studies we begin to understand the role of angioarchitecture on blood perfusion in the brain.

27, April 2014 (Sunday)

Neurode(re)generation

9.00 – 10.30
chaired by: Patrik Verstreken (University of Leuven, VIB, Belgium)

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1. **Targeting mitochondrial dysfunction in Parkinson's disease**

Patrik Verstreken

VIB Center for the Biology of Disease, Department of Human Genetics, KU Leuven, Belgium

Mitochondrial dysfunction has been linked to Parkinson's disease and likewise, genetic models that were generated to recapitulate features of the disease also show mitochondrial defects. To understand the molecular nature of these defects we have focused on Pink1, a mitochondrial kinase mutated in Parkinson's disease and we have analyzed *pink1* mutant fruit flies, mouse knock out cells and patient derived cells. While Pink1 has mostly been studied for its role in the regulation of Parkin-dependent mitophagy, we have found very specific defects at the level of the electron transport chain in these mutants in that they fail to couple electron transfer between complexI and ubiquinone. While much more work is needed, the discovery of electron transport chain defects in pink1 mutants now provides a therapeutic window and I will discuss our efforts to bypass the mitochondrial defects using expression of a yeast enzyme, photostimulating a specific component of the electron transport chain and the effect of vitaminK2 as an alternative electron carrier in mitochondria. Taken together, our work indicates pink1 regulates mitochondrial function by promoting electron transport at complexI and promoting mitochondrial activity may be a prosperous strategy to rescue *pink1* deficiency.

2. ***Herpes simplex virus type 2 induces the apprearance of Alzheimer´s disease-like neurodegenrative markers***

Henrike Kristen, Jesus Aldudo, Maria Jesus Bullido

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Mounting evidence suggest that HSV-1 is involved in the appearance of the biochemical anomalies characteristic of Alzheimer´s disease (AD) brains. Nevertheless, the relationship between HSV-2 and AD-like neurodegenerative markers has not been extensively studied. The present work reports that HSV-2 infection leads to a strong intracellular accumulation of the β-amyloid peptides Aβ40 and Aβ42, and a marked reduction in the amount of secreted Aβ. Further, decreased amounts of α-C-terminal fragment (α-CTF) and secreted APPα have been observed due to reduced α-secretase activity. These results indicate the inhibition of the non-amyloidogenic pathway and probably the impairment of Aβ secretion in HSV-2 infected human neuroblastoma cells. Microscopy experiments showed that intracellular Aβ is located in late endosomes, suggesting an involvement of this cellular compartment in Aβ generation. In addition, HSV-2 induces an increase in LC3 lipidation provoking the accumulation of intracellular autophagic compartments. Studies with the mCherry-GFP-LC3 reporter indicate the inefficient fusion between autophagosomes and lysosomes, suggesting a failure in the autophagic flux. Taken together, these data suggest that HSV-2 modulates the autophagic process and processing of APP leading to intracellular accumulation of Aβ and autophagosomes, characteristic hallmarks of AD brains, and might therefore contribute to the pathogenesis of sporadic AD.

3. ***TIMP-1 loaded nanoparticles: a therapeutic strategy for neuroprotection***

Mayank Chaturvedi, Yves Molino, Sreedhar Bojja, Michel Khrestchatisky, Leszek Kaczmarek

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Matrix Metalloproteinase-9 (MMP-9) is directly involved in excitotoxic neuronal death. Therefore, inhibition of MMP-9 is considered as a potential therapeutic target for neuroprotection. Hence, in this study, we planned to evaluate neuroprotective effects of an endogenous inhibitor of MMP-9, Tissue Inhibitor of Matrix Metalloproteinase-1 (TIMP-1), which is a 28 KDa protein. However, the major obstacles of using TIMP-1 as a neuroprotective agent are its in vivo short half-life and low brain permeability. Hence, we planned to explore a nanotechnological approach for delivery of TIMP-1, by using poly lactic-co-glycolic acid (PLGA) based Nanoparticles (NPs), so in the future it can be developed as a

neuroprotective agent. Here, we have developed TIMP-1 loaded PLGA NPs which can deliver TIMP-1 in a sustained release manner and can cross the blood brain barrier (BBB). We have evaluated whether these NPs have BBB penetration and any toxic effects on endothelial cells. The results have shown that NPs are non-toxic and they have BBB penetration. Finally, we evaluated their neuroprotective effects on organotypic hippocampal slice culture using propidium iodide staining and LDH assay, which showed that TIMP-1 and TIMP-1 loaded have neuroprotective effects against Kainic Acid (KA) induced excitotoxicity. Moreover, we have shown through gelatinase assay that these effects are mediated through MMP-9 inhibition.

4. ***Distinct neuronal differentiation of induced Pluripotent Stem Cells (iPS) into dopamine and neuromelanin producing cells***

Maciej Sułkowski, Bogna Badyra, Tomasz Adamus, Paweł Konieczny, Przemysław Płonka, Marcin Majka

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Department of Transplantation, Collegium Medicum Jagiellonian University, Krakow, Poland

Induced Pluripotent Stem cells (iPS) are unlimited source of different cell types. Thanks to their traits they can found application not only in clinic but also as in vitro models of diseases. One important type of cells which can be generated from iPS cells are dopamine producing cells. They are particularly vulnerable to degeneration in many neuronal disorders such as Parkinson's disease (PD). IPS-derived dopamine producing cells in vitro comprise perfect model not only for drug testing but also for elucidating pathogenesis of PD. Here we present distinct protocol for neuronal differentiation of iPS cells. Neuronal differentiation is a multi-step procedure. Firstly, iPS cells cultured on feeder layer were transferred to suspension culture. In next step Neuronal Progenitor Cells (NPC) were selected and expanded in serum-free medium. In final step NPC cells were terminally differentiated into dopaminergic neurons. On each step cells were characterized for expression of specific markers (neuronal - Nestin, Tuj-1, TH, DAT, Tyrosinase and embryonic) on the level of mRNA (by RT-PCR) and protein (by immunocytochemistry). Dopamine production was proved by HPLC and appearing black pigment was identified as melanin by EPR and Fontana-Masson staining. Acquired cells were also able to integrate into rats' striatum as shown by immunohistochemical staining. We show protocol for iPS cells differentiation into dopamine and melanin producing cells. Our model is useful for pharmacological tests both in vitro and in vivo but moreover it is valuable in deciphering pathogenesis of neurodegenerative diseases. Authors acknowledge the financial support from the project Interdisciplinary PhD Studies "Molecular sciences for medicine (co-financed by the European Social Fund within the Human Capital Operational Programme).

Psychopathology in Neuroscientific Research

9.00 – 10.30

chaired by: Adrianna Mendrek (Bishop's University, Canada)

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1. ***Sex, drugs and the brain***

Adrianna Mendrek

Department of Psychology, Bishop's University, Sherbrooke & Centre de recherche de l'Institut universitaire en santé mentale de Montréal, Canada

Drug use and drug addiction have been traditionally considered to be a male problem, however the gender gap has been decreasing over the past few decades. Women appear to be more prone to develop drug dependence, suffer more severe physical and psychological consequences of drug abuse, and have more difficulties quitting the habit. Numerous psychological, socio-cultural and biological factors have been implicated in these changing statistics. For example, there is now evidence that dopamine system, which for decades has been strongly implicated in drug reinforcement, is sexually dimorphic. In the present talk I will present various factors contributing to sex/gender differences in drugs use and abuse and then concentrate specifically on nicotine and present some recent findings from my lab. Although overall more men than women smoke cigarettes, women and girls take less time to become dependent after initial use and have more difficulties quitting the habit. One of the factors contributing to these differences may be that women crave cigarettes more than men and that their desire to smoke is influenced by hormonal fluctuations across the menstrual cycle. Thus, in our recent study we examined potential sex/gender differences in functional neuroanatomy of craving and delineated neural correlates of cigarette cravings in women across their menstrual cycle. Fifteen tobacco-smoking men and 19 women underwent a functional MRI during presentation of neutral and smoking-related images, known to elicit craving. Women were tested twice; once during early follicular (low levels of estradiol and progesterone) and once during mid-luteal (high levels of estradiol and progesterone) phase of their menstrual cycle. The analysis did not reveal any significant sex differences in the cerebral activations associated with craving. Nevertheless, the pattern of activations in women varied across their menstrual cycle. They showed significant activations in the precuneus, anterior and posterior cingulate, medial frontal, inferior temporal and angular gyrus during follicular phase, and only

limited activations in the right hippocampus during the luteal phase. These results, together with existing neurobiological and epidemiological data, indicate that sex-related biological and psychosocial factors must be taken into consideration while evaluating and treating men and women with drug addiction problem.

2. *Incidental threat during visuo-spatial working memory in adolescent anxiety: An emotional memory-guided saccade task*

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Pediatric anxiety disorders are among the most common psychiatric mental illnesses in children and adolescents, and are associated with perturbed emotion-related processing. While recent studies in adults suggest a possible modulatory role of threat on working memory, little is known about such interaction in adolescents, particularly those affected with clinical anxiety. Thirty-three children/adolescents diagnosed with an anxiety disorder and 22 age-matched healthy comparisons participated and completed a novel eye movement task, an affective variant of the memory-guided saccade task. This task assessed the influence of incidental threat on visual-spatial working memory processes during high and low cognitive load. Healthy but not anxious children showed slowed saccade latencies during incidental threat in low-load but not high-load working memory conditions. However, this effect was modulated by state anxiety in the anxious group. By comparison, accuracy in anxious participants was reduced relative to comparisons under high load. Comorbid depression did not impact the findings. The current data suggest that incidental threat affects spatial working memory differently in anxious relative to healthy adolescents, particularly during low-load task. The findings are discussed along current theoretical accounts of anxiety in adults and their applicability for pediatric anxiety.

3. *Schizophrenic patients show abnormal early brain activation during lateralized visual stimulation*

Ingrida Antonova[a], Claudia van Swam[b], Daniela Hubl[b], Thomas Dierks[b], Inga Griskova-Bulanova[a], Thomas Koenig[b]

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The right hemisphere is dominant in visuospatial perception. However, left hemisphere deficits can also contribute to impaired visuospatial perception in schizophrenia. We aimed to find the link between hemispheric specialization and schizophrenia by relating differences in the activity of hemispheres during a lateralized choice reaction task (CRT) to schizophrenic psychopathology. Healthy controls (n=28), schizophrenic patients with hallucinations (n=18) and without hallucinations (n=11) performed a simple 4-choice reaction time task with stimuli presented to four lateralized visual fields, while EEG was recorded from 76 channels. ERP components were identified and quantified as function of visual field and eccentricity. Stimulation induced predominant activity in the contralateral hemisphere, and it was smaller in patients than in controls. However, an early co-activation of the ipsilateral hemisphere was also observed in all three groups. Compared to controls, this co-activation was less prominent in patients with hallucinations, and it was more prominent in non-hallucinating patients. Differences were statistically significant ($p=0.05$) between groups in left-right by medial-lateral interactions. Differences in an early activation show changes in an early visuospatial processing in two patient groups. This study highlights the importance of understanding the pathophysiology of schizophrenia in the context of hemispheric specialization and primary sensory processes.

4. *Developmental Disregard in children with unilateral Cerebral Palsy - A spatial attention deficit?*

Ingar Zielinski, C. Marjolein Baas, Pauline BM Aarts, Bert Steenbergen, Marijtje LA Jongsma

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Some children with unilateral Cerebral Palsy (uCP) disregard the preserved capacity of the affected upper limb, known as Developmental Disregard (DD). Using Event-Related Potentials (ERPs) it was shown that children with DD require a disproportional amount of attention when preparing a response with their affected hand, which may explain the underuse of that hand. This was however only observed in a dual-hand task situation requiring shifts in spatial attention. In line, it was stated that DD conceivably is a neurological based phenomenon similar to neglect, as neglect is characterized by spatial attention deficits leading to an underuse of one side of the body. The goal of this study is to investigate the spatial attention processes preceding goal-directed behavior in children with DD. Twenty-four children with uCP participated in the study. Twelve were diagnosed with DD. All

participants performed a dual-hand inhibition task. The ERP components elicited by lateralized cue, target and stop stimuli were analyzed. In children with DD the N1 component following cue and target stimuli was significantly diminished. This component is known to reflect aspects of spatial attention. We propose that DD can be linked to deficits in spatial attention, as it is the case in neglect.

PLANARY LECTURE:
11.00 – 12.00

Neurobiological mechanisms underlying the regulation of negative emotion

Angela Roberts

University of Cambridge, UK

Dysregulated emotions are a core feature of many neuropsychiatric disorders and are often associated with altered activity in limbic emotional circuitry that includes the amygdala, hippocampus and prefrontal cortex (PFC). Altered activity in serotoninergic forebrain systems has also been implicated and currently, the front-line treatment of these disorders includes drugs that target the serotonin system. However, our understanding of the interaction between these brain structures, and their modulation by serotonin, in the control and regulation of emotion is only in its infancy. Much insight has been gained recently into the role of the medial PFC in the regulation of the amygdala-dependent freezing response to a fear conditioned stimulus, primarily from studies in rodents. However, the neuroimaging of patients with mood and anxiety disorders have revealed structural and activity changes not only in the medial but also the ventral PFC, including orbitofrontal and ventrolateral PFC. These regions are at their most highly developed in primates and thus, to further our understanding of the regulation of amygdala-dependent emotional learning and expression by the ventral PFC we have developed models of negative emotional learning and expression in a new world primate, the common marmoset. Since emotional responses are composed of both physiological and behavioural components we use an automated telemetry system to allow the simultaneous measurement of behavioural and cardiovascular e.g. heart rate and blood pressure, emotional responses in freely moving marmosets. This also helps bridge the gap between current human and rodent studies in which the primary measures of emotional expression are autonomic activity and behaviour, respectively. I shall describe two main experimental approaches that we have adopted to study the neurobiological mechanisms underlying the regulation of emotion. The first is the temporary or permanent manipulation of specific brain regions or neurochemical pathways to establish the causal role of such neural systems in emotion regulation. The second is the investigation of known genetic and behavioural risk factors for developing emotional dysregulation. Using the first approach we have identified the critical role of the anterior orbitofrontal cortex (antOFC) in the regulation of both positive (Reekie et al, 2008) and negative (Agustin-Pavon et al, 2012) conditioned emotional responses, responses that we have already shown to be dependent upon the amygdala. We have also revealed the parallel contribution made by the ventrolateral (vl)PFC. In addition, we have determined the critical role of serotonin in modulating the processing of positive and negative feedback within the amygdala and ventral PFC, dissociating it's role from that of dopamine. Our more recent studies, exploring prefronto-amygdala and prefronto-hippocampal circuits in the context of avoidance behaviour and decision-making, are beginning to differentiate the contributions of the vlPFC and the antOFC to emotion regulation. They are also providing insight into the specific role of the antOFC in the modulation of negative emotional memories through its interactions with the amygdala and hippocampus. Using the second approach we have developed a model of trait anxiety in the marmoset and identified independent, behavioural and cardiovascular biomarkers of this trait, which appear to support the existence of multiple underlying phenotypes. These different phenotypes may, in turn, be linked to altered cognitive processing in separable neural circuits involving the antOFC and vlPFC (Shiba et al, 2014). In addition, we have discovered a novel functional polymorphism within the serotonin transporter (5-HTT) repeat promoter region of marmosets and shown its association with 5-HTT expression levels, emotional responses to threat and altered 5-HT2a binding in the anterior insula, along with structural morphological changes in the anterior hippocampus. We also show that 5-HTT expression correlates with variant-specific, differential transcription factor binding and have begun to identify those factors that may ultimately contribute to individual differences in affective behavior. Using these two different approaches we hope to provide converging evidence for the role of parallel prefrontal circuits, and their interaction, in the control of emotional regulation that will have prognostic, diagnostic and therapeutic potential.

Learning and memory

14.30 – 16.00

chaired by: Ewelina Knapska (Nencki Institute of Experimental Biology, Warsaw, Poland)

1. *A cure for fear: apart or together?*

Ewelina Knapska

Nencki Institute of Experimental Biology, Warsaw, Poland

Fear extinction is a useful model for exposure-based therapies for the treatment of human anxiety disorders, such as phobias and posttraumatic stress disorder. During fear extinction, a previously conditioned stimulus (CS) is repeatedly presented in the absence of the unconditioned stimulus (US), a procedure that induces a progressive decrease in the magnitude and probability of learned fear responses. During extinction of conditioned fear a new memory trace is formed; it is however neither stable nor does it obscure completely the previously formed association. Examples of such phenomena include fear renewal (re-emerging of fear if CS is presented outside the extinction context) and spontaneous recovery of fear (re-emerging of fear with the passage of time after extinction); their neuronal basis has not been fully understood yet. During the lecture, I am going to talk about neuronal circuits involved in the context-dependent retrieval of recent and remote extinguished fear memories. I will explain how, by using a new visualization technique (anterograde tracing in a transgenic rat in which neurons express a dendritically targeted PSD-95:Venus fusion protein under the control of a *c-fos* promoter), we found functional interaction between the amygdala, hippocampus and prefrontal cortex underlying fear extinction and renewal. I will also describe how we developed new animal models of social renewal of conditioned fear and avoidance responses and show how fear and its extinction can be modulated by social context. All these results provide a framework for therapeutic manipulations of the characterized circuits.

2. *Diverse patterns of behavioral deficits in subjects being genetic mouse model of Fragile X syndrome*

Alicja Puścian, Ksenia Meyza, Szymon Łęski, Ewelina Knapska

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Loss-of-function mutations in the fragile X mental retardation protein result in fragile X syndrome (FXS) characterized by intellectual disability and autistic behaviors. FXS is a trinucleotide repeat disorder in which a CGG element located within the 5' untranslated region of fmr1 gene expands and becomes hypermethylated. Earlier studies reveal that individual capabilities of FXS patients are related to the FMRP expression and methylation level, but the observed variability is not fully explained by this factor. In our studies we exploited a mouse model of FXS with identical, non-functional FMR1 genotype. Using fully automated IntelliCage tests we showed significant variability in cognitive and social functioning within the FMR1 knock-out population. We observed subgroups of knock-out mice differing in their performance in place preference learning, as well as in social approach behavior. Interestingly, the levels of cognitive and social performance were correlated only in some animals. Our findings suggest that, in addition to CGG repetitions, there exist different mechanisms leading to altered cognitive and social functioning in animals lacking a functional fmr1 gene. The designed behavioral paradigm enables us to investigate characteristics which can be observed only in a continuous, long-lasting study and holds promise of revealing mechanisms underlying the observed phenomenon.

3. *Delay discounting behaviour in dopamine D1 mutant and wild type rats*

Jeffrey Martin, Judith Homberg

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Donders Institute for Brain, Cognition & Behaviour, Nijmegen, the Netherlands

The role of D1 receptors in cognition and behaviour has remained mysterious, despite great strides being made in the understanding of their diverse functions. A particularly interesting facet of behaviour yet to be explicated is their precise role in the economic process of delay discounting behaviour - a proxy for cognitive impulsivity and disorders of decision making. In this study, a delay discounting task was designed and administered to homozygous and heterozygous DRD1 mutant rats, as well as their wild type equivalents. Homozygous animals were unable to learn the task or acquire stable behavioural responding. Heterozygous and wild type animals did not differ in the majority of test metrics, but showed significantly different delay discounting curves, with heterozygous animals discounting less steeply and thus showing a reduced sensitivity to delay compared to wild types. This finding partially elucidates the role of the

D1 receptor, as well as reiterating the importance of defining the optimal level of a particular neurotransmitter only in context - where appropriate behaviour is determined by the environmental conditions; that is, a tendency toward impulsive choice is either adaptive or not depending on the conditions in which the choice is taking place. Further study is required to completely explicate the relationship between genetic, behavioural, receptor, and environmental optima.

4. *Inhibition of glycogen metabolism in astrocytes positively influence on the synaptic plasticity in old rats*

Dominika Drulis – Fajdasz[a], Marcin Wawrzyniak[c], Jakub Włodarczyk[c], Jerzy W. Mozrzymas[a,b], Dariusz Rakus[a]

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Over the last years growing body of evidence has accumulated that glycogen metabolism in astrocytes modulates synaptic plasticity and its abnormality may be related to various pathologies. In the present study we have asked whether the inhibition of astrocytic glycogenolysis influences the synaptic plasticity in the old rats (P550-700). We focused on CA3-CA1 pathway of glutamatergic transmission in hippocampal slices. We recorded the field excitatory postsynaptic potentials in different glucose or lactate concentrations, and with addition of BAY-U6751 (glycogen phosphorylase inhibitor). We analyzed their amplitudes to characterize: basal synaptic transmission; input output curves; paired pulse facilitation ratio; long-term potentiation (LTP) (HFS=4x100Hz) and measured for 90 minutes. Surprisingly, our results indicated that for all analysed ACSF compositions, extent of LTP was significantly higher in group treated with the BAY inhibitor (p=0.05 from 15' to 60'). Qualitatively opposite results were obtained in the group of juvenile rats (P30). The morphometric analysis of spines in neurons confirmed that after HFS synapses were more matured in samples treated with BAY. Spines were statistically shorter, more circular and with larger area than in controls. We provide the first evidence that inhibition of glycogen metabolism in astrocytes might upregulate the LTP maintenance in old rats.

SSVEP Frequency Responses in Human EEG Studies

14.30 – 16.00
chaired by: Jarosław Żygierewicz (University of Warsaw, Poland)

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1. *Quantification of SSVEP Frequency Responses in Human EEG related to BCI*

Jarosław Żygierewicz

Faculty of Physics, University of Warsaw, Poland

A problem of a brain-computer interfaces (BCI) based on Steady State Visual Evoked Potentials (SSVEP) will be discussed. One of the important issues is the selection of the a-priori most suitable frequencies for stimulation. Previous electrophysiological works related to this problem were done with measuring systems that have little in common with actual BCI systems on small group of subjects. In the case of BCI, the frequencies are often adapted individually for each user. The selection of these frequencies, however, was not justified in quantitative group-level study with proper statistical account for inter-subject variability. The aim of the reported study is to determine the SSVEP response curve, that is, the magnitude of the evoked signal as a function of frequency. The SSVEP response was induced in conditions as close as possible to a BCI system, using actual BCI appliance, for a wide range of frequencies (5–30 Hz, in step of 1 Hz). The data were obtained for 10 subjects. SSVEP curves for individual subjects and the population curve was determined. Statistical analysis were conducted both on the level of individual subjects and for the group. The main result of the study is the identification of the optimal range of frequencies, which is 12–18 Hz, for the registration of SSVEP phenomena. The applied criterion of optimality was: to find the largest contiguous range of frequencies yielding the strong and constant-level SSVEP response.

2. *SSVEP-BCI based on the phase relationship of the stimulus and response*

Anna Chabuda, J. Żygierewicz

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Steady state visual evoked potential (SSVEP) is the response of the brain to visal stimulation with regularly flickering light. This response can be observed in the EEG signal and it can be used in the brain-computer interface. SSVEP is

phase-locked to the stimulus and has a characteristic subject-dependent structure resulting from different composition of the harmonics. An attempt to take into account the typical response is the classification of the reaction using a pattern, which is based on the phase relationship with the stimulus. This method takes into account contribution of the stimulus frequency, harmonic components, and the relationships between them. The aim of this study was to try to build a classifier based on these dependencies. A method presented in this work gave promising results.

3. *Habituation of Steady State Visual Evoked Potentials*

Maciej Łabęcki, Magdalena Zieleniewska, Piotr Suffczyński

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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. Many scientists have been using SSVEP in various applications without validation of the original assumption. In this study we examined stability of SSVEP in large group of subjects. The analysis was done using EEG signals recorded during series of 60-seconds long stimulation periods interleaved with 30-seconds rest periods. The SSVEP strength was estimated by the instantaneous power of the EEG signal that was band-pass filtered in a narrow band around the stimulation frequency. We showed that for the large majority of subjects instantaneous power of SSVEP decrease significantly during stimulation. Two types of habituation may be distinguished. In some subjects power of SSVEP decrease continuously during the stimulation. In other subjects the habituation is rapid and is observed only during the first part of stimulation period, and afterwards the SSVEP power remains stable. Still there is small group of subjects with no habituation.

4. *Time evolution of Steady State Visual Evoked Potentials for different stimulation frequencies*

Maria Nowicka, Maciej Łabęcki, Anna Chabuda, Piotr Suffczyński

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Steady State Visual Evoked Potentials (SSVEP) are the steady state responses elicited in EEG signal by flicker stimulation. Frequency of oscillation of these responses corresponds to the stimulus frequency and its harmonics. In an earlier study we showed, using single stimulation frequency, that in majority of subjects instantaneous power of SSVEP decreased in time. The aim of this study was to investigate time evolution of SSVEP for different stimulation frequencies. The analysis was done using EEG signals recorded during series of 60-seconds long stimulation periods interleaved with 30-seconds rest periods. We used four stimulation frequencies, i.e, 5, 10, 20 and 40 Hz, which were randomly changed between the trials. For each subject 5 hours of EEG signal were collected – 50 trials for each frequency. In this work we present results of initial experiment performed on three subjects. The analysis shows that time evolution of SSVEP varies between stimulation frequencies. For low frequencies (5 Hz) the power of response increases in time while for higher frequencies the habituation of power is observed. The possible explanation of these results is that SSVEP propagate by two different visual streams, which may have different, frequency dependent properties.

5. *Comparison of LDA and SVM classifiers in classification of motor imagery based on EEG*

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A multiclass brain–computer interface (BCI) based on the modulation of sensorimotor oscillations by imagining movements is described. The aim of the work was to differentiate three states: imageries of a) a right hand movement, b) a left hand movement, c) a leg movement based on EEG signal analysis. Subjects were trained by neurofeedback platform to work out a set of useful imageries. Features (acquired for classification process) consisted of power estimates for mu (7-13Hz) and beta band (13-30Hz) for components obtained as a result of blind source separation for consecutive time windows. A Linear Discriminant Analysis, regularized LDA, Linear Support Vector Machine, Gaussian SVM classifiers were compared. The initial results show that linear analysis is not only less computationally expensive but also more effective. Three subjects was examined. The best efficiency obtained in case of three-class LDA classifier was 55%, and in two-class 90% and in case of three-class SVM classifier was 43% and in two-class 86%. The results show that problem is linearly separable - linear SVM had better results than Gaussian. The obtained results can be applied in Brain-Computer Interfaces in movement imagery paradigm.

6. ***Spatio-Temporal Dictionaries for Multivariate Matching Pursuit Decompositions of Evoked Brain Responses in MEG***

Paweł Kordowski, Artur Matysiak, Reinhard König, Cezary Sielużycki

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We introduce a novel algorithm to the Multivariate Matching Pursuit (MMP) decomposition of evoked related fields. We termed it Multivariate Spatio-Temporal Matching Pursuit (MSTMP), since it allows dealing simultaneously with spatial and temporal aspects of MEG signal by using a spatio-temporal dictionary. We evaluate the feasibility of this approach using an illustrative MEG data set obtained from a measurement in which one subject was exposed to a repeated auditory stimulation with sinusoidal 1-kHz tones. We focused on a time window around the most prominent late auditory evoked magnetic field, the M100 component. Furthermore, we assessed the robustness of the performance for various signal-to-noise ratios using a permutation test. MSTMP is an independent source localization strategy free of setting any regularization parameters, in contrast to classical MMP preprocessing approaches, where decomposing a signal containing contributions of temporally related but not identical activities yields one waveform addressing both activities, which is then followed by applying an inverse solution with an unknown number of sources. MSTMP is able to separate such activities, resulting in more specific waveforms and allows to avoid such intricate inverse solutions, as one signal component addresses the activity of exactly one dipolar source.

CLOSING LECTURE:
16.15 – 17.15

Neural mechanisms of auditory perception: regularity encoding and deviance detection from brainstem to cortex

Carles Escera

Institute for Brain, Cognition and Behavior (IR3C), Department of Psychiatry and Clinical Psychobiology, University of Barcelona, Spain

How do we perceive the auditory world? This remains as a mystery, but recent research has suggesting that the auditory system extracts regularities from the ongoing acoustic input to build up auditory object representations. In my talk, I will discuss recent evidence obtained in our laboratory with the complex Auditory Brainstem Response (cABR), the Middle Latency Response (MLR), Magnetoencephalography (MEG), and functional Magnetic Resonance Imaging (fMRI) demonstrating that human regularity encoding, as demonstrated by deviance detection, occurs at latencies and in neural networks comparable to those revealed in animal studies of single-neuron activity. Our results demonstrate that the encoding of simple acoustic-feature regularities and detection of corresponding deviance, such as an infrequent change in frequency or location, occur in the latency range of the MLR, in separate auditory cortical regions from those generating the mismatch negativity (MMN) long-latency evoked potential, and even at the level of human auditory brainstem. In contrast, violations of more complex regularities, such as those defined by the alternation of two different tones or by feature conjunctions (i.e., frequency and location) fail to elicit MLR correlates but elicit sizable MMNs. Taken together, these findings support the emerging view that regularity encoding, as revealed by deviance detection, is a basic principle of the functional organization of the auditory system, one that it is organized in ascending levels of complexity along the auditory pathway expanding from the brainstem up to higher-order areas of the cerebral cortex.

POSTER SESSION I

April 26, 2014 (Saturday)
16.30 – 18.15

NEUROPATHOLOGY

1. Apoptotic response differentiates lymphocytes from sporadic and familiar Alzheimer`s disease patients

Joanna Wojsiat, Katarzyna Sawicka, Emilia Białopiotrowicz, Jacek Kuźnicki, Urszula Wojda

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Our aim was to compare apoptotic response to oxidative stress in EBV-immortalized B-lymphocytes from healthy individuals and patients with familiar (FAD) and sporadic form of AD (SAD). We found that 24h after 40mM 2-deoxy-D-ribose (2dRib) treatment, the percentage of surviving lymphocytes in MTT assay was significantly decreased in SAD comparing to the age-matched controls (p=0,05) and FAD (p=0,005). In agreement with these data, early apoptosis measured by AnnexinV staining was higher in SAD lymphocytes than in control (p=0,05) and FAD (p=0,005) cells. Also measurements of mitochondrial membrane potential (MMP) using cationic dye JC-1 showed differences in the response to 2dRib between SAD and FAD: MMP of SAD lymphocytes was significantly decreased comparing to control (p=0,05) and FAD (p=0,005) cells. Accordingly, SAD lymphocytes showed increased percentage of cells in SubG1-phase when compared to control and FAD cells (p=0,05). Comparing the response in two control groups, age-maching FAD and SAD, respectively, we found that the differences between SAD and FAD cells are not due to aging. Altogether, our results showed that SAD lymphocytes are more vulnerable to 2dRib than control and FAD cells and thus that mechanism of apoptosis differentiates cells from SAD and FAD patients.

2. Impact of global brain ischemia on BH3-only proteins, Bad and PUMA

Katarína Klačanová[a], Ivana Pilchová[a], Mária Chomová[b], Zuzana Tatarková[a], Dušan Dobrota[a], Peter Račay[a]

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Global brain ischemia has impact on all cellular pathways including mitochondrial apoptosis. The crucial roles in ischemia-induced neuronal death have regulators of mitochondrial apoptosis, BH3-only proteins. The aim of this study was to investigate impact of global brain ischemia on BH3-only proteins, Bad and PUMA. Rats were subjected to 15 minutes of global brain ischemia using four vessel occlusion model, followed by 1, 3, 24 and 72 hours of reperfusion. Global brain ischemia did not affect total level of Bad and PUMA but led to the significant accumulation of Bad in mitochondria isolated from hippocampus of rats subjected to ischemia and reperfusion. Since activity of Bad is regulated with Akt kinase, we have also investigated the impact of global brain ischemia on phosphorylation of Akt on Ser473. We have incubated neuroblastoma SH-SY5Y cells with Akti1/2 to confirm involvement of Akt kinase in the mechanism of ischemia-induced translocation of Bad to mitochondria. Incubation of cells was associated with cell death but we did not observe changes of Bad level. Our study confirmed possible involvement of Bad in ischemia-induced cell death. The exact mechanism of Bad activation after brain ischemia remains to be further investigated (Supported by APVV-0245-11).

3. Association of BsmI gene polymorphism of VDR gene with susceptibility to Multiple Sclerosis

Peter Dubovan, Čierny, D.[a], Michalik, J.[b], Kurča, E [b], Lehotský, J.[a]

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Vitamin D alters immune system responses and can improve clinical course of MS or prevents the onset of the disease. Dihydroxycholekalciferol exerts its biological functions after binding to vitamin D receptor (VDR). The aim of our preliminary study was to uncover potential role of the BsmI gene polymorphism of VDR in MS susceptibility. We

genotyped 57 Slovak patients with MS and 57 healthy controls. DNA samples were isolated from peripheral leucocytes. DNA was amplified by PCR reaction and BsmI genotypes were identified by restriction analysis. We found 57 % incidence of susceptible allele b in MS patients compared to 56% in healthy controls. There was 31,6 % incidence of homozygotes bb in MS patients and 33,3 % in healthy controls. In our preliminary study, we did not find any significant differences among allele or genotypic frequencies between the groups of MS patients compared to controls. To confirm these findings, the role of BsmI gene polymorphism in MS susceptibility will be further studied in larger cohort of individuals. This work was supported by the grant 2012/30-UKMA-7 Biological and molecular markers of MS and ITMS: 26220220114 Identification of novel markers in diagnostic panel of neurological diseases.

4. HMG-1 as a potential marker of disease progression in multiple sclerosis

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High mobility group protein 1 (HMG-1) is an important mediator of inflammation, actively secreted by immune cells. Changes in plasma levels of HMG-1 are observed in some cases of neurodegenerative diseases. The aim of our study was to detect the association between HMG-1 plasma levels and variable degrees of disease severity in multiple sclerosis (MS) patients. The concentration of HMG-1 in plasma was analysed by ELISA (Human HMGB1 ELISA kit) in 40 MS patients (MS Centrum, UH and JFM CU Martin), divided according MSSS into 2 groups – 19 patients with slow progressing and 21 with rapid progressing form of multiple sclerosis. We did not detect any statistically significant differences in plasma concentration of HMG-1 between slow progressing and rapid progressing group of MS patients. Our results do not indicate for the relevant association of HMG-1 plasma levels with various progression forms of multiple sclerosis. It is suggested to determine plasma levels of HMG-1 in larger groups of MS patients. This work was supported by grant 2012/30-UKMA-7 Biological and molecular markers of MS and ITMS: 26220220114 Identification of novel markers in diagnostic panel of neurological diseases.

5. The ischemic preconditioning and his influence on the ROS formation and apoptotic markers in the nervous tissue aggravated by hyperhomocysteinemia

Martin Petráš, Mária Kovalská[b], Zuzana Tatarková[a], Silvia Mahmood[a], Ján Lehotský[a], Anna Drgová[a]

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Brain ischemia causes the death and the disability of adults worldwide and the reperfusion may produce the ischemia-reperfusion (IR) injury. The ischemic preconditioning (IPC) can help to improve neuronal survival after ischemia. The hyperhomocysteinemia (hHcy), aggravating the IR damage, results in increased reactive oxygen species formation (ROS), homocysteinylation of enzymes and proteins. We focus attention on markers of ROS and apoptosis in the cortex after induced hHcy and IPC. The male Wistar rats divided into four groups (control group, hyperhomocysteinemic group, IR and IPC group with hHcy) were used in our experiments. Homogenized cortex and mitochondria were used for biochemical and histological analysis. Our results showed the significantly increased DCF formation and decreased the Bcl-2/Bax ratio after long-lasting reperfusions after IPC. The immunohistochemical analysis was in correlation with the Western blot analysis (WB). Changes in 3-NT production were not significant, however the WB showed the increased amount of nitrated proteins. These results indicate the increased post-translational modifications of proteins, due to the hHcy and the increased level of apoptotic markers, moreover the protective effect of IPC prior to ischemia and 1h reperfusion. (Supported by VEGA 1/0213/12 and project Identification of Novel Markers in Diagnostic Panel of Neurological Diseases“, code:26220220114).

6. Animal model of induced hyperhomocysteinemia in association with Alzheimer's disease-like pathological features

Maria Kovalska, Libusa Kovalska, Martin Petras, Zuzana Tatarkova, Marian Adamkov, Jan Lehotsky

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Alzheimer's disease (AD) is a progressive neurodegenerative disorder that results in dementia and death. A high level of plasma homocysteine (Hcy) is an independent risk factor for stroke. AD commonly co-occurs with stroke. A recent studies showed hyperhomocysteinemia to be a strong risk factor also for AD. The molecular mechanisms underlying these mechanisms are not fully understood. Therefore, we investigated the effect of ischemia-reperfusion injury (IRI) in combination with hHcy on neurodegeneration in rat brains. We have studied neurodegeneration as well as post-translation changes in MAPK (mitogen-activated protein kinase) pathways after global IRI in rat hippocampus in association with hHcy. Global forebrain ischemia was induced by 4-vessels occlusion, a 15 min of ischemia followed by 72h and 7 days reperfusion. hHcy was induced by methionin diet (0.2g/kg) in duration of 30 days. We demonstrated occurrence of degeneration of selectively vulnerable neurons after IRI as well as after hHcy. Western blot study and imunohistochemical analysis suggested that IRI and also hHcy down-regulates the p-ERK protein, which is associated with survival of neural cells. These findings suggest that IRI after induced hHcy could have a neurodegenerative role on global brain ischemia in rats. Our results also indicate that this model of combined insults could lead to progression of AD-like pathological features. Supported by VEGA 213/12, 1/0050/11 and by project: "IDENTIFICATION OF NOVEL MARKER IN DIAGNOSTIC PANEL OF NEUROLOGICAL DISEASES co-financed from EU sources and European Regional Development Fund.

7. Effect of histone acetylation on expression and processing of amyloid precursor protein

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The generation of β-amyloid plaques and tangles are considered as the hallmarks of Alzheimer's disease. The expression and subsequent processing of the amyloid precursor protein (APP) determines the amount of present β-amyloid. Several molecular mechanisms, including epigenetic, can regulate the expression of β-amyloid and members of its processing pathway. Therefore, to investigate the role of histone acetylation status on the expression of APP and its processing, the human neuroblastoma cells SH-SY5Y were cultured in a presence of histone deacetylase inhibitors, trichostatine A and valproic acid. Immunoblotting analysis was used to estimate the levels of APP and its fragments after 72 hour incubation in presence of trichostatine A or valproic acid. Our results revealed that trichostatine A and valproic acid had no effect on the level of APP, but trichostatine A increased the level of 40 and 43 kDa fragments generated by partial proteolysis of APP. Our results indicate that histone acetylation is linked with higher rate of APP processing in non-amyloid pathway and is in agreement with recent consideration to use histone deacetylase inhibitors as neuroprotecting compounds. in a wide range of neurodegenerative disorders including Alzheimer's disease. This work was supported by projects VEGA grant 1/0242/13, VEGA 1/0260/14;"Competence Center for Research and Development in the diagnosis and therapy of oncological diseases" code ITMS 26220220153; "The increasing of opportunities for career growth in research and development in the medical sciences", code ITMS: 26110230067.

8. Changes in the expression of markers of the inflammatory response under the influence of α-synuclein in the brain of mice

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The researches for possible causes of the neurodegeneration in Parkinson\'s Disease (PD) are still far from conclusion. However, it has been already confirmed that α-synuclein protein (ASN), together with other proteins, is the principal component of Lewy pathology and influences strongly the pathogenesis of PD. The increased level of ASN protein causes microglia response. Microglial activation leads to the increased expression of inflammatory agents in the central nervous system (CNS) and the infiltration of peripheral immune cells into the CNS. Recent evidence suggests that reactive microglia cells may actively participate in the damaging of dopaminergic neurons. Furthermore, we examine the potential role of recombinant monomer of ASN as a major pathogenic factor causing the inflammatory reaction in CNS. We investigate the effect of high concentrations of human recombinant ASN proteins on some pro- and anti-

inflammatory cytokines as well as trophic factor and adhesion molecule in mice striatum (ST). The clarification of the exact role of ASN in the inflammation in PD may likely lead to the understanding the molecular mechanisms resulting in the dopaminergic cells degeneration.

9. Salsolinol – the effect on the glutamate-induced cell apoptosis pathway

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The endogenous neurotoxin, 1-methyl-6,7-dihydroxy-1,2,3,4-tetrahydroisoquinoline (SAL), has been considered a potential neurotoxin in the etiology of Parkinson's disease. The synthesis of SAL as the concentration product of dopamine and acetaldehyde, the first metabolite of ethanol, suggested also its involvement in alcohol addiction. To investigate the effect of SAL on the glutamate-mediated apoptosis pathway. Methods: evaluation the effect of SAL (50, 100 and 500μM) on glutamate-induced apoptotic and neurotoxic parameters, and comparison of biochemical data with cellular analyses, including Hoechst 33342 and calcein AM staining. SAL (50μM) significantly inhibited the pro-apoptotic and neurotoxic effects caused by glutamate treatment. Hippocampal tissues responded to the inhibitory action of SAL on glutamate-activated caspase-3 and LDH release from the damaged cells. Additionaly, SAL (50μM) inhibited of glutamate-induced loss of membrane mitochondrial potential. It also diminished the number of bright fragmented nuclei with condensed chromatin and increased cell survival in Hoechst 33342 and calcein AM staining in hippocampal cultures. Only the highest dose of SAL (500μM) enhanced the excitotoxicity caused by glutamate. SAL possess neuroprotective effects at low micromolar concentrations. This findings may have important implications for the development of new strategies to treat or prevent neural degeneration.

10. Influence of physical training on diminished motor learning abilities in MPTP-mouse model of Parkinson's disease

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Motor therapy in animal models of Parkinson's disease (PD) has neuroprotective and neuroregenerative effects. However, the mechanism of motor therapy effects is unknown. Fundamental research relies on good animal models that demonstrate the hallmarks of PD. Chronic treatment with MPTP and probenecid in mice produced long-lasting dopamine cell loss and motor deficits. Overreaching aim of the present study was to examine efficacy of physical training on changes in the motor learning in MPTP model. Three-months old, male C57BL/6 mice were injected with 10 doses of MPTP (12,5mg/kg subcutaneously) in combination with probenecid (250 mg/kg, intraperitonealy) on 5 week schedule. The motor learning was assessed in RotaRod test. Motor performance was assessed as maximal rpm sustained for each trial on RotaRod. Behavioral tests were performed before treatment and immediately and four weeks after treatment. Before treatment mice doubled maximal sustained rpm during 4 consecutive days of RotaRod training. Immediately after treatment MPTP-mice lowered the maximal learned speed and did not improve during training. Tested four weeks later MPTP-mice were able to increase their speed during learning and finally achieved the pre-treatment level. Contrary to the claimed sustainability of motor impairment caused by MPTP/probenecid treatment in our study some forms of motor learning recovered spontaneously and some other were not affected at all. Supported by NCN grant 2011/01/D/NZ7/04405

11. Markers of a systemic inflammation following LPS injection in two age groups of rats

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Several animal models of sepsis have been developed to explore nature of inflammation. Most of them are based on intra-abdominal injections of agents initiating systemic inflammation like bacterial lipopolysaccharide (LPS). This approach mimics pathophysiological changes in septic patients.The present study focuses on changes in blood levels of two proinflammatory cytokines TNFα and IL-6 as markers of systemic inflammation. LPS was injected intraperitoneally (2 mg/kg b.w.) to six- or 30-day-old Wistar rats (P06s and P30s, respectively). Blood samples were obtained from the animals before and 2, 4, 6, and 24 hours after the injection and centrifuged. Thereafter, the serum levels of TNFα and IL-6 at different time points after LPS injection were determined using the ELISA method. In both age groups, high levels of TNFα and IL-6 were observed 2 and 4 hours after LPS injection. In P06s, however, the increased levels remained up till 6 hours following the injection. Generally, the concentration levels of TNFα and IL-6 at those time points were higher in

P06s than in P30s. The results indicate that intraperitoneal injection of LPS caused a systemic inflammation in rats at different developmental stages. Supported by the National Science Centre, grant UMO-2012/05/B/NZ4/02406.

12. Pre-chiasmatic arterial subarachnoid hemorrhage leads to generalized neuronal damage and astrocyte activation in rat brain

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Our aim was to develop model of arterial bleeding into the pre-chiasmatic cistern resembling subarachnoid hemorrhage (SAH) from aneurysm rupture in the anterior part of the circle of Willis and to explore different aspects of its effect upon adjacent as well as distant areas of rat brain. Pre-chiasmatic SAH (pSAH) was produced by injection of 200uL of fresh autologous arterial blood into pre-chiasmatic cistern in rat brain. Brains were coronally cryosectioned and stained with Fluoro Jade C (FJC, selective specific marker for degenerating neurons) and immunostained to visualize cleaved caspase 3 and GFAP. We found numerous FJC positive neurons around the site of blood application as well in more distant areas. The number of FJC cells was especially high in somatosensory cortex and hippocampus. Distribution of caspase 3 positive cells was similar to that for FJC. Additionally we found astrocytes with morphological alterations characteristic for their activation: thick processes and enlarged cell bodies, mainly located in the hippocampus and do not co-localized with FJC positive cells. Obtained results indicate that administration of blood directly to pre-chiasmatic cistern leads to neuronal damage and stimulation of astrogliosis not only in the vicinity of injection site but also in more distant regions.

13. Myelin abnormalities in the brain of the mice lacking St8sia2 gene - a new model of Schizophrenia

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Polysialylation is a posttranslational modification of NCAM proteins carried out by two polysialytransferase II (ST8SIAII) and IV (ST8SIAIV). The attachment of polysialic acid chains to NCAM results in the reduction of NCAM-mediated cell-adhesion in the brain. Mice knock-out for St8sia2 gene has been shown to display schizophrenia-like phenotype including enlarged ventricles, decreased thalamus and thalamocortical disconnection. Similar morphological abnormalities have been observed in schizophrenic patients. These data suggest that an impaired expression of St8sia2 and a deficit in polySia-NCAM contribute to the etiology of schizophrenia. To explain the role of ST8SIAII in the brain physiology and pathology, we compared hippocampal proteome of St8sia2-/- mice and their WT littermates, using mass spectrometry (iTRAQ). We detected lower levels of Myelin Basic Protein (MBP) and Myelin Proteolipid (PLP1) in St8sia2-/-. Immunoblot analysis confirmed this result, and revealed the same changes in cortical areas, suggesting that ST8SIAII is implicated in myelin formation. Finally, we used Black Gold II to stain myelin proteins in brain tissue, and showed that the impairment of myelin is developing with age. Here, we propose that myelin abnormalities in schizophrenic might be a consequence of low expression level or activity of the ST8SIA2 enzyme, what remains to be established.

14. Disturbances in ERK1/2 signalling and function of 26S proteasomal complex do not affect level of selected proteins from Bcl-2 family after global brain ischemia

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ERK1/2 kinases are members of signalling pathway involved in modulation of mitochondrial pathway of apoptosis by phosphorylation of some proteins from Bcl-2 family which are consequently degradated in 26S proteasomal complex. Global brain ischemia is accompanied with disturbances in ERK signalling and inhibition of 26S proteasomal complex, leading to iniciation of mitochondrial apoptosis and neuronal cell death. Our study is focused on impact of global brain ischemia on level of proteins from Bcl-2 family(BIM, Bad, Mcl-1) which are regulated by ERK1/2 and 26S proteasome. Global brain ischemia in rats was induced using 4-VO model, followed by 1,3,24 and 72h of reperfusion and relative level of selected proteins was evaluated in hippocampal tissue by western blot analysis. Proteasomal stress was detected 1 and 3 hours after ischemia in form of massive aggregation of polyubiquitinylated proteins associated with significant decrease of free ubiquitin. Cellular stress response in form of increased level of Hsp70 was induced 24 and 72 hours

after ischemia. Immediately after ischemia we observed transient decrease of phospho-ERK1/2 which is considered as a marker of ERK1/2 activation. Interestingly, neither ischemia nor ischemia with reperfusion had significant impact on the level of investigated proteins from Bcl-2 family. Supported by APVV 0245-11.

15. The effect of kinin peptides on the neurodegeneration development in a cellular model of Parkinson's disease

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Kinins, the known pro-inflammatory peptides are proposed as important factors involved in the development of several neurodegenerative diseases, including Parkinson's disease (PD). The aim of this study was to examine the effect of the most representative kinins - bradykinin and des-Arg10-kallidyn on neurodegenerative processes in a cellular model of PD, which was obtained after stimulation of a human neuroblastoma cell line (SK-N-SH) with the neurotoxin - 1-methyl-4-phenylpyridine (MPP+). An increased release of pro-inflammatory cytokine interleukin 6 was observed after stimulation of the PD cellular model with kinins. In addition, the Alamar Blue Cytotoxicity and Caspase 3/7 assays showed a significant decrease in the survival of cells treated with both kinins and neurotoxin. On the other hand, RT-PCR analysis suggested an increased gene expression of the kinin and dopamine receptors after cell stimulation with MPP+. Moreover, the mRNA quantity of tyrosine hydroxylase and α-synuclein was also altered in this cellular model. The obtained outcomes indicate a significant role of inflammation in neurodegenerative diseases development and suggest that both dopamine and kinin receptors may be involvement in this activity. These results might open new ways for the treatment of PD throughout the manipulation of kinin receptors.

16. The influence of the increased concentration of α-synuclein on dopamine metabolism and transport in mice

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Parkinson's disease (PD) is one of the most common neurodegenerative disorders. It is characterized by two major processes: a progressive loss of dopaminergic neurons, which occurs mainly in the substantia nigra (SN), accompanied by a decreased concentration of dopamine (DA) and its metabolites in the striatum (ST) and an accumulation of intraneuronal Lewy bodies containing misfolded fibrillar α-synuclein (ASN). Mechanisms and etiology of the neurodegeneration in PD remain still unknown. The aim of our study was to examine the influence of recombinant monomers of ASN on dopaminergic system. 1-year-old male C57Bl mice were used in this study. ASN was bilateraly administered into SN or ST. To evaluate the influence of the ASN on the neurodegeneration concentrations of striatal DA and its metabolites were measured by high performance liquid chromatography (HPLC). The expression of dopamine transporter (DAT) was measured by western blot method. We observed changes in dopamine metabolism after ASN monomers administration. Our study also showed statistically significant influence of ASN on dopamine reuptake via DAT. Further research must be conducted to better understand the crucial role of ASN in the neurodegenerative process in PD.

17. Chronic mild stress attenuates lipopolysaccharide-induced oxidative stress

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Lipopolysaccharide (LPS) is a major cell wall molecule of Gram-negative bacteria. The majority of LPS enters the host (both in normal and pathological states) through the gastrointestinal tract and liver, which is strategically located at the gateway draining gastrointestinal tracts. Intraperitoneal LPS administration leads to its rapid accumulation and detoxification in hepatic Kupffer cells. LPS challenge stimulates hepatic Kupffer cells to synthesize and secrete toxic metabolites, such as reactive oxygen species (ROS) which cause oxidative stress. The present study aimed to investigate the putative destructive effect of chronic stress on LPS-induced oxidative stress in liver. Animals were subjected to

chronic mild stress (CMS) procedure for 8 weeks and than half of the animals were challenged with LPS. Four hours after LPS injection liver samples were collected. Animals subjected to CMS or LPS revealed an increase in ROS synthesis (respectively by 19% and 31%) and in hepatic lipid peroxidation estimated by malonodialdehyde (MDA) level (respectively by 55% and 100%). LPS injection to chronically stressed animals did not increase levels of markers of oxidative stress. Moreover reduction of MDA level by 21% in comparison to LPS-treated animals was observed. Chronic stress may induce protective mechanisms against acute liver LPS-induced injury.

18. Influence of ibudilast on the glia reaction in the mouse model of Parkinson's disease induced by 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)

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Ibudilast (IBU) (3-isobutyryl-2-isopropylpyrazolo-[1,5-a]pyridine), non-selective phosphodiesterase inhibitor is a well-known anti-asthmatic agent with anti-inflammatory potency. Therefore, IBU may raise expectations as a potential neuroprotectant agent for the treatment of neurodegenerative diseases. In the present pilot study for the first time was examined efficacy of IBU in the animal model of Parkinson's disease caused by MPTP. 3 months-old male C57Bl/10Tar mice were treated IBU b.i.d. for 9 days with subcutaneous injections [0, 20, 30, 40 or 50 mg/kg], beginning 2 days prior to MPTP (60 mg/kg) intoxication. Locomotor activity was examined by the RotaRod performance test. Expression of mRNA cytokines (TNFα, IL-6, IL-1), trophic factor (GDNF) was examined by the Real Time RT-PCR method. Behavioral study indicated dose-dependent trends toward improvement in the locomotor activity and significant result in the group of mice treated with 40 mg/kg IBU prior to MPTP administration. The RT-PCR analyses revealed significant reduction in mRNA expression of all investigated pro-inflammatory cytokines and increase in GDNF production in the striatum in the dosage range. In agreement with our results, IBU may have some therapeutic potential, but there is still need to examine its effects on the degeneration of neurons.

19. Effect of glucocorticoid receptor ablation in adrenergic cells on inflammatory response in female mice

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Noradrenergic neurons with terminals in the hypothalamus are known to regulate activity of the hypothalamic pituitary adrenal (HPA) axis. The aim of the study was to evaluate whether glucocorticoid receptor (GR) ablation in adrenergic cells affects the inflammatory response in CNS and functioning of immune organs, under inflammatory conditions. The experiments were carried out on female C57BL/6N GRDBHCre and littermate wild type mice. Conditional ablation of GR was achieved using the Cre/loxP system. Resulting GRDBHCre mutant mice, showed lack of adrenaline but no differences in corticosterone level. The animals were injected intraperitronealy with a single dose (700 ug/kg) of lipopolisacharide (LPS). Expression of adrenergic receptor (AR) genes, selected cytokine genes (in hypothalamus) and cytokine production by spleen and thymus was measured. LPS increased the alpha1B- AR expression in hypothalamus, both in mutant and wild type mice. Ablation of GR attenuated LPS-induced expression of proinflammatory cytokines in the hypothalamus and Concanavalin A induced proinflammatory cytokine synthesis in splenocytes. Our results suggest that ablation of GR in noradrenergic system does not affect an afferent inflammatory signal from the periphery and, unexpectedly, attenuates inflammatory response in hypothalamus and spleen. Supported by program "Interdisciplinary PhD Studies: Molecular Sciences for Medicine founds.

20. Identifying multiple sclerosis biomarkers in the cerebrospinal fluid using nuclear magnetic resonance (NMR) spectroscopy

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This study employed nuclear magnetic resonance (NMR) spectroscopy to search for low molecular weight biomarkers in the cerebrospinal fluid (CSF) of patients shortly after the onset of the disease (clinically isolated syndrome, CIS) and with diagnosed MS. CSF was collected from 26 patients with CIS, 17 patients with MS and 25 control patients. It was analyzed using 800MHz NMR spectrometer. The spectra were phase and baseline corrected, the peaks were integrated and scaled relative to glucose. Statistical analysis was conducted using R-CRAN. Package ChemoSpec was employed to

perform principal component analysis (PCA). Statistical analysis was conducted on separate integrated peaks in order to find the possible biomarkers (p=0.05). Forty seven percent of MS patients and 15% of CIS patients were identified outside control group using PCA. We identified 11 peaks that significantly differed MS and control group and 10 peaks that identified differences between CIS and control group. Three peaks were overlaping in both comparisons. Only one peaks significantly differed in the CIS and MS group (chemical shift of 3.35 ppm). Virtually no difference between MS and CIS populations indicate common biochemical nature of those disorders. It suggests that metabolomic features of MS are present early in disease development.

21. Quantitative morphometric analysis of seizure-induced hippocampal microglia activation in normal and dysplastic rat brains

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Epileptic seizures induce local microglial activation – a process in which "resting microglia lose their robust branched morphology, transforming into a macrophage-like "active phenotype. Prenatal gamma irradiation is a method used in animal research to generate morphological features, such as cerebral dysplasia and heterotopias, similar to human dysplasia. Alterations induced at distinct stages of prenatal development differentially affect seizure susceptibility in adulthood. Here, we used Sholl-based morphometry to quantify microglial alterations in response to seizures in rats with irradiation-induced cerebral dysplasia. Adult male rats irradiated at prenatal day 17 as well as untreated controls were given i.p. injections of kainic acid. Seizures were assessed over a 6h period with a modified Racine scale. After 72h the animals were sacrificed, brains were cut into 30µm sections and stained immunohistochemically for Iba-1, a microglial marker. Digital images of microglia from hippocampal subarea CA1 and dentate gyrus were extracted and thresholded. Sholl analysis was performed and polynomial functions were fitted to data points. The properties of the resulting curves were used to describe cell morphology. Microglia from the dentate gyrus exhibited greater changes, both in dysplastic and normal rats. A strong relationship between seizure intensity and microglial activation was observed. Supported by NCN grant: 2012/05/N/NZ2/00641.

22. Morphological approach to brain contusion-timing in forensic medicine – initial results from the study on the deceased

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In forensic pathology determination of the age of injuries is extremely important, as it allows to establish the time of trauma. The purpose of our study was to analyze changes in the neurofilament architecture following the brain contusion and relate them to the length of the time of survival. The available literature lacks any data dealing with brain trauma related temporal changes in the neuronal cytoskeleton which could be used for forensic wound age estimation. Brain tissue samples collected during medicolegal autopsies have been analyzed using immunohistochemical procedures. The material was divided into nine subgroups (10 cases each) according to the time of death of persons: immediately at the accident site, 12 hours, 24 hours, 2, 3, 4, 5, 6 and 7 days after head trauma. Immunostained neurofilaments were evaluated quantitatively using the novel Met-Ilo digital morphometric application. The initial results were analyzed statistically with the one way analysis of variance (ANOVA) and the least significant difference (LSD) tests. It was calculated that there are significant differences in numbers and area fractions of neurofilaments within 7 days after head trauma. It should be concluded that morphometric analysis of neurofilaments may be a promising method but further studies are still required.

LEARNING AND MEMORY

23. Intracerebroventricular adminstration of oxytocin is related to increase of neurotrophins expression in the brain and behavioral changes

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Neuropeptide oxytocin is known for its effects on behavior and memory,however mechanisms of its action on neuronal tissue is not clear. Aim of our study was to analyze influence of central oxytocin administration on expression of cytoskeletal proteins (nestin and microtubule-associated protein 2), and growth factors (brain-derived neurotrophic factor and nerve growth factor) in rat hippocampal tissues. Male Wistar rats were infused continuously from a subcutaneous osmotically driven mini-pump via a lateral cerebral ventricle with oxytocin (20ng/ µl) for 7 days; the infusion rate was 0,5 µl/h; controls were infused with vehicle.Behavior evaluation and recognition tests were performed on 7th day and hippocampal tissues were collected for gene expression and western blot analysis. Total exploration activity of oxytocin treated rats was increased. Object recognition test showed, that oxytocin rats significantly prefered unknown object. Oxytocin treatment significantly increased gene expression and protein levels of cytoskeletal proteins and growth factors in comparison with control group. In conclusion, central oxytocin changes markers of brain plasticity and has functional effect on memory related behavior.Our data support assumption that, brain oxytocin might contribute to maintaining of cognitive functions. Supported by grants of APVV-0253-10 and VEGA 2/0132/12

24. Influence of ketamine and nicotine on rats' performance in the odor span test

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Ketamine, the noncompetitive NMDA receptor antagonist, is commonly used to mimic schizophrenia-like symptoms, including working memory (WM) deficits, in animal and human tasks. On the other hand, activation of nicotinic acetylcholine receptors (nAChRs) can improve various indices of cognitive functioning, as for example working memory capacity (i.e. the number of items that can be concurrently held in WM). Hence, we examined whether ketamine (3 and 10 mg/kg) can affect working memory capacity that is assessed in the Odor Span Test (OST). Nicotine (0.05 and 0.1mg/kg) was used as a positive control. Rats were trained to detect a novel odor from an increasing number of odors, according to a nonmatching to sample rule. Span length, considered as a number of correct and consecutively chosen cups minus 1, as well as the number of errors were counted during the session. Nicotine caused a statistically significant improvement of the span length and significantly decreased a number of errors. Ketamine had a tendency to impair OST performance, but this effect did not reach statistical significance. Present findings demonstrates the utility of the OST in detecting compounds with cognitive-enhancing properties. Further studies are required to determine the impact of NMDA receptor antagonists on WM capacity.

25. A 'near-miss' effect enhances reward expectancy in gambling behaviors during performance on the rat slot machine task

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Pathological gambling (PG) is, according to DSM-V, behavioral addiction. It has been revealed that multiple similarities exist between PG and the substance use disorders, including neurobiological overlap. Rodent models provide a useful tool for modeling and studying of PG as well as for examining the role of different neurotransmitters in these processes. Therefore, we have employed the modified version of a rat slot machine task (rSMT). This model of PG is based on an observation that phenomenon of unrestrained will of gambling (despite no rewards) results from an experience of "near-miss events. It is believed that cue signaling "near-miss could suggest direct reward and enhance conviction about expecting reward, which in turn drive further play. In the rSMT, subjects responded to a series of three flashing lights (analogous to the wheels of a slot machine). A winning trial was signaled if all three lights were illuminated. At the end of each trial rat chose between responding on the 'collect' lever, resulting in reward on win trials, but a time penalty

on loss trials, or starting a new trial (i.e. responding on the roll lever). Our preliminary results confirmed that rats usually interpret both two and three illuminated lights trials as win trials, suggesting enhanced reward expectancy following near-misses similar to wins.

26. Instrumental conditioning in transgenic mice lacking NMDA receptors on dopamine neurons

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Dopamine release from the ventral midbrain dopamine neurons underlies positive reinforcement and has been proposed to be the basis of behavioral conditioning. Here, we examine how the loss of the NMDA receptors on dopamine cells (the NR1DATCreERT2 mouse strain) affects instrumental learning related to various types of reward. Animals were food-deprived (80-85% of their initial weight) and then introduced to Skinner boxes, where exploration of active operant (nose poke) would trigger the delivery of a food pellet. Mice quickly learned to perform the instrumental response to obtain food (75 responses/session) with no difference between mutants and controls. Likewise, the mutation had no effect on responding under the progressive ratio and variable interval schedules. However, when we tested mice for operant sensation seeking in the same boxes, mutants did not acquire the instrumental behavior. This prompted us to conduct a saccharine preference test in the IntelliCage apparatus, where animals had to respond under FR3 schedule to obtain 0.1% saccharine solution. The NR1DATCreERT2 mice showed on average 60% preference for saccharine whereas control mice reached 100% preference. In conclusion the loss of the NMDA receptors on dopamine cells caused inhibited instrumental responding for non-essential reward.

27. Habitual behavior in mice lacking NMDA receptors in catecholaminergic neurons

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Frequently repeated behaviors may become habits. Their execution becomes automatic in response to associated cues, thus freeing brain's resources for other tasks. However, habits may become pathological, inflexible and persist though they lead to no benefit or even harm, as is classically observed in addictions. Here we investigate the neural mechanisms underlying the development of habits, the NMDA-dependent plasticity of catecholaminergic neurons. We used NR1DATCreERT2 and NR1DBHCre transgenic mice lacking the NR1 subunit selectively in dopamine and noradrenergic neurons respectively. Animals were trained in operant chambers under random interval schedule of reinforcement, which generates habitual responding. After several days of extensive training a reward devaluation procedure (open access to the reward prior to testing) was used to test for habit formation. During training, NR1DATCreERT2 mice shows significantly less responses than wild type and NR1DBHCre mice, which would suggests that they failed to develop habitual responding, despite extensive training. NR1DBHCre mice in turn, did not differ from the control animals, however the tendency towards increased responding was visible. Furthermore NR1DBHCre mice, contrary to NR1DATCreERT2 mice were insensitive to reward devaluation and shows increased responding in an extinction test, which suggests shift from goal-directed to habitual behavior in these animals. These preliminary results indicate an opposing role of NMDA receptors in dopamine and noradrenergic neurons in control of habitual behavior. However, their precise functions need to be further determined.

28. Role of SRF-dependent transcription in homeostatic plasticity

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Homeostatic plasticity is a neuronal ability to maintain a stable level of activity in the face of sustained alterations in synaptic stimulation. Regulation of this form of plasticity is based on global changes of synaptic strength known as synaptic scaling, involving changes in receptor levels on postsynaptic membrane. Synaptic scaling is controlled on transcriptional level. The aim of our study was to investigate which transcription factors play a role in the regulation of homeostatic synaptic plasticity. To modulate synaptic activity, we used global pharmacological treatment of hippocampal neuronal cultures with gabazine (GABAA antagonist) resulting in chronic network hyper-activation. We showed, that treatment of neurons with gabazine results in the induction of Serum Response Factor (SRF)- driven transcription. In addition, Arc (Activity-regulated cytoskeleton-association protein), one of the major regulator of synaptic scaling, was expressed at a higher level during over-excitation in vitro. Arc protein production was also significantly up-regulated

after injections of WT but not the SRF KO animals with pentylenetetrazole (PTZ, another GABAA antagonist). Altogether, these results suggest that SRF may play an important role in the regulation of gene expression underlying synaptic scaling.

29. Behavioural correlates of between-subject transfer of emotional information in c57BL/6J mice

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Empathy is often considered to be a human-specific emotion. Growing evidence shows, however, that other species are capable of using emotional information obtained from their conspecifics to adjust their behaviour to environmental challenges. Here we present two behavioral models of transfer of emotional information using the c57BL/6J mouse, the most commonly used background strain, used for development of autism-related mouse models. Both models are based on remote transfer of fear, where Observer animal does not witness the aversive stimulation experienced by Demonstrator mouse, but relies on information obtained from Demonstrator during exposure time immediately following the aversive event. First model uses two unfamiliar individuals which are allowed to interact with one another across a cage divider. The other uses animals which have been housed together for 4 weeks and are allowed to interact freely upon return of Demonstrator to the home cage. Both models show differences between the behaviour of Observers exposed to non-stressed and stressed Demonstrators. The first shows behavioral withdrawal and elevated stress response of the Observer (more time spent away from the cage divider and increased production of boli), while the second shows much more approaching behaviour (increased following, sniffing of head and anogenital regions of Demonstrator).

30. Stimulation of the central nucleus of the amygdala influences corticosterone level and locomotor activity in the new environment in rats

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The amygdala is a limbic structure involved in mood regulation, associative learning, fear conditioning and modulation of cognitive functions. This structure also participates in neuroendocrine response to stressful stimuli and today is one of the most heavily studied brain areas. In our previous study, we found that central nucleus of the amygdala (CeAm) also influences immune function. In the present study, we investigated the influence of 14-day electrical stimulation of the CeA on corticosteron level (COR; determined by radioimmunoassay) and locomotor activity in the new environment (measured in the Opto Varimex Minor actometer). Male Wistar rats implanted with stimulating electrodes into the CeA were divided into groups: CeA 14–day electrical stimulation (n=20) and CeA sham (n=18). Current intensity (70-120 μA; 50Hz) was raised incrementally in 30-s trials until behavioral reaction was observed. Electrical stimulation of the CeA caused augmentation of COR level ($p=0.001$) correlated with an increase in the average number of movements in horizontal and vertical plane ($p=0.001$) imitating escape behavior. We suggest the hormonal response to of the CeA stimulation plays a crucial role in the regulation of the behavioral response. Supported by The National Science Centre, grant number: NN303819040.

31. Cognitive judgement bias in the amphetamine-induced model of mania in rats

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Chronic amphetamine administration is a frequently used, however unspecific, model of mania in rodents. In our study, we investigated whether chronic administration of d-amphetamine may produce in rats, also more specific, affective symptoms of mania, such as the hyperoptimistic cognitive judgement bias. To accomplish this goal, after initial behavioural training, 2 groups of rats were subjected either to 3 weeks of chronic d-amphetamine treatment or physiological saline injections. Before, during and after the treatment the animals were tested with ambiguous-cue interpretation paradigm. We report that chronic amphetamine administration does not produce optimistic judgement bias in rats. This work was supported by Polish Ministry of Science and Higher Education (Research grant: Iuventus Plus IP2011047271 to RR) and the statutory funds of the Institute of Pharmacology Polish Academy of Sciences

32. Types of social contacts coordinate behavior during competition

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Social hierarchies tend to be quite stable over long period of time but the insertion of new individuals can have important consequences for future behavioural interactions and fitness. The aim of our study was to analyze if rats' behavioural indices registered in a social competition test depending on a type of their social contacts. In one type of contacts animals were housed in pair in the same cage (LT group). In a second type of contacts rats were housed in different cages and met together only during competition test (ST group). Control group was represented by animals which were taken into experiment separately. During test rats competed in pairs for sugar pellets The number of pellets consumed by each rat was recorded. Rats with higher number of consumed pellets were identified as dominants, those with the lower as subdominants. Analysis showed that number of interactions between rats from LT group was higher than in ST group. The rats from LT group presented also higher locomotor activity in comparison with animals from ST group. The obtained data indicate that competitive behaviour of rats depends on the type of familiarisation.

33. How does chemical signals inform us about brain asymmetry?

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In various human psychopathologies dysfunction of brain asymmetry were shown to be involved, what is probably due to disturbances in asymmetry of neurotransmitter systems. In the present study we compared the dopaminergic system activity in the central part of amygdala (CPA) of left and right hemisphere in rats exposed to one of the stages of the elevated plus maze test (EPM) i.e., without EPM (wEPM), before EPM (bEPM) and after EPM (aEPM). The rats of group bEPM were placed in the EPM for 5 seconds. Group aEPM included animals subjected to 5-min lasting EPM. The concentration of dopamine (DA) and its metabolites - 3,4-dihydroxyphenylacetic acid (DOPAC) and homovanilic acid (HVA) were determined in the CPA using high-performance liquid chromatography with electrochemical detection. Statistical analysis revealed that concentration of DA in the right CPA was reduced in comparison with the contralateral part of examined brain area of wEPM and bEPM rats. Moreover, the exposition of rats on the first seconds of EPM was accompanied by significant increase in index of metabolism of DA, measured by DOPAC/DA and HVA/DA ratio in the right CPA. Our findings confirmed statement about considerable involvement of right hemisphere in the central regulation of stress reaction.

34. How does caffeine affect social behaviour of workers of the red wood ant Formica polyctena?

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Caffeine, one of the methylxanthines, is commonly used as a neurostimulant to increase behavioural activity in humans. While caffeine is known to act as inhibitor of insect development and insecticide, its impact on behavior remains relatively little known. Effects of chronic caffeine administration include changes in locomotory activity patterns in Drosophila melanogaster and disruption of it's daily rhythm. Caffeine was recently shown to "boost memory of honeybee Apis mellifera, both on behavioural and neurobiological level. We examined how chronic oral caffeine treatment modificate behaviour of the red wood ant Formica polyctena during nestmate reunion tests. Ants were fed 0ppm, 25ppm and 200 ppm caffeine diluted in aqueous sugar solution for 14 days. We induced social isolation, after which ants were placed in two combined test-tubes with cotton plugs. We found, that caffeine exerted a suppressing effect on resting behavior of workers. It also stimulated their exploratory behavior, such as contacts with cotton plug or test-tube. What is the most important, we found, that caffeine exerted self-grooming and social contacts with the nestmate, such as allogrooming and trophallaxis. Effects were stronger with ants, which were isolated for two days.

NEUROPSYCHIATRY

35. Repeated cocaine treatment during adolescence induces long-term neuroplastic changes in the medial prefrontal cortex of adult rats

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It is well known that adolescence represents a factor of vulnerability for drug abuse although the molecular correlates of such increased sensitivity remain elusive. Adolescent rats were exposed to cocaine (20 mg/kg), from postnatal day (PND) 28 to PND 42, and the animals were sacrificed at PND 90. Molecular analyses were carried out in the medial prefrontal cortex (mPFC) using Real Time-PCR and western blot techniques. We found enhanced BDNF mRNA and protein levels in the mPFC of PND 90 rats exposed to cocaine during adolescence. Such effect resulted in the activation of the trkB/AKT pathway which, through increased S6 kinase phosphorylation, increased Activity Regulated Cytoskeletal-associated protein (Arc) in the nucleus and the crude synaptosomal fraction. We also analyzed the inhibitory and degradative pathways regulating Arc expression and found reduced FMR1 and Ube3a mRNA levels as well as increased GRM5 mRNA levels. The up-regulation of Arc protein led, in turn, to reduced AMPA GluA1 mRNA and protein levels, indicating that long-term abstinence alters markers of synaptic plasticity thorugh different, but converging, mechanisms. Our findings demonstrate that abstinence from developmental exposure to cocaine dysregulates BDNF, Arc and AMPA transmission in the mPFC of adult rats.

36. The association between serotonin-related gene polymorphisms (5-HT2A and 5-HTT) and the occurrence of depressive symptoms in obese patients

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The role of serotonin in eating disorders is indisputable, it causes weight loss. It is also known that obese patients often experience depression. The aim of this study was to determine the association between the occurrence of gene polymorphisms: 5-HTT serotonin transporter gene (5-HTTLPR) and the 5-HT2A serotonin receptor gene and the presence of depressive symptoms in obese patients. The study involved 180 (138 female) patients diagnosed as obese (mean age 40,0±12,9 years; mean BMI 43,7±7,8). Physical examination, metric measurements and genotyping were performed. The intensity of depressive symptoms was measured with Beck Depression Inventory (BDI) and Hamilton Depression Rating Scale (HAM-D). 1) Clinically relevant depressive symptoms were diagnosed in 39% of subjects. 2) Patients with the least advanced obesity presented the lowest values of depressive symptoms intensity (ns.). 3) Small, but not statistically relevant, differences were shown in obesity indicators (but not in depressive symptoms intensity) between 5-HTTLPR polymorphism. 4) In patients with different 5-HT2A gene polymorphisms no significant differences were demonstrated among particular obesity parameters and in depressive symptoms intensity. Almost 40% of subjects experienced depressive symptoms. No statistically relevant association between 5-HT2A and 5-HTT gene polymorphisms and depressive symptoms were found.

37. Evaluation of anxiolytic-like properties of new GABA reuptake inhibitors

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Gamma-aminobutyric acid (GABA) is the major inhibitory neurotransmitter in the mammalian central nervous system. The enhancement of GABAergic neurotransmission exerts anxiolytic and anticonvulsant effects. To determine anxiolytic-like properties of nine new GABA reuptake inhibitors (GAT transporters inhibitors; compounds named GT),

the four-plate test and elevated plus maze test were performed. Tiagabine (inhibitor of GAT1) was a reference compound. The compounds were administered intraperitoneally (suspended in 1% Tween 80) to Swiss Albino mice 1h before each test. In the four-plate test three compounds: GT53 and GT54 at a dose of 30 mg/kg and tiagabine at a dose of 8 mg/kg caused a statistically significant increase in the number of punished crossings by 98,03%, 73,29% and 79,07% respectively. In the elevated plus maze test compounds: GT55, GT57 and GT62 at a dose of 30 mg/kg exerted a statistically significant prolongation of the time spent in open arms (in the range of 42,73%-65,87%) when compared to the control group, yet the action of tiagabine (8 mg/kg) was more potent (189,62% vs. control). The examined compounds presented anxiolytic-like activity that was less pronounced than in case of tiagabine. High affinity for GAT1 seems to determine anxiolytic-like properties. Supported by DEC-2012/05/B/NZ7/02705

38. Alterations in the level of NMDA receptor subunits in the medial prefrontal cortex in neurodevelopmental model of schizophrenia

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NMDA receptor (NMDAR) dysfunction in the medial prefrontal cortex (mPFC) is suggested to be involved in cognitive symptoms observed in schizophrenia. In the present study, the level of NMDAR was determined in the neurodevelopmental model of schizophrenia based on postnatal injections of CGP 37849, a competitive antagonist of NMDAR (1,25 mg/kg on days 1, 3, 6, 9; 2,5 mg/kg on days 12, 15, 18; 5,0 mg/kg on day 21). The levels of NMDAR subunits (NR1, NR2A, NR2B) were analyzed in mPFC membrane fraction in 60-day old rats using Western Blot method. Postnatal CGP injection did not affect the level of NMDAR subunits. However, alterations in NMDAR subunit levels were correlated with fear memory deficit observed in CGP-treated rats in trace, but not delay fear conditioning (TFC or DFC, respectively). NR1 protein level was increased only in TFC in CGP-treated group. However, CGP administration induced the decrease in the level of NR2B subunit in TFC, but the increase in DFC memory retrieval. No changes in NR2A level were observed. The obtain results indicate that changes in levels of NMDAR subunits in mPFC observed in TFC memory retrieval might be involved in impairment of fear memory induced by postnatal blockade of NMDAR.

39. Studies on hypothalamic adult neurogenesis in rats treated with selected antipsychotics

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Among many factors influencing adult neurogenesis, pharmacological modulation have been broadly studied. It is proven that neuroleptics (antipsychotics) positively affect new neuron formation taking place in canonical sites – subgranular zone of the hippocampal dentate gyrus and subventricular zone of the lateral ventricles. Latest findings suggest, that adult neurogenesis occurs also in several additional regions, for example hypothalamus, amygdala, neocortex, striatum and spinal cord. As hypothalamus is considered as an important target of neuroleptics, hypothesis can be made, that these substances are able to modulate local neural proliferation. Experiments were carried out on adult male rats injected for 28 days by three neuroleptics: olanzapine, chlorpromazine and haloperidol. Immunohistochemistry was used to determine expression of cell proliferation and differentiation markers (Ki-67,DCX, nestin, NeuN) which may inform about potential drug influence on adult neurogenesis at the level of hypothalamus. It was proven that after olanzapine and chlorpromazine administration there was a significant increase of DCX expression and cell proliferation in hypothalamus. The opposite effect was observed after haloperidol. The results confirm existence of hypothalamic neurogenesis and help to better understand the neuroleptics mechanism of action. They can also suggest ways of pharmacomodulation of neurogenesis process which has a potential clinical application.

40. Subdiaphragmatic vagotomy and crowding stress affects hypothalamic COX and NOS response to acute restraint

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Stress response involves activation of hypothalamic-pituitary-adrenal axis and expression of nitric oxide synthase (NOS) and cyclooxygenase (COX) in different brain regions. This study evaluated whether alterations in hypothalamic COX and NOS isoenzymes levels in response to acute restraint are affected by vagotomy and prior crowding stress. Subdiaphragmatic vagotomy or sham surgery was performed 10 days before experimental procedure. Adult male Wistar rats were subjected to crowding stress for 3 days, then exposed to 10 min restraint and decapitated immediately after stress or 1, 2 and 3 hours later. Western blot analyses were performed to determine the level of COX-1, COX-2, nNOS and iNOS in hypothalamus. Acute restraint significantly decreased hypothalamic COX-1 in sham-operated rats but increased COX-1 parallel to decreasing of COX-2 in vagotomized animals. After vagotomy basal nNOS level in hypothalamus was increased compared with sham-operated rats, but nNOS expression was insignificantly affected by restraint. Regardless of vagotomy hypothalamic iNOS level decreased in response to acute restraint. Prior crowding stress moderately intensified COX and NOS response to acute restraint. Results indicate that acute restraint functionally affect hypothalamic COX and NOS systems which appear to be under the influence of the vagus. Crowding stress sensitized COX/NOS response to acute restraint.

41. The impact of chronic antidepressants administration on the insulin receptor adaptors protein in the brain of prenatally stressed rats

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Recent data indicates that there are strong bi-directional links between depression and diabetes. Antidepressant drugs are widely used to eliminate a number of depression syndromes but there has been very little investigation into the relationship between depression treatment and function of insulin receptor and insulin brain signaling. Pregnant Sprague-Dawley rats were submitted to stress sessions- from 14th day of pregnancy until delivery. At 3 months of age, control and prenatally stressed rats were treated with antidepressant drugs (10mg/kg i.p.) for 21 days. RT-PCR and ELISA methodology were applied to investigate the changes of gene and protein expression in the hippocampus and frontal cortex. Our purpose was to find out the effect of chronic treatment with imipramine, fluoxetine and tianeptine on the Shc1 gene and protein expression in the brain structures of prenatally stressed rats. The main finding of our research was that prenatal stress decreased Shc1 protein level in the frontal cortex and hippocampus. Treatment with all antidepressants led to normalization of Shc1 protein level in the hippocampus whereas in the frontal cortex imipramine was the only effective drug. This work was supported by the project Interdisciplinary PhD Studies Molecular sciences for medicine(co-financed by the ESF within the Human Capital Operational Programme).

42. Effect of combined treatment with risperidone and mirtazapine on MK-801-induced deficits in the social interaction test in rats

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Several clinical reports have suggested that the mirtazapine-induced augmentation of risperidone activity may effectively improve the treatment of negative and some cognitive symptoms of schizophrenia. The aim of the present study was to evaluate the effect of mirtazapine and risperidone, given separately or jointly, on the MK-801-induced deficits in a social interaction test in rats. Mirtazapine (2.5 or 5 mg/kg) and risperidone (0.01 mg/kg) were given 60 and 30 min before MK-801(0.1 mg/kg), respectively. The social interaction of rats was evaluated for 5 min, starting 4 h after MK-801 administration. The obtained results showed that in the social interaction test, MK-801induced deficits in either parameters studied, the number of episodes and time of interactions. Risperidone at a higher dose (0.1 mg/kg) reversed that effect. Co-treatment with an ineffective dose of risperidone (0.01 mg/kg) and mirtazapine (2.5 or 5 mg/kg) reversed the effect of MK-801, while locomotor activity of those rats was not altered in any of the treatment groups. The obtained results suggest that mirtazapine may enhance the antipsychotic-like effect of risperidone in the

animal test modeling some negative symptoms of schizophrenia. Further studies are necessary to elucidate its mechanism of action. This study was financially supported by statutory funds of the Institute of Pharmacology, Polish Academy of Sciences, Kraków, Poland.

43. Carnitine-mimicking drug mildronate protects against haloperidol-induced disturbances in memory and brain protein expression

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Recently, harmful influences on memory after a long-term use of psychotropic drugs, particularly neuroleptics (Breggin, 2011) have been demonstrated. However, etiopathogenetic causes of these influences have not been well clarified. Neurotrophins and enzymes related to cholinergic and glutamatergic systems are considered as critical molecules that maintain synaptic plasticity and memory formation. Mildronate, a carnitine-congener, which previously demonstrated memory-enhancing and protein expression-regulating activities (Klusa et al., 2013), was expected as beneficial protector against alterations caused by haloperidol. Haloperidol-amnesia in rats was modeled by 3-week haloperidol (1 mg/kg, i.p.) administration in rats. Spatial memory was assessed in Barnes maze. The expression of hippocampal and striatal BDNF, AChE and GAD67 were analysed by WB (Western blot) and IHC (immunohistochemically). Mildronate (50 mg/kg) was administered per se and in haloperidol-treated rats. Haloperidol treatment impaired spatial memory, that coincided with the significantly reduced hippocampal BDNF and AChE expression (WB), while in the striatal tissue (ICH) the number of BDNF-, AChE- and GAD67-positive cells were considerably increased. Mildronate normalized memory and all altered biomarkers. Haloperidol caused deteriorating influence on protein expression and memory, that was protected by mildronate which effectiveness in the combined therapy with antipsychotics in schizophrenia patients is suggested.

44. Antipsychotic properties of newly synthesized analogues of arypiprazole

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The aim of this study was to examine a receptor binding profile and antipsychotic properties of 7 newly synthesized indoloamine derivatives, analogues of arypiprazole. Radioreceptor binding assays were carried out to assess affinity of studied compounds to monoaminergic receptors. D-amphetamine (AMP)- and MK-801-induced locomotor hyperactivity in mice paradigms were conducted to evaluate potential antipsychotic properties. All of the tested compounds display a significant affinity to D2, 5-HT1A, 5-HT2A, 5-HT6 and 5-HT7 receptors (Ki < 100 nM), with the exception of compound ADN-1321 that has no affinity for 5-HT7 ones. ADN-1336 (2.5 mg/kg), ADN-1320 (5 mg/kg) and ADN-1319 (20 mg/kg) attenuated the AMP-induced hyperactivity at minimum effective doses, that had no influence on spontaneous locomotor activity (by 57%, 57% and 60%, respectively). ADN-1321 (40 mg/kg) and ADN-1322 (10 mg/kg) produced non-specific antipsychotic effect. Only AND-1319 (10 mg/kg) and 1320 (1.25 mg/kg) significantly decreased MK-801-induced hyperactivity by 43% and 56 % in mice, respectively, at minimum effective doses, that had no influence on spontaneous locomotor activity. ADN-1321 (40 mg/kg) and ADN-1307 (5 mg/kg) evoked non-specific antipsychotic activity in that test. The obtained results suggest that the tested compounds possess potential antipsychotic activity and may find an application in the treatment of schizophrenia.

45. Effects of acute and repeated administration of tianeptine on the level of endocannabinoids and endocannabinoid-like molecules in different rat brain structures

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In recent years there has been highlighted the potential participation of the endocannabinoid system in the pathogenesis of depression and in the action of antidepressants. The aim of this study was to investigate the effect of the clinically effective atypical antidepressant - tianeptine (TIA, 10 mg/kg), on the level of endocannabinoids anandamide (AEA) and 2-arachidonoylglycerol (2-AG) and of endocannabinoid-like molecules palmitoylethanolamide

(PEA) and oleoylethanolamide (OEA) in different rat brain structures. Administered acutely TIA resulted in decreased levels of PEA in the hippocampus. The chronic TIA administration increased the AEA levels in the hippocampus and dorsal striatum and the 2-AG levels in the frontal cortex and dorsal striatum as well as a decrease of PEA and OEA in the hippocampus and prefrontal cortex was reported. Tianeptine-free period (10-day washout period) evoked enhancement in the accumbal OEA and PEA concentration and reduction in the cortical 2-AG level. Our data suggest the engagement of the endocannabinoid system in the effects of TIA, but the more detailed explanation of this mechanism requires further investigations.

46. Exposure to enriched environment blocks the decrease in H3K9ac level induced by prenatal MAM administration in mPFC of rats

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Schizophrenia is a neurodevelopmental disease with the interface of genetic and environmental risk factors regulated by epigenetic mechanisms. Our previous study showed that prenatal administration of methylazoxymetanol (MAM, 22mg/kg, ip, E17), modeling neurodevelopmental aspects of schizophrenia, induced the decrease in the level of acetylation form of histone H3 at lysine 9 (H3K9Ac) in the medial prefrontal cortex (mPFC) during rat postnatal life. In the present study we investigated, whether the exposure to enriched environment (EE) during adolescence (23rd to 29th day) or early adulthood (63rd to 69th day) of postnatal life is able to modulate MAM-induced alternations in H3K9ac level at 30- (P30) or 70-day-old-rats (P70), respectively. It was found that exposure to EE during adolescence prevented the decrease in H3K9ac proteins induced by MAM at P30, which might be connected with decrease in histone deacetylase HDAC1 level evoked by EE in MAM group. Moreover, exposure to EE during adulthood reversed the decrease in H3K9ac level induced by MAM at P70, but the mechanism might not be related to alterations in the deacetylase levels. The obtained results indicate that exposure to EE influences the acetylation of H3K9 and affects MAM-induced decrease in H3K9ac level in pre- and post-puberty.

47. Effect of caffeine and selective antagonists of adenosine A1 and A2A receptors on DA and 5-HT release induced by methamphetamine and 3,4-methylenedioxymethamphetamine in the mouse striatum

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MDMA (3,4-methylenedioxymethamphetamine), recreationally used psychostimulant is the main component of ecstasy tablets. MDMA and caffeine (CAF) are often used in combination to gain stronger stimulatory effect. Pharmacological mechanism of CAF is based on blockade of adenosine A1 and A2A receptors. Our earlier data have shown that CAF (10 mg/kg) given together with MDMA (20 or 40 mg/kg) potentiated stimulatory effect of MDMA on extracellular level of dopamine (DA) and serotonin (5-HT) in the mouse striatum. In a present study we aimed to understand if potentiating effect of CAF on DA and 5-HT release produced by MDMA occurs via blockade of adenosine A1 and A2A receptors. Mice were treated with selective adenosine A1 and A2A receptor antagonists, DPCPX and KW-60002 (1.25 - 2.5 mg/kg, respectively) alone or in combination with MDMA and the release of DA and 5-HT was assayed using microdialysis in freely moving mice. The extracellular level of DA and 5-HT was determined by HPLC with coulochemical detection. Both adenosine A1 and A2A receptor antagonists enhanced DA and 5-HT release increased by MDMA. It can be speculated that CAF effect on DA and 5-HT release may be caused by blockade of A1 and A2A adenosine receptors.

48. Impact of prenatal stress on the IGF-1 and IGFBP's concentarion in the olfactory bulbs of adult rats offspring

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Theories regarding the origins of depression suggest that prenatal stress impacts embryonic development of the nervous system and alters the behavior of affected individuals in later life. Stress procedure can affect the developing brain through changes in the levels of neurotrophic factors (e.g. IGF-1), which modulate neurogenesis, cell differentiation, and synaptogenesis. The aim of present study was to examine whether prenatal stress influence the IGF-1 system in the olfactory bulbs of adult rats offspring. Pregnant Sprague-Dawley rats were subjected to stress sessions from 14th day of pregnancy until the delivery. Control pregnant females were left undisturbed. At 3 months of

age, rats were tested for behavioral changes in the sucrose preference test. Animals were sacrificed and the olfactory bulbs were rapidly dissected. Levels of IGF-1 and IGFBPs were determined in tissue homogenates by ELISA assays. We found that prenatally stressed male rats consumed significantly less sweetened water revealing anhedonic-like behavior. Moreover, a significant reduction in the amount of IGF-1 protein level and dysregulation in IGFBPs network in the olfactory bulbs of stressed animals was detected. Our study confirmed that prenatal stress causes long-lasting behavioral alterations. Reduction of IGF-1 level and changes in IGFBPs network may lead to observed behavioral changes.

49. May repeated mild stress preconditioning alter the effect of asenapine on the FOS expression in neurons of frontal brain areas?

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Asenapine (ASE) is a novel atypical antipsychotic developed for treatment of schizophrenia. Main brain areas of its effects are striatum, septum, and prefrontal cortex. This study was aimed to reveal whether preconditioning with an unpredictable variable mild stress lasting 21 days may alter effect of asenapine treatment on Fos expression in mentioned areas. Stress paradigms included: restraint (in plastic tubes), social isolation and crowding (in home cage), swimming (in glass cylinders), and cold (in cold room at 4°C). On the 22nd day rats received single injection of vehicle (saline 300 µl/per rat s.c.) or ASE (0.3 mg/kg s.c.). Animals were sacrificed 90 min after drugs injection. Fos protein was visualized by ABC immunohistochemistry with nickel intensification of endprodukt. Four groups of animals were evaluated: controls-vehicle (CV), controls-ASE (CA), stressed-vehicle (SV), and stressed-ASE (SA). Immunolabeling showed low Fos expression in CV and SV, while intensive Fos immunolabeling was observed in CA and SA groups of animals in each structure investigated. Significant differences in Fos response were found not only between the individual structures, but also within same structure. Stress preconditioning had no significant effect on spatial distribution or quantity of Fos profiles in the structures investigated. (Supported by 2/0069/12 VEGA grand).

50. Pro-oxidant action of imipramine induced antioxidant enzyme activites

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Imipramine is a dibenzazepine-derived tricyclic antidepressant which acts by inhibition of serotonin and norepinephrine reuptake within synaptic clefts in the central nervous system. Imipramine is indicated for therapy of depression and is widely used, more than 1 million prescriptions being filled yearly. Imipramine is also used for childhood enuresis. Liver test abnormalities have been reported to occur in up to 20% of patients on long-term therapy with imipramine. The mechanism by which imipramine causes liver test abnormalities is not known but probably oxidative stress is involved in this process. Oxidative stress occurs when the synthesis of oxygen free radicals exceeds the body's ability to offset them with antioxidant molecules. In present study we examined the effect of chronic imipramine treatment on oxidative stress in liver estimated by levels of reactive oxygen species (ROS), malondialdehyde (MDA), non-protein sulfhydryl groups (NPSH) and sulfane sulfur (SS) groups as well as by catalase activity (CAT), glutathione peroxidase activity (GPx), superoxidase dismutase activity (SOD). Chronic imipramine administration were associated with increase of ROS level and lipid peroxidation as well as with enhancing activities of key antioxidant enzymes such as CAT and GPx and with increase of NPSH level. This work was supported by grant POIG.01.01.02-12-004/09-00

51. Impact of prenatal stress procedure on the expression of MCP-1 and CCR2 receptor system in brain of adult offspring

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Recently a lot of attention is paid to the role of chemokines in brain neuromodulation. Monocyte chemoattractant protein (MCP-1/CCL2) is a chemokine involved in communication between damaged neurons and surrounding glial cells. Moreover, MCP-1 plays a crucial role in the brain inflammatory regulation. The main purpose of our study was to

determine whether prenatal stress - an animal model of depression - provokes changes in CCL2-CCR2 system. Pregnant Sprague- Dawley rats were subjected daily to 3 stress sessions from 14th day of pregnancy until delivery. Control pregnant females were left undisturbed in their homecages. At 3 months of age male offspring from both group was tested behaviorally in order to verify used model of depression. 48 hours later animals were decapitated and the hippocampi and frontal cortices were rapidly dissected out. mRNA and protein levels of CCL2 and CCR2 were determined. Behavioral tests revealed depression-like behavior in prenatally stressed animals. Furthermore behavioral changes were correlated with modifications in mRNA and protein levels of CCL2 and CCR2 in both brain structures. In summary, it may be suggested that disturbances, caused by prenatal stress procedure, in CCL2-CCR2 system can be involved in pathological processes leading to development of depressive disorders.

52. Antipsychotic activity of positive allosteric modulator of the mGlu4 receptor, Lu AF21934

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Preclinical studies exploiting the modulation of the glutamatergic system in brain via metabotropic glutamate (mGlu) receptors suggest the potential therapeutic utility of this biology. Lu AF21934, a positive allosteric modulator of the mGlu4 receptor, was previously shown to reverse behavioral phenotypes in animal models thought to mimic positive, negative and cognitive symptoms of schizophrenia. To begin elucidating the brain circuitry involved in mGlu4 receptor pharmacology and add mechanistic support to Lu AF21934-induced phenotypic responses, the potential involvement of 5-HT1A receptors in these antipsychotic-like effects was explored. The tests used were: MK-801-induced hyperactivity, 2,5-dimethoxy-4-iodoamphetamine (DOI)-induced head twitches in mice, MK-801-induced disruptions of social interactions, novel object recognition, spatial delayed alteration test. Effects of Lu AF21934 were inhibited by administration of the selective 5-HT1A receptor antagonist WAY100635 (0.1 mg/kg). That inhibition was observed across all models used. Moreover, the concomitant administration of sub-effective doses of Lu AF21934 and asub-effective dose of the selective 5-HT1A receptor agonist tool compound (R)-(+)-8-hydroxy-DPAT hydrobromide (0.01 mg/kg) induced antipsychotic-like effect in all the procedures used. The actions of Lu AF21934 are 5-HT1A receptor-dependent. Activation of the mGlu4 receptor may be a promising mechanism for the development of novel antipsychotic drugs, efficacious towards all schizophrenia symptoms.

53. Prenatal stress decreases the concentration of glucagon-like peptide-1 receptors in the hypothalamus

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Recent findings indicate that disturbed brain glucose metabolism may play a role in the pathogenesis of depression. Insulin and glucagon-like peptides (GLPs) are involved in the regulation of peripheral glucose metabolism, however their central role is so far poorly understood. The aim of the present study was to investigate the effect of prenatal stress (an animal model of depression) on the amount of GLP-1 and its receptor in selected brain structures. Prenatal stress model of depression was obtained and verified as described earlier (Budziszewska et al., 2010). A part of prenatally stressed male rats was subjected to immobility stress while other animals received glucose (1 g/kg, oral). After isolation of brain structures, levels of GLP-1 and its receptor were measured using specific ELISA kits. Prenatally stressed rats were characterized by significantly higher immobility time in Porsolt test. Although prenatal stress had no effect on GLP-1 concentrations in the examined brain structures, it significantly decreased level of GLP-1 receptor in the hypothalamus. Obtained results suggest that attenuated central incretin hormone signaling may contribute to metabolic and synaptic plasticity disturbances, evident in depression. This work was supported by the Operating Program of Innovative Economy 2007-2013, grant No. POIG.01.01.02-12-004/09

54. Chronic fluoxetine treatment decreases cognitive abilities and synaptic plasticity in wild type mice

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Fluoxetine, a selective serotonine reuptake inhibitor, is commonly used to treat different psychiatric disorders. The available data show that fluoxetine has limited side effects and that it may improve patient\'s cognitive abilities. However, the mechanisms by which fluoxetine affects cognitive processes are largely unknown. Since we have

previously shown that MMP-9 (matrix metaloproteinase 9, an enzyme involved in synaptic plasticity) knock-out mice are impaired in appetitively motivated discrimination learning in the IntelliCage, in presented study we investigated the effects of the long-term fluoxetine treatment on learning in this behavioral paradigm. Before the behavioral training MMP-9 knock-out and wild-type mice were treated with fluoxetine or saline for 41 days. After this treatment we observed significant impairment of reward-motivated discrimination learning in wild-type mice and a slight improvement in MMP-9 knock-outs. As it was established that appetitively motivated discrimination learning depends on MMP-9 activity in the central amygdala, we also assessed fluoxetine influence on dendritic spine formation in this structure. Interestingly, observed behavioral deficits were accompanied by changes in morphology of dendritic spines in the central amygdala. The obtained results suggest that chronic fluoxetine treatment results in deterioration of reward-motivated discrimination learning in wild-type mice affecting neuronal plasticity in the central amygdala.

55. Changes in the level of endocannabinoids after acute and repeated administration of imipramine with simultaneous blockade of CB1 receptors in different rat brain structures

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The role of the endocannabinoid system in the pathogenesis of depression and in the action of antidepressants has been highlighted. The aim of this study was to investigate the effect of the imipramine (IMI, 15 mg/kg), on the level of endocannabinoids anandamide (AEA) and 2-arachidonoylglycerol (2-AG) with using simultaneous blockade of CB1 receptors by a selective antagonist AM251 (1 mg/kg) in different rat brain structures. Administered acutely AM251 reversed the effect of acute administration of IMI on the AEA levels in the frontal cortex and hippocampus (decreased or increased, respectively) and on the 2-AG levels in the cerebellum and corticolimbic structures (decreased or increased, respectively). The chronic CB1 receptor blockade restored to the basic levels of the increased AEA levels in the hippocampus and dorsal striatum. The increased 2-AG levels in the frontal cortex and dorsal striatum or decreased 2-AG levels in the hippocampus and cerebellum after chronic IMI treatment were restored to the basic levels after simultaneous administration of AM251. Our data suggest the engagement of the CB1 receptors in the effects of IMI. This study was supported by the research grant UMO-2012/05/B/NZ7/02589 from the National Science Centre, Kraków, Poland.

56. The level of glutamate transporters: xc- and EAAT2 in selected brain structures in animals who underwent phenotypic differentation in conditioned place preference test with cocaine

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Cocaine-addiction studies prove the phenotypic vulnerability to addiction development. Moreover, literature data indicate that decreased activity of glutamate transporters: EAAT2 and xc- generated in animals by cocaine simplify craving and relapse to addiction. On the basis of this reports, we aimed to investigate the xc- and EAAT2 level in addiction-vulnerable and in addiction-resistant animals brains. For this purpose, male Wistar rats (260-340g) underwent a 10-day conditioned place preference with cocaine (15 mg/kg, ip) after which they were divided in addiction-vulnerable and addiction-resistant animals. After immediate decapitation, xc- and EAAT2 levels were determined using Western blot. Data were analyzed using one-way ANOVA followed by the Bonferroni test. The results showed no decrease in the level of xc- and EAAT2 in addiction-vulnerable group. Interestingly, we found a statistically significant increase in the EAAT2 and xc- level in prefrontal cortex and enhanced level of EAAT2 in nucleus accumbens in addiction-resistant animals. In conclusion, our findings indicate that at this stage of addiction (no abstinence period) the level of xc- and EAAT2 were not decreased in addicted animals in this model, but the xc- and EAAT2 appear to play a possible role in the mechanism of resistance for the development of cocaine addiction.

57. Study of neurodegenerative action of N-benzylpiperazine – a model compound from the group of "legal highs

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N-benzylpiperazine (BZP) – a model compound from the "designer drugs of abuse belongs to central nervous system

psychostimulants. Effects of BZP are defined as 10-times weaker than d-amphetamines, while mechanism of action is compared to Ecstasy (MDMA). Aim: Due to reports of neurotoxicity of this substance, an attempt to explain its apoptotic effect on glial cancer cells, LN-18, was made. Methods: Apoptotic effects such as: cytotoxicity through an evaluation of LDH released into culture medium, changes in mitochondrial membrane potential ($\Delta\psi_m$) and generation of reactive oxygen species (ROS) using flow cytometry, changes in ATP level and caspase-3 activity using luminescent and fluorescent methods and the increasing of oxidative DNA damage marker (8-OHdG) by ELISA were analyzed in cells incubated with BZP for 24 h. Results: the highest used concentration of BZP (300 □g/mL) in the cell line disturbed mitochondrial function through statistically significant changes in decreased ATP and increased ROS production, increased mitochondrial membrane potential as well as causing activation of caspase-3 and DNA oxidative damage probably through ROS activity. Conclusions: The results may indicate that BZP in high doses induces apoptosis in LN-18 cells through disrupting mitochondrial function, which could indicate the neurodegenerative properties of this drug. Financial support from the Interdisciplinary PhD Studies project "Molecular sciences for medicine (co-financed by the European Social Fund within the Human Capital Operational Programme).

58. Traits "pessimism" and "optimism" are associated with different levels of motivation in rats

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Present study has been designed to investigate whether traits optimism/pessimism are associated with different levels of motivation in laboratory animals. For this, the natural propensity of rats to interpret environmental stimuli in a positive or negative manner has been established using a number of ambiguous-cue interpretation tests. We isolated two groups of animals that significantly and persistently differed in their interpretation of the ambiguous-cue over time: the "optimists and "pessimist. To investigate purported differences in the level of motivation between "optimisms and "pessimists we used an operant procedure known as the progressive ratio schedule of reinforcement. In this task, subjects are required to make an increasing number of operant responses for each successive reward. The number of responses made to obtain the last reward, termed the breakpoint, serves as an index of motivation. For the first time we demonstrate that traits optimism" and pessimism" are associated with different levels of motivation in laboratory animals. This work was supported by the National Science Centre (Research grant: Sonata bis dec-2012/07/E/NZ4/00196) and the statutory funds of the Institute of Pharmacology Polish Academy of Sciences.

59. Cognitive judgement bias is a stable and enduring behavioural trait in rats

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In humans, cognitive judgement bias (CJB) has both; enduring trait and transient state components. Present study has been designed to investigate whether CJB can be considered as an enduring behavioural trait also in animals. For this, the natural propensity of rats to interpret environmental stimuli in a positive or negative manner has been established using the ambiguous-cue interpretation (ACI) test. In this test, the rats are trained to press one lever in response to one tone to receive a reward and to press another lever in answer to a different tone to avoid punishment. Cognitive judgement bias is than tested by measuring the pattern of animals' responses to a tone of intermediate frequency (ambiguous-cue). On the basis of a number of ACI tests, we isolated two groups of animals that significantly and persistently differed in their interpretation of the ambiguous-cue over time. This difference turned out to be stable and enduring. We demonstrate that in rats, similar to humans, the valence of CJB may be considered as a behavioural trait. This work was supported by the National Science Centre (Research grant: Sonata bis dec-2012/07/E/NZ4/00196) and the statutory funds of the Institute of Pharmacology Polish Academy of Sciences.

VISUAL PERCEPTION & COGNITIVE PROCESSES

60. Endogenous and exogenous cuing of attention in rapid serial visual presentation task. The consequences for the left visual field advantage

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When two streams of stimuli are rapidly presented left and right, the second target (T2) is better identified in the left (LVF) than in the right visual field (RVF). This asymmetry may reveal easier voluntary allocation of attention to the LVF or easier involuntary attraction of attention by targets events to the LVF. In Study 1 explicit information indicated the target location, and in Study 2 the visual cue shortly before T2 onset exogenously attracted attention to valid or invalid location. If those attentional mechanisms contribute to the LVF advantage, then endogenous right-T2 will improve more then left-T2. In turn, invalid cue should particularly impair the identification of right-T2, because attention engaged first to the LVF will be less effectively shifted to the RVF. These predictions were confirmed: Valid cue decreased and invalid cue increased the asymmetry by influencing right-T2 more than left-T2. ERPs analysis revealed that the cue elicited larger and more prolonged negativity when it was valid, confirming that attention was first attracted by the cue and then redirected towards T2. Both, cue- and T2-evoked negativity was earlier when evoked by stimuli in the LVF suggesting the predisposition of the right hemisphere in orienting of attention.

61. Does P3 reflect a link between perception and action? Evidence from the guessing task

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It has been proposed that the P3b component of event-related EEG potentials reflects a process of activating relevant stimulus-response links when perceiving the corresponding stimulus. However, it has often been shown that outcome stimuli in guessing tasks, though not requiring any response, nevertheless still evoke large P3bs. Thus, in the present study, we tested the hypothesis that the P3b evoked by the guessed stimuli does, in fact, reflect links from stimuli to actions (though not reactions), namely to the guess actions preceding the outcome stimuli. Sixteen participants were asked to predict occurrence of two alternative stimuli, one frequent and one rare. The rare one was expected to evoke a large feedback-P3 (a P3 oddball effect). If the frequency of guess-to-outcome relations is decisive, rather than the frequency of outcome stimuli per se, then large P3b\'s should also be evoked by incorrectly predicted frequent stimuli. This was indeed the case. The results suggest that P3b amplitude is a function of the frequency of stimulus-action links, rather than of the frequency of stimuli only, thereby supporting the bridge hypothesis of P3b's function.

62. Spatial-numerical association observed for vulgar but not for decimal fractions

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Brain representations of numbers are spatially organized along the mental number line. The example of this spatial-numerical relationship is the SNARC (Spatial Numerical Association of Response Codes) effect. It refers to the faster responses with the left than right hand to low magnitude numbers and vice versa to high magnitude ones. We investigated the question whether the SNARC effect is related to the number magnitude of fractions (both vulgar and decimal). During control blocks participants responded if the number magnitude of displayed fraction was lower or higher than the reference magnitude. In experimental blocks the number magnitude of presented fractions was task-irrelevant and the participants were asked to respond to their colors. 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 demonstrated the interaction between congruency and magnitude, but no SNARC effect. It was observed only in case of high number magnitude of fractions, however not in the case of decimal ones. Moreover, this results pattern was obtained only in the group of participants who were highly skilled in a magnitudes comparison task, what suggests the role of experience in the spatial-numerical association development.

63. P300 as a marker of solving the trade-off between exploration and exploitation in value-based decision-making

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Value-based decision making often involves choosing between different alternatives characterized by multiple attributes. One of the typical problems connected with this type of decisions is whether we have enough information to choose the best option or should we seek for more. We assumed that this problem is an example of solving trade-off between exploration and exploitation. Potential neural mechanism responsible for solving this trade-off is Locus Coeruleus-Norepinephrine system (LC-NE). LC-NE system operates in two modes: the "phasic" LC mode is hypothesized to drive exploitation of the environment, whereas the "tonic" mode induces exploration of different opportunities. The main aim of presented study was to determine if P300 differentiates between decisions to search for more cues (exploration) and decision to finish this process and choose one of the alternatives (exploitation). 18 participants conducted probabilistic inference task in which they had to infer which of two options was better on the basis of sequential acquisition of cues. The results show that P300 amplitude is larger in reaction to last cues revealed before the final decision in comparison to the penultimate ones, indicating that this component of event-related potential could be the marker of switching between exploratory and exploitative behavior.

64. Space-positional and pure-motion SRC effects may be underlined by different functional mechanisms: further evidence from distributional RT analysis

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Our previous research on the space-positional stimulus response correspondence (SRC) and pure-motion SRC effects with the use of a reaction time (RT) distribution analysis suggested that different mechanisms may underlie these effects. Present study, explored this issue. In the first experiment, both SRC effects were pitted against each other in one visuo-motor task. It appeared that both effects did not affect each other, which might indicate the relation of independence between them. Furthermore, the patterns of RT distribution functions for both effects were different in shapes demonstrating that space-positional SRC effect decreased with longer RTs while the pure-motion SRC effect increased with longer RTs. In the second experiment, we examined whether adding a cognitive task (decision about stimulus location and motion) to the visuo-motor task from the first experiment resulted in the impairment of the pure-motion SRC effect, while the space-positional SRC effect remained intact. This allowed for verification of the claim that pure-motion SRC effect is based on more cognitive mechanisms than the space-positional SRC effect. Present study brings more evidence in support to the idea that different mechanisms govern these two SRC effects. The study results contribute also to the discussion about neural correlates of the SRC phenomena.

65. Induced inter-ocular suppression reflected in evoked corical oscilations

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In normal humans, binocular sensitivity has been shown to be superior to monocular sensitivity. Similarly, cortical visual evoked potentials evoked by binocular stimulation are generally larger in amplitude than those evoked by monocular stimulation - binocular summation or facilitation phenomenon. As mechanism of physiological binocular rivarly is largely explored, thus neuronal processes related to pathological inter-ocular suppresion found in strabismic and anisometropic subjects, are still hardly understood. The aim of the study was to explore cortical oscillations related to inter-ocular suppression compared with normal binocular viewing. Using multichannel EEG and time-frequency analysis, interaction between different brain areas related to binocular viewing, could be indicated. Twelve young subjects with corrected refractive errors and induced inter-ocular suppression were examined. Cortical activity was measured with 64 channels (Quick Amp). Reversed pattern checkerboard (box size 15') was presented with 0.6 Hz frequency. Three different visual conditions

(dominant eye (DE), nondominant eye (NDE) and both eyes (BE)) were tested in two different forms: no-suppresion (NS) and induced inter-ocular suppression (IS). For exploring evoked brain oscillations wavelet transform (Morlet Complex) was performed on averaged trials what gave information about evoked rhythms (phased/coherent oscillations). Binocular viewing induced increased delta-power compared to monocular viewing, and it was evident in 50-250 ms post-stimulus. This effect was not dependant on suppression condition. In early phases of processing (50-200 ms post-stimulus), no effect of binocular facilitation and no effect of inter-ocular suppression was found in alpha-band. But in later processing stage (200-250 ms post-stimulus), significant inhibition of occipital alpha-power was observed in the IS condition. In beta-band, significant facilitation in occipital area (50-150 ms) was observed for no-suppression (NS) condition, and the lack of facilitation in induced suppression (IS) condition. Increase in gamma-power was found in occipital cortex in 50-100 ms time window for no-suppression (NS) condition, but the lack of facilitation in induced suppression (IS) condition was observed. Normal binocular viewing was related to increase in occipital delta, beta and gamma-power. Inter-ocular suppression evoked inhibition in alpha-band oscillations. No facilitation for induced inter-ocular suppression condition was observed in high frequency rhythms (beta and gamma).

66. JLab - development and validation of new software for visual field diagnosis

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The rapid development of computers during last years provides a lot of new possibilities – one of them is visual field examination based on wide available personal computers and freeware, specialized software. Development and validation of such new software for visual field diagnosis is the main subject of this work. Each newly emerging diagnostic tool must, however, be examined and validated before it goes to new users. Therefore, a validation study was performed using simulated deficit in the temporall part of right eye visual field. The study involved 20 people divided equaly into two groups – one with simulated deficit and the other without it. The main task of both groups was to respond to on-screen points display in different locations and to fixation point changes. Conducted analysis showed significant differences ($F(1, 18) = 44{,}987$; $p=0{,}001$; $\eta 2 = 0{,}714$) between both groups in the level of performence of the procedure for the left part of the visual field indicating the suitability of the software for the diagnosis of visual field deficits. Supported by ERA-NET Neuron grant REVIS.

67. Deficient beta band information flow in ADHD children during attention demanding task

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Attention deficit hyperactivity disorder (ADHD) is a common behavioral diagnosis based on the presence of developmentally inappropriate levels of inattentiveness, overactivity and impulsivity. The aim of the study was to investigate differences in information flow between ADHD children and matched controls. Electroencephalograpic (EEG) data was collected from clinical group aged 11-16 and compared with healthy, age- and sex- matched controls. EEG signal was recorded while the participants performed the Posner's Attention Network Test (ANT). This test combines cue detection (Posner, 1980) with a flanker-type paradigm (Eriksen and Eriksen, 1974) and allows for the behavioral assessment of attention - alerting, orienting, and executive function. Independent Component Analysis (ICA) was performed for every subject, afterwards components were localized using DIPFIT EEGlab plug-in. The obtained dipoles were then clustered according to their position and time-frequency response to the cue. We chose six clusters that maximized the number of participants having dipoles in all chosen clusters. Then for each participant multivariate autoregressive model was fit to the Independent Components that were included in selected clusters and normalized partial directed coherence was computed for the model. We show that cue-evoked parieto-temporal flow in beta band is significantly lower in ADHD participants. This result is discussed in context of current views on attentional networks and the function of beta band oscillations.

68. Does action video game training improve temporal accuracy of information processing? Pilot study on finger tapping task

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Video games training seems to be promising form of enhancing various cognitive capacities. So far mechanism of broad transfer of cognitive improvement reported in many recent studies is not completely understood. The most important dimension shared by all cognitive functions is time, conceptualized as temporal structure appearing in information processing. Aim of the study was to investigate whether action video game training improves temporal information processing (TIP) in the range of hundreds milliseconds. Thirty non-gamer females (19-26 years old) participated in the study. Procedure contained two randomized groups: (1) action video game and (2) non-action video game. TIP in the range of hundreds of milliseconds was assessed using synchronization tapping task. The tapping task consisted of a synchronization phase and a continuation phase, divided into 4 sets of intervals: 500, 700, 1000 and 1500 milliseconds. Action video game players showed better performance in finger tapping task. Accuracy and precision of particular finger tap series seem to be enhanced after this non-specific cognitive training. This project was financially supported by Dean of Faculty of Psychology, University of Social Sciences and Humanities (WP/2013/A/29) and Dean of Faculty of Humanities, Nicolaus Copernicus University.

69. Action video game training influences the temporal information processing in the range of tens of milliseconds

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Numerous interventional studies suggest that there is a causal relationship between action video game training and improvement across a broad range of cognitive tasks – from many aspects of visual attention, decision making, mental rotations to contrast sensitivity. In this study we want to investigate whether cognitive benefits after this kind of cognitive training may be mediated by improvement in temporal information processing (TIP) in the range of tens milliseconds. We used visual inspection time task and auditory temporal-order judgment task as a measures of TIP in the range of tens milliseconds. All subjects (thirty non-gamers) were randomly assigned into one of the two training groups: (1) an action game group and (2) a non-action game one. TIP tasks was performed twice – before and after 10 hours of video game training. We found a greater TIP improvement after action-game training than the control training. Our results suggest that improvement in temporal information processing in the range of tens of milliseconds may underlie general cognitive benefits observed in previous studies using action video game training. This project was financially supported by Dean of Faculty of Psychology, University of Social Sciences and Humanities (WP/2013/A/29) and Dean of Faculty of Humanities, Nicolaus Copernicus University.

70. EEG components of the Social Simon Effect

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Research in social cognitive neuroscience has shown that cognitive processes underlying action planning and control can not be fully explained without taking into account their social context. Previous studies indicate that perceiving another\'s action activates similar representations in an observer\'s action system. These mechanisms can be observed in EEG signal recorded during simple go/no-go task performed alone and with another person. This task performed individually is known as Simon task. The aim of our study was to investigate in more detail EEG components (event-related potentials, ERPs) of go/no-go task which was performed alone (individual condition) and together (group condition). Ten right-handed subjects took part in this study. Both EEG signals and response times were recorded. Comparing specific ERP components in those two different settings indicates significant changes in ERP's.

71. Inhibitory Control in Nonsuicidal Self-Injury: Even-Related Potentials in the Stop-signal Paradigm

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Many authors indicate a relationship of impulsivity and inhibitory control to Nonsuicidal self-injury (Herpertz et al. 1997, Simeon and Favazza 2001, Glenn and Klonsky, 2010). In the present study we investigated inhibitory control in individuals with self-injury and non-self-injurers. We were inspired by a comparative research on self-injury and inhibition control with a stop-signal task (Glenn and Klonsky, 2010). In this study, subjects were asked to distinguish between visual stimuli and respond to them or – when a sound (stop signal) appeared - inhibit their response. The results of this research showed no difference in inhibitory control between the groups. However, neither the electrical activity of the brain nor the impact of negative emotions on inhibitory control was investigated. Therefore in our study we compared the two groups at both levels - a behavioral one (reaction time and number of inhibited responses) and physiological (latency and amplitude of endogenous potential). Additionally, in both groups we investigated the effect of negative emotions on inhibition. The results indicate no differences between groups in the number of inhibited responses. Self-injurers due to experiencing negative emotions increased the number of inhibited responses, which indicates an increase in inhibition control. No such differences were seen in control group.

MEDICAL CASE REPORTS & CLINICAL NEUROSCIENCE

72. Verbal fluency in schizophrenia and bipolar disorder

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Verbal fluency is one of the most useful neuropsychological tests, that assesses memory, speaking and executive functions. In this research we examined Schizophrenia and Bipolar Disorder patients with verbal fluency tests in order to measure their cognitive and language impairments. One-minute Phonological Verbal Fluency Test (PVF) for words starting with the letter K and one-minute Semantic Verbal Fluency Test (SVF) for the category of animals have been used for assessment of 28 Schizophrenia and 12 Bipolar Disorder patients treated with atypical neuroleptics, comparing with 18 healthy Adult Control Group. One-way ANOVA and Tukey\'s Test were used for statistical analyses. The only statistically significant difference has been found between Schizophrenia Patients and Control Group in the SVF Test (p=0,001), whilst no statistically significant differences have been found in the PVF Test. These results indicate that one-minute Semantic Verbal Fluency Test is suitable for differentiating Schizophrenia patients (not BP) from healthy control only. Therefore one-minute Phonemic Verbal Fluency Test is unsuitable for these purposes.

73. Fine motor behaviour in schizophrenia patients

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Clinical picture of schizophrenia includes affected motor functions, which has been shown by research to date. We take a novel approach in measuring those disturbances using a new, more sensitive equipment - computerized pursuit rotor test with a digital tablet allowing for tracking the target. 26 schizophrenia patients, treated with atypical

neuroleptics (olanzapine, clozapine, quetiapine) and 13 healthy controls (matched in age and gender) were tested using a Psychology Experiment Building Language (PEBL) pursuit rotor task. The test was performed on a computer equipped with a tablet. Patients were asked to track the target using the tablet on 8 full circles. We found significant (p = 0,0009) difference in total time on target between schizophrenia patients and the control group, in favour of the latter. Total deviation from target was higher in schizophrenia patients (p = 0,001). Our results show that fine motor behaviour is significantly affected in schizophrenia patients. Further analysis on factors such as age and how hey affect the results is necessary.

74. Fine motor behaviour is affected in bipolar disorder patients

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Disturbances in motor functions in bipolar disorder are not well researched, and can be clinically easily dismissed. However, research suggests similar neurobiological mechanisms in etiology of bipolar disorder and schizophrenia, where affected motor functions are a part of clinical picture. We measured fine motor behaviour in bipolar disorder patients using a computerized pursuit rotor test and a digital tablet for tracking the target. We evaluated 10 bipolar disorder patients diagnosed based on DSM IV TR criteria, trated with atypical neuroleptics (olanzapine, quetiapine, clozapine, aripiprazole), using a computerized pursuit rotor task programmed in the Psychology Experiment Building Language (PEBL). Patients were asked to track the target on 8 full circles using a digital tablet. Their results were compared to those of sex- and age-matched 13 healthy controls. The bipolar disorder patients had significantly less time spent on target compared to healthy controls (p = 0,0002). Their total deviation from target in this task was also significantly higher (p = 0,0004) than in control group. Our data shows that fine motor behaviour is affected in bipolar disorder patients. Further analyses are needed, especially to show how age affects those results.

75. Is Bipolar Disorder associated with spatial short-term memory impairment?

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Growing number of evidence show that bipolar disorder is not only associated with affective symptoms but also with cognitive impairments. An example of such cognitive deficit is a prospective memory impairment. The purpose of this study was to prove the deficits in other areas of memory, particularly in spatial short-term memory. 21 patients with bipolar disorder (diagnosed by DSM-IV-TR) and 16 healthy controls performed computer version of the Corsi-block-tapping task. The task is to memorize the sequence of squares displayed on a computer monitor and then reconstruct the sequence by clicking the mouse on the squares in the correct order. Memory span was determined by the maximum length of the correctly reproduced sequence. Mean memory span of the two groups were compared using Tukey's test. Patients had significantly lower memory span (M=3,79) than healthy controls (M=5,19; p=0,002). Further analysis demonstrated moderate negative correlation between the memory span and the age of patients (r=-0,49, p=0,045) and strong negative correlation between memory span and the length of a treatment (r=-0,61, p=0,035). No such correlation was noted in the control group. Patients with bipolar disorder show impairment of spatial short- term memory, which may progress with age or the duration of treatment.

76. Ghrelin level is Parkinson's Disease patients treated with subthalamic nucleus deep brain stimulation

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Deep brain stimulation of subthalamic nucleus (STN-DBS) is a treatment option with well-established therapeutic benefits, performed in patients with advanced Parkinson's Disease. One of the adverse effects of STN-DBS is weight

gain. Ghrelin is an orexigenic hormone produced in the gastrointestinal tract. It has effects on regulation of energy homeostasis by stimulating appetite and therefore increasing body weight. It has been identified that ghrelin may play a neuroprotective role towards dopaminergic neurons in PD patients. We measure the fasting plasma concentration of ghrelin in PD patients before they underwent the STN-DBS procedure and compare it to the fasting serum concentration of the hormone after the surgery and with healthy controls. Blood samples for identifying the ghrelin levels were collected from 6 PD patients qualified to STN-DBS surgery before and 3 months after the procedure, each time at least 12 hours from last meal. Ghrelin levels were compared in groups before and after surgery, and to healthy controls. No significant difference in fasting ghrelin levels were found between groups 'before' and 'after' surgery and between 'after' group and controls. There was a statistically significant difference between 'before' group and controls (p=0,03). Further research with a larger sample size is necessary to confirm those preliminary findings.

77. Language impairments in patient after right cerebellar hemisphere lesion

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Cerebellum is considered to be a main coordinator of fine motor acts. Participation of the cerebellum in the speech was mainly perceived by its function in coordinating its motility. New reports indicate that the cerebellum is also involved in higher cognitive functions associated with language. This function is assigned mainly to the right cerebellar hemisphere. Here we present a case of 38-year old female patient after an excision of medulloblastoma in fourth ventricle, attached to the vermis and the right cerebellar hemisphere. In order to assess the language skills several test were applied: verbal fluency task, measurement of voice onset time and verb generation task. Patient performed tasks very slowly and showed problems with response inhibition. Apart from the classical cerebellar symptoms such as dysathria, patient presented discreet aphasia and impairments in other cognitive language tasks. Neuropsychological assessment revealed i.a. weakening of semantic and formal verbal fluency. Described example of the patient seems to confirm that the right hemisphere of the cerebellum may be related to language.

78. Spatial short term memory deficits in Schizophrenia

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Schizophrenia is associated with cognitive impairments such as working memory deficits. While most of the recent research focuses on the verbal memory, the data regarding visuo-spatial memory is scarce. The aim of this study was to examine the spatial working memory span in schizophrenia. 30 patients with DSM-IV-TR diagnosis of schizophrenia and 16 healthy controls were examined using The Corsi block tapping task. Their task was to recreate the sequence of highlighted squares, displayed on the monitor, by pressing them in sequence with the mouse. Memory span was determined by the maximum length of the sequence which was correctly reproduced by the participants and then compared using Tukey test. Memory span in patients' group was also controlled for age of the participants, length and type of treatment. Patients revealed lower memory span (M=3,89) than healthy controls (M=5,19). The difference was statistically significant (p=0,004). There was no significant correlation with the patients' age, length and type of treatment. Our results confirm the presence of the deficit in spatial working memory, additionally to the previously reported verbal working memory deficits.

79. Lexical retrieval in schizophrenia assessed with the verb generation task

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Patients with schizophrenia present disruption of fronto-cerebellar dysfunctions, that may impair language tasks based on lexicon retrieval. Verb generation task is a well-known psychological test evaluating retrieval of semantic information. Our aim is to assess lexicon retrieval in schizophrenia patients with the verb generation task. 25 patients with DSM-IV-TR diagnosis of schizophrenia and 17 healthy controls performed the verb generation task. 20 nouns were

presented on computer screen and in audio forma via headphones. Data was recorded and analyzed in terms of adequacy. U Mann-Whitney test showed that schizophrenia patients presented statistically significant (p=0,01) lower number of proper verbs (mean=14,64; median=17) than control group (mean=18,94; median=20). Those impairments are not correlated with medication or with years of treatment. Patients with schizophrenia reveal lexical retrieval impairments, seemingly associated the disease but not with the treatment duration. These deficits can be assessed with the use of verb generation task.

80. Coexpression of PrPc and Aβ protein in Alzheimer-type pathology

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Findings of concomitant accumulation of PrPc and Aβ in brain tissue revealed new traces important to understand mechanism of neurodegenaration. In our previous work we have summarized putative role of cooperation of those proteins and its possible contribution in the cognitive decline. As the next step of our research we aim to evaluate coexpression of PrPc and Aβ in the brains showing signs of Alzheimer-type pathology. 8 autopsy investigated cases with Alzheimer type pathology (Aβ immunopositive neuritic plaques) – age: 61-86 were included in the study. Immunohistochemical staining for prion protein, tau, and Aβ was performed. Prion proteins were presented within neuritic plaques in 7 out of 8 patients and within neurons in 6 out of 8 cases. 8/8 brains showed Aβ positive plaques and 6/8 presented tau pathology (NFT's and neuropiles threads). Coexpression of PrPc and Aβ protein within neuritic plaques seems to be a commonplace phenomenom.

81. Progressive supranuclear palsy - clinicopathological view

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Progressive supranuclear palsy, also known as Steele-Richardson-Olszewski disease is a very rare neurodegenerative disease, associated with progressive loss of motor and cognitive functions, leading to death in approximately 5 – 10 years. Case of 51 year old female patient is presented. In 2010, the patient was admitted to the clinic with the symptoms of gait abnormality, dysphagia, dysarthria and blurred vision. General condition of the patient deteriorated quickly, with the loss of verbal contact and symptoms of severe dystonia. In 2011 the patient was admitted again, due to progressive dementia and cerebellar syndrome. During hospitalization, patient suffered from cardiopulmonary failure, resulting in death. Neuropathological investigation revealed signs of neurodegenerative process i.e. taopathy and ubiquitin immunopositivity of substantia nigra. This case presents clinico-pathological view of this multisymptomatic severe neurodegenerative disorder.

82. Implicit motor learning in bipolar disorder

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Patients with bipolar disorder present motor dysfunctions and suffer from impaired plasticity, which reveal itself during adaptation of reflexes tasks. We suggest that those impairments combined will be revealed during implicit motor learning, which relies on improving sequence of motor acts through their repetition without conscious awareness of the exposure of the task. The aim of this study is to assess implicit motor learning with the use of Serial Reaction Time Task (SRTT). 21 patients with DSM-IV-TR diagnosis of BD patients treated with atypical antipsychotics, and 22 healthy controls were tested with the use of SRTT. During that test participant's task was to push an adequate button corresponding to the number on the screen. Task consisted of 5 blocks, in the first and fifth block the numbers were displayed randomly. Blocks 2-4 consisted of ten 10-items long sequences. Each subject performed the task with the right and the left hand separately. In the control group we noted a rebound of the reaction time between the fourth and the fifth block, suggesting that the group have learned the sequence. No such effect appeared in patients with BD. BD patients reveal implicit motor learning impairments.

83. Bilateral impairment of procedural learning in schizophrenia

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Schizophrenia (SZ) patients present impairments of procedural learning. Paradigms evaluating those functions, like Serial Reaction Time Task (SRTT) are usually performed by dominant hand. The aim of study was to verify, if this impairment is bilateral. 24 patients with DSM-IV-TR diagnosis of SZ treated with atypical neuroleptics and 22 healthy controls were tested with the use of SRTT. Participant's task was to push an adequate button corresponding to the number on the screen. Task comprised 5 blocks, in the first and fifth block numbers were displayed randomly. Blocks 2-4 consisted of ten 10 items long sequences. Each subject performed the task with the right and the left hand separately. Only control group presented rebound of the reaction time between the fourth and the fifth block in both the right and the left hand. This suggests that the group have learned the sequence. SZ patients did not present this effects neither in the right not the left hand. Schizophrenia patients present bilateral implicit motor learning impairments.

84. Is semantic retrieval impaired in bipolar disorder?

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Bipolar Disorder (BD) is a complex mental disorder mainly associated with various affective impairments. However, growing number of evidence suggest cognitive dysfunctions in this disease. Despite the growing popularity of cognitive research in BD, data concerning language impairments in this clinical group is scarce. The aim of this study was to evaluate semantic lexical retrieval in BD with verb generation task. We tested 12 patients with DSM-IV-TR diagnosis of BD patients, treated with atypical antipsychotics, and 17 healthy controls, matched in age and gender. During the verb generation task the participants were asked to generate verbs to 20 nouns presented visually on the computer monitor and auditorly via headphones. BD patients produced lower number of adequate verbs (median: 18, mean: 14.5) than healthy controls (median: 20, mean: 18, 94), but the difference did not reach the statistical significance (p=0,07). Despite the dysfunctions that may be spotted during clinical practice, our preliminary data suggests that lexical retrieval might not be impaired in BD patients. Research on bigger BD group is needed to fully evaluate those results.

85. Does asymmetric onset of Essential Tremor influence severity of the symptoms and progression of the disease?

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Essential Tremor (ET) is the most common cause of the upper limbs tremor, however relationship between asymmetry and clinical course of the disease remains elusive. To compare clinical features and parameters of tremor in patients with symmetrical and asymmetrical hands tremor at the onset of the disease. 99 ET patients, diagnosed according to NIH Collaborative Genetic Criteria, were assessed clinically and objectively by computerized method of Quantitative Tremor Analysis by Digitizing Tablet (QTADT). The Tremor Disability Questionnaire (TDQ) was also collected. 60.4% patients reported asymmetry of hand tremor at the onset of ET. Groups with symmetric and asymmetric onset did not differ in gender, family history nor frequency of tremor. Patients with asymmetric onset were older (39.0 vs. 30,.8 years, p=0.003), had shorter duration of symptoms prior to the diagnosis (11.7 vs. 15.3 years p=0,02), more frequent of both resting tremor (67.2% vs. 50.0%, p=0,01) and intermittent tremor (33.9% vs. 18.4%, p=0.04), lower tremor amplitude and intensity. TDQ score was significantly lower in asymmetrical group as well (3.5 vs. 5.6, p=0.006). Asymmetric onset of ET is associated with later onset, slower progression of the disease and lower amplitude of tremor.

86. Diagnostics of multifocal motor neuropathy with conduction block in a 57-year-old woman

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This case is a report of the diagnostic process in which multifocal motor neuropathy with conduction block (MMNCB) was confirmed. This rare disease needs differentiation with other types of neuropathies, as well as with motor neuron

diseases. MMNCB is most probably an autoimmunological disease but its' causes are yet not completely known. A 57-year-old woman was admitted to the hospital due to progressive flaccid paresis of all four limbs. The symptoms had started approximately 1,5 years before – at first the patient noticed flopping of the left foot, which got better after rehabilitation, but worsened again after some time. Then the patient presented weakness of consecutively: right upper limb, left upper limb, and then both lower limbs. The patient is suffering also from muscle atrophy (lost 7kg in few months), tremor and problems with balance. Neurological examination has shown flaccid paresis of upper limbs (R>L) and lower limbs, absent reflexes on lower limbs and hyporeflexia of upper limbs. The patient walks stork-like due to the paresis of the feet. She presents no loss of sensation. The diagnosis of multifocal motor neuropathy with conduction block has been made, based on several diagnostic criteria, such as asymmetric paresis, slow progression, temporary improvement, no loss of sensation and absence of upper motor neuron signs. Blood and urine examination have shown no abnormalities. Electromyography has ultimately confirmed MMNCB. Treatment with Kivig 30g was started. Diagnosis of multifocal motor neuropathy with conduction block requires conscientious review of the history and thorough examination of the patient. Since MMNCB may have similar manifestation but better prognosis than other neurological disorders (such as amyotrophic lateral sclerosis), it requires precise differentiation.

87. MoCap method in the assessment of rest tremor in patients with Parkinson's disease treated with deep brain stimulation (DBS) surgery

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Rest tremor is one of the main symptoms of Parkinson's disease (PD). According to various authors parkinsonian tremor (PT) is characterized by frequency (f) of 3-7 Hz. The treatment of severe PD is a challenge for modern neurology, where drug therapy is not only insufficient but also may provoke dyskinesia. This is an indication for deep brain simulation (DBS) which is well proven and effective treatment for PD but with debatable evaluation of therapeutic effect in reduction of tremor. In our study, the analysis of PT was performed in Motion Capture Studio of the Polish-Japanese Institute of Information Technology in Bytom. The method allows to analyze the motion in three dimensions by using markers placed on the patient's body. The trial included 7 patients (mean age 52 yrs) who were treated with DBS surgery between April 2008 and December 2010. Four sessions were recorded: patients without medications or DBS stimulation, only DBS, only drugs, DBS and drugs. Data analysis was performed with MatLab software. The presented method of PT measurement is repeatable and allows for quantitative assessment the impact of different DBS treatment methods on the severity of PD symptoms. DBS reduces the PT in patients with severe PD.

88. Usefulness of the MOCAP method in the assessment of freezing of gait in patients with Parkinson's disease treated with deep brain stimulation (DBS)

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The freezing of gait (FOG) is one of the least understood motor symptoms of Parkinson's disease (PD), described as a sudden appearance of OFF state during gait. Recent studies focus on assessing the influence of freezing on life quality and risk of falls with use of the FOG-Q questionnaire. More precise and objective measurement methods seem important for propper evaluation of the effect of various therapies on FOG. Analysis of the usefulness of Motion Capture (MOCAP) in the assessment of FOG intensity in PD patients treated with Deep Brain Stimulation (DBS). The study included PD patients, who underwent DBS-STN (subthalamic nucleus) therapy in Silesian Parkinson's Disease Treatment Centre in Katowice and were subjected to MOCAP analysis. FOG intensity was independently evaluated by 4 researchers based on video recordings. Results were compared with FOG-Q score and MOCAP analysis using: A. Pearson cross-correlation to assess stride-to-stride variation, B. changes of iFOG-MOCAP ratio. Influence of DBS therapy on FOG intensity was assessed using data from four sessions: S1– patient without medication and DBS stimulation, S2– DBS only, S3– drugs only, S4– DBS and drugs. MOCAP can be used as an objective method for the assessment of FOG intensity.

89. MoCap method in assessment of postural instability in patients with Parkinson's disease (PD) treated with Deep Brain Simulation (DBS) surgery

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In addition to the typical motor symptoms, many patients with idiopathic PD develop balance disorders. These disorders are the main cause of falls in PD. One of the most innovative method of objective analysis of movement disorders in PD patients is Motion Capture. The main objective was to determine the usability of MoCap in the quantitative assessment of balance in PD patients and also analysis of the impact of DBS surgery on postural stability in this group. The trial included 12 patients treated with DBS in our facility. Motion analysis was performed in the Polish-Japanese Institute of Information Technology in Bytom. The study compared the average sway radius measured with MoCap (Centre of Mass – COM) and with force platform (Centre of Pressure – COP). For the assessment four sessions were recorded: without DBS and medication; DBS only; medication only; with DBS and medication. Positive correlation between average sway radius of COM and average sway radius of COP was shown. Reduction of sway radius in patients with DBS was shown. The tested method of postural stability assessment is objective, repeatable and shows positive correlation with the analysis of movement trajectory of COP. Research in progress.

90. Non-motor function in Parkinson's disease patients after Deep Brain Stimulation of Subthalamic Nucleus

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Deep Brain Stimulation of Subthalamic Nucleus (DBS STN) is an effective method for motor symptoms in Parkinson's disease (PD) patients. However, its impact for non-motor functions remains controversial. We assessed how DBS STN influences cognitive functioning and daytime sleepiness in PD patients. 6 PD patients eligible for DBS STN and 7 PD patients after STN DBS were enrolled to the study. To assess cognitive functions we used Montreal Cognitive Assessment (MoCA), Frontal Assessment Battery (FAB), Trail Making Test A and B (TMT A and B), Stroop Test (ST), verbal fluency test (VFT) (semantic: animals and sharp objects, letter: K and S). To assess daytime sleepiness we used Epworth Sleepiness Scale (ESS). PD patients after DBS STN presented lower performance in ST, VFT (semantic and letter category), FAB and lower daytime sleepiness in ESS. However, observed differences were not statistically significant, Cohen's d value indicated large to medium effect size. That may suggest that observed differences may be clinically significant. DBS STN may cause a selective decrease in some aspects of cognitive functions and an improvement in daytime sleepiness in PD patients. Further studies of DBS STN effects on non-motor functions in PD patients are warranted.

91. The effects of the high dose nicotine product Snus on academic performances of medical students

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Snus is a high-dose smokeless tobacco product commonly used amongst Scandinavian medical students. Compared to cigarettes, a dose of Snus provides 3-8 times higher concentrations of nicotine and has a longer duration of exposure. Nicotine has been shown to improve short-term episodic memory, working memory, and attention. It affects memory by acting on nicotinic acetylcholine receptors (nAChRs) in the hippocampus and basolateral amygdala. It also stimulates presynaptic nAChRs to trigger the release of neurotransmitters involved in cognition. Studies about the effects of Snus on cognition and memory however are limited. The aim of our study was to determine if high doses of nicotine improved or impaired academic performance. A total of 152 students enrolled in the first three years of medical school volunteered for our retrospective-prospective study, of which 25% were Snus users. Examination results were collected for all participants and analysis showed that the use of Snus and examination scores were associated ($p=0.03$). Academic performance was not improved by the use of Snus, with most users scoring within 0.5 standard deviations of the mean. These results suggest that higher doses of nicotine do not confer the same cognitive benefits as lower doses.

92. Memory Rehabilitation 10 Years Post Stroke: a Case Report

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Neurorehabilitation is usually described in the context of early post-stroke stages. Within that period, most of the patients do not restore their premorbid functioning. Thus, attention should also be given to rehabilitation years after stroke. This report presents a case of successful memory-focused rehabilitation implemented 10 years after stroke. A.L., a 55-year-old female, experienced left-hemisphere ischemic stroke 10 years earlier. Patient's subjective opinion on own cognitive functioning was assessed using a semi-structured interview. A.L. reported memory problems to significantly disturb her daily functioning. Verbal memory and learning was assessed using California Verbal Learning Test (Łojek & Stańczak, 2010) which revealed functioning within average to high range. Intervention comprised 15 weekly sessions, in which memory enhancement techniques were presented and practiced. Post-intervention subjective and objective measures were administered. Due to A.L., intervention positively influenced her functioning as she used the acquired memory techniques in everyday activities. Moreover, the level of memory and learning functioning increased from the pre- to post-intervention standardized assessment. This case report emphasizes the effectiveness of memory rehabilitation in terms of elevating subjective as well as objective well-being of the patient, even if implemented as long as 10 years after stroke.

93. The influence of genes associated with stress response and the risk of depression and bipolar disorder

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In this project I have been examined the role of genetic variation in the dysregulation of hypothalamic–pituitary–adrenal axis (HPA axis) that underlies pathogenesis of bipolar and unipolar disorders including differential clinical subtype. Molecular analysis of genetic polymorphisms of genes: Molecular analysis have been included 7 polymorphisms in the following genes: FKBP4, BAG1, STIP1, DUSP1, GLCCL1, SRD5A1. Determination of genetic polymorphisms of selected genes have been made using sets of primers and probes TaqMan SNP Genotyping Assays (sets of two primers and fluorescently labelled TaqMan probes, each specific for one allele) (Applied Biosystems). The reaction have been performed using the real time nucleic acids detection system ABIPrism7900HT (Applied Biosystems), in the 384-well microplate module. It was found that excessive stress response underlies the pathogenesis of psychiatric disorders. Qualitative and quantitative composition of chaperone proteins suggesting their important role in the pathogenesis of mood disorders such as depression and bipolar disorder. Regarding their function, the most important proteins include FKBP4 protein, to support the function of the BAG1 protein, related to hsp90 and hsp70 and STIP1, GLCC1, SRD5A1, DUSP1 protein.

94. Patterns of synchronous population activity in the neocortex of patients with epilepsy or tumor, in vitro

Katharina Hofer, Hungarian AcadKinga Tóth, Ágnes Kandrács, Csilla Szabó, Attila Bagó, Loránd Erőss, László Entz, István Ulbert, Lucia Wittner

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Epilepsy is thought to be related to hyperactivity of neuronal circuits. Surgical tissue removal in patients who resist pharmacotherapy offers a possibility to study living human tissue involved in the generation of this neurological disorder. Similar to interictal spikes recorded on scalp EEG, synchronous population activity (SPA) has been shown to be spontaneously generated in epileptic human tissue in vitro. Tissue slices were prepared from neocortical tissue of patients with epilepsy and as a control of patients with tumour but without epilepsy. The local field potential gradient was recorded using a laminar microelectrode. Neurons were characterized in simultaneous intracellular recordings. SPA consists of high frequency oscillations and elevated cell firing superimposed on a local field potential transient. Several patterns of SPA could be differentiated, but it was generated most frequently in the supragranular layers. Cell clustering analysisshowed most neurons elevated their firing rate. Our results suggest that supragranular layers have a leading role in the initiation of the SPA, in which both excitatory and inhibitory neurons participate. The cellular and network properties of SPAs were similar in tissue slices derived from epileptic and tumour patients. This indicates that in vitro occurring SPA cannot be directly related to epileptic processes.

95. Are patients with schizophrenia able to infer communicative interactions from biological motion?

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Deficits of social cognition are frequently observed in patients with schizophrenia. However, the ability to discriminate communicative from individual actions from biological motion has not yet been investigated in schizophrenia. We examined this issue by applying point-light methodology. Nineteen patients with schizophrenia (SCZ) and nineteen matched healthy controls (HC) watched video-clips depicting actions of two point-light agents. After each video-clip, participants were asked to a) decide whether the two agents were communicating vs. acting independently of each other, and b) to select the correct action description between 5 response alternatives. Participants completed also Emotional Intelligence Scale - Faces. Patients were significantly less sensitive in discriminating the communicative from individual actions (d: SCZ 1,05+/-0,77 vs HC: 2,00+/-1,25; U=266,5; p=0,05) and were outperformed by HC in both parts of the task. Discriminating communicative from individual actions was significantly correlated with basic social cognition skills in HC (r=,64; p=0,01), but not in SCZ. This results are in line with previous findings of deficient attribution of social meaning in schizophrenia. Furthermore, dissociation between various aspects of social cognition skills may be observed in schizophrenia.

96. Diagnosing consciousness - first attempts to use fMRI to assess awareness in Polish patients with disorders of consciousness

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Severe brain injury results often in so called disorders of consciousness (i.e. coma, vegetative state, minimally conscious state, locked in syndrome). The assessment of voluntary behaviour in non-communicative patients is challenging. Especially problematic is diagnosis of vegetative state in which patients who just emerged from coma appear awake, but with no clear signs of retained awareness. Diagnosis of the vegetative state is a process based on interpretation of overt behavior. But lack of overt signs of consciousness can be misleading duo to possible severe motor dysfunctions. As a result rate of misdiagnosis is very high (as high as 40%). Therefore, many attempts has been undertaken to use neuroimaging methods to assess signs of conscious processing in the brain. One of the approaches, which is simple and ingenious at the same time, use fMRI to track neural correlates of spatial vs motor imagery while patients are being guided to imagine one of the two events in a meaningful sequence. Here we present results of first attempt to use this method to diagnose consciousness in brain injured Polish patients. Moreover we present data from pilot study aiming to find best task for use in motor imagery paradigm.

97. Chasing the consciousness - implications for diagnostic purposes

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Adequate diagnosis of patients with disorders of consciousness (DOC) who may not be able to move or communicate while retaining conscious experiences is still a challenge. The principal goal of this work is to develop or test some methods based on EEG measurement that could be used as a diagnostic tool to assess patient condition. Several EEG paradigms were tested. Two methods; auditory steady-state responses (ASSRs) and somatosensory steady-state evoked potentials (SSS - EP, Colon, 2012) were used to assess the level of consciousness in healthy participants in deep NREM sleep compared to wakefulness condition. In the following studies patients after severe brain injuries underwent ASSR protocol together with partially modified command-following procedure developed by Guger et al. and Cruse et al. (Guger et al., 2003; Cruse et al., 2011, 2012a, 2012b). We suggest that all presented methods could be performed complementary in determining the actual state of brain functions in DOC patients. The results of ASSR responses in patients group suggest that some frequencies (20Hz and 40Hz) could be the promising markers of their condition. The usefulness of command-following procedure in the diagnosis of DOC was not unequivocally confirmed. SSS-EP paradigm succeeded in discriminating between the two conditions, although some frequencies of stimulation proved more useful and reliable.

POSTER SESSION II

April 27, 2014 (Sunday)
13.00 – 14.30

BASIC NEUROSCIENCE

1. Voltage-sensing domain mutations in the´split´Kv 10.1 channel

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Opening and closing of voltage-gated ion channels (also called chanel gating) is a mechanism of utmost importance to physiological processes based on electrical excitability, like nerve signaling or heartbeat. The widely accepted model of channel gating assumes that a charged domain of the channel protein moves within the transmembrane electric field, thereby exerting a mechanical force on the pore domain through a cytoplasmic linker. In our lab we investigate channel gating using the 'split' Kv 10.1 potassium channel which consists of two halves, expressed from 2 independent cRNAs in Xenopus laevis oocytes. In the 'split' channel the voltage-sensing domain and the pore domain are no longer linked by a peptide bond. We show that such a construct retains voltage-dependency of activation. Introducing mutations to the voltage-sensing domain shifts the dependency of activation in either depolarizing or hyperpolarizing direction. Interestingly, the direction of the shift is conserved, when the same mutations are made to the 'split' channel. What changes dramatically is the time constant of activation in the voltage range where the open probability of the channel is subjected to greatest change. Our results indicate that the idea of mechanical coupling as a means of voltage-gating needs further refinement.

2. Genetic approaches to the study of peripheral cold thermoreceptors

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Primary sensory neurons are morphologically and functionally diverse. Typically, subclass identification is based on their response pattern to a battery of physical (thermal, mechanical) and chemical stimuli or by immunohistochemistry. This problem is specially limiting in the study of cold thermoreceptors because they comprise only about 5-10% of all sensory neurons identified in culture or on histological sections, an added difficulty in their biochemical and functional characterization. To facilitate the characterization of TRPM8-expressing neurons we adopted a genetic strategy, generating a mouse line expressing the yellow fluorescent protein (YFP) under the control of the TRPM8 promoter, using in vitro modification of a bacterial artificial chromosome (BAC) that harbor a long stretch of DNA (<200 kb) around the TRPM8 gene locus. We developed a simple method using fluorescent activated cell sorting (FACS) to purify and characterize TRPM8-expressing neurons obtained from DRGs. We combined this approach with a gene expression analysis in this population of purified neurons and we found an unexpected enrichment of several ion channels in cold thermoreceptors. In conclusion, these methodology results in interesting possibilities for the easy identification and molecular characterization of cold TRPM8(+) thermoreceptors, an approach applicable to other subclasses of sensory neurons.

3. Immunoreactivity of galanin and galanin receptor 2 in the preoptic area of the female guinea pig

Beata Hermanowicz, Krystyna Bogus-Nowakowska, Maciej Równiak, Witold Żakowski, Barbara Wasilewska, Janusz Najdzion, Anna Robak

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Galanin (Gal) has a widespread distribution in the central and peripheral nervous systems of mammals and diversity of biological effects. These include nociception, cognition, feeding behavior and reproduction. The molecular actions of

galanin are mediated through three membrane receptor isoforms, including GalR2. The aim of this study was to examine the immunoreactivity of galanin and galanin receptor 2 (GalR2) in the preoptic area (POA) of the female guinea pig. The tissue blocks containing the preoptic area were processed for routine single-labelling immunofluorescence. Gal and GalR2 were present in all POA parts, Gal in perikarya and fibers, whereas GalR2 occurred in perikarya only. Gal- and GalR2- immunoreactive (–ir) perikarya were the most numerous in the medial preoptic area (MPA) with the highest reactivity in its dorsal part. In the median preoptic nucleus and periventricular preoptic nucleus only single Gal-ir and GalR2-ir neurons were observed. The highest density of Gal-ir fibers was revealed in the periventricular preoptic nucleus (PPN) and the lowest in the lateral preoptic area (LPA). The present results indicate that the distribution patterns of Gal-ir and GalR2-ir cells were very similar, especially in the MPA. This may suggest galanin receptor 2-dependent activity in this brain region.

4. Immunohistochemical identification of orexin A and B in nucleus incertus of the rat

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Relaxin-3 (RLN3) is a recently discovered brain neuropeptide. The main source of RLN3 is nucleus incertus (NI) – a small GABAergic brainstem structure located in the pons near the IV ventricle. Physiological functions of NI and RLN3 are related to arousal, feeding behavior, stress response and hippocampal theta rhythm. Another neuropeptides involved in regulation of sleep-wake behavior and arousal are orexins (OX), synthesized in the lateral hypothalamus. Moreover, orexins modulate feeding behavior, activity and energy expenditure of the animal. Orexin A and B bind to orexin type 1 and 2 receptors with different affinities. Both peptides and receptors are differentially expressed throughout the rat brain, including the brainstem. Although some functions of both RLN3 and orexins are similar, interactions between them have not been precisely investigated yet. Results of our recent immunohistochemical studies reveal the presence of orexin A and B fibers in the NI of male Wistar rat. Moreover, synaptic contacts between orexin fibers and RLN3 positive neurons have been confirmed. Microscope image processing has shown that orexin A fibers within the NI are more abundant than orexin B fibers what raises the possibility that there are differences in the functional roles of OXA and OXB within the brain.

5. Falcarinol influences GABAergic currents mediated by different types of receptors

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γ-aminobutric acid (GABA) is the most important inhibitory neurotransmitter in the adult brain of Mammals. GABAA receptors (GABAAR) demonstrate functional and structural diversity with 19 different subunits cloned so far. Receptors with αβγ subunit arrangement are usually localized synaptically and mediate high intensity phasic currents. αβδ and αβ GABAARs are found extrasynaptically and mediate persistent low intensity currents. One of the challenges of modern pharmacology is a search for subunit specific GABAARs modulators. Therefore we investigated falcarinol - a natural product common in plants from the Apiaceae family (e.g. carrot). We used recombinant GABAARs with different stoichiometry expressed in HEK cells. Current responses to low GABA concentration were measured in voltage-clamp mode of the patch-clamp technique. Interestingly, the effect of falcarinol strongly depended on the compound concentration and receptor subunit composition. Low falcarinol concentration (0.1 - 1μM) potentiated currents mediated by αβδ and αβγ GABAARs, and inhibited those mediated by αβ. Responses to high concentration (3μM) mediated by αβγ showed use-dependent amplitude reduction, suggesting an open channel block. In conclusion, we provide first evidence that this polyacetylene have subunit selective effect on GABAARs. Further investigation will help to establish mechanisms of GABAARs modulation by falcarinol.

6. Differences in the number of binding sites of dopamine D2 receptors labeled by various radioligands

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Radioligand binding studies frequently show differences in the number of binding sites labeled by various radioligands. It has been shown that [3H]raclopride labeled more sites in the presence of sodium ions, however specific binding of [3H]spiperone was unaffected by sodium ions and revealed similar number of sites as labeled by [3H]raclopride in the presence of sodium ions. Since these observations are not consistent and have been made using saturation binding

methodology, we performed an autoradiography analysis using three different radioligands, i.e. [3H]spiperone, [3H]raclopride and [3H]quinpirole. Dopamine D2 receptor autoradiography was made on the naïve mouse brains. Mice were decapitated immediately after, as well as 3 days after forced swim test (FST). The highest binding was observed for [3H]spiperone in opposite to [3H]raclopride for which we observed only ~30% of specific binding as compared with [3H]spiperone. Only for [3H]raclopride and [3H]quinpirole we observed changes in specific binding immediately after FST. However, the character of changes was different for both radioligands. [3H]quiniprole revealed decrease, and [3H]raclopride – an increase in specific binding. Such result indicate the reduction of number of receptors in high affinity state upon acute stress. When experiments were made 3 days after FST, the specific binding returned to control level for both radioligands. Supported by grant DeMeTer (POIG.01.01.02-12-004/09; 3.6).

7. Synthesis and evaluation of new indole derivatives as aminergic GPCR ligands

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Aim: Developement of new series of indole and other priviledged structures derivatives as new aminergic GPCR ligands. Screening of active compounds towards 5-HT6 selectivity in the search of therapeutics and neuroimaging agents.
Methods:
Total synthesis, purity examination via LC-MS, NMR and elemental analysis. Structure determination via 1D and 2D NMR. Binding affinity measurement on a 96-well plate using appropriate GPCR-overexpressed HEK293 cells and specific radioligands. CNS screening for alpha-1 and alpha-2C adrenergic, dopamine D3, muscarinic M1 and M5, serotonine 5-HT2C and 5-HT3 done by CEREP.
Preliminary results:
Series 1:
Very high binding affinity for 5-HT6R (Ki = 2-14nM) and selectivity over D2, 5-HT1A, 5-HT7 in the range of 9 to 574 fold. Low affinity towards adrenergic and muscarinic receptors.
Series 2:
Compounds contain iodine atom which can be substituted with 127I; binding affinity for 5-HT6R Ki<50nM.
Acknowledgements:
This study was partly supported by the project UDA-POIG.01.03.01-12-063/09-00 \"Antagonists of 5-HT6 receptor as advanced antipsychotic drugs with pro-cognitive properties\" co-financed by European Union from the European Fund of Regional Development (EFRD).

8. Acute and chronic administration of glucocorticoids affect expression of glucocorticoid receptor and target genes in astrocytes *in vitro*

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Chronic stress associated with glucocorticoid (GC) hormone release has been linked to development of mood disorders such as depression. Alterations in both astrocyte numbers and astrocytic genes' expression were reported in animal models of chronic stress and in brains of depressed patients. We have previously shown that astrocytes are a major target of acute GC action in the central nervous system through glucocorticoid receptor (GR)-mediated transcriptional response, while the effects of chronic stimulation remain unknown. Here we treated murine astrocytes with GR agonist, dexamethasone (DEX). Single short exposures to DEX (5-30 min) resulted in a rapid accumulation of GR protein, followed by upregulation of GR target gene proteins SGK1 and FKBP5 at longer times, corroborating earlier results of mRNA analysis. Repeated DEX treatments resulted in a significant attenuation of induction of GR targets, suggesting that chronic glucocorticoids may affect GR not only in neurons, but also in astrocytes, which could contribute to astrocytic alterations under chronic stress. [This work was supported by grant 2011/03/B/NZ3/01683 from National Science Centre].

9. Glycinergic neurons innervate basal forebrain cholinergic neurons in mice

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Glycine is a major inhibitory neurotransmitter and an important regulator of glutamate neurotransmission; its extracellular concentration is regulated by glycine transporters (GlyT-1 and GlyT-2). The aim of the present study was to reveal whether (1) GLYT1- and/or GLYT2-immunoreactive (IR) cells are in morphological relationship with cholinergic neurons and (2) glycine has direct effect on these neurons in the basal forebrain (BF). GLYT-2-immunoreactivity (a marker of glycinergic neurons) was detected in axons which established appositions on ChAT-IR cells. Track tracing experiments identified a glycinergic input of BFC neurons from the raphe magnus. Correlated electron microscopic processing of the appositions revealed synapses between glycinergic axons and ChAT-IR neurons in the BF. The confocal microscopic detection of glycine receptor (GlyR)-IR sites in ChAT-IR neurons and recording strychnine-sensitive postsynaptic currents in cholinergic neurons at concurrent ionotropic glutamate and GABA receptor blockade suggest that glycine has a direct influence on BFC neurons. By using confocal and electron microscopy, GLYT1-IR glial processes were observed in the vicinity of ChAT-IR neurons in BF suggesting a local tight regulation of extracellular glycine levels. Our results strongly support glycine's involvement in the regulation of BFC neurons. Identification of the behavioral consequences, however, needs further studies. Supported by OTKA K101326, OTKA K83710, OTKA K100722, TAMOP 4.2.1.B-11/2/KMR-2011-0002, FP7/2007-2013 Grant Agreement 245009 and NIH/NINDS grant NS023945 (LZ).

NEUROPHYSIOLOGY

10. The orexin B mediation of hippocampal formation theta rhythm in anasthetized rats

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Orexins are represented by two neuropeptides – orexin A and orexin B - which exert their effects via membrane receptors – OxR1 and OxR2. They are synthesized mainly in the area of hypothalamus. Their send axons projections to many brain parts including cerebral cortex, thalamus, brain stem and the hippocampal formation (HPC). The aim of the study was to investigate the effect of intrahippocampal injection of orexin B and blockers of orexin receptors – SB (antagonist of OxR1) and TCS (antagonist of OxR2). Experiments were conducted on anasthetized rats. Initially spontaneous theta rhythm recorded from HPC was blocked by the intravenous injections of atropine. When the HPC theta disappeared, the rats were subjected the local injection of orexin B and mixture of: orexin B and SB, orexin B and TCS, and orexin B, TCS and SB in separate experiments. In the first and second experiment theta activity was still observed but with a lower frequency and amplitude in comparison to theta recorded after orexin B injection. After intrahippocampal injection of mixture of orexin B, SB and TCS in EEG no theta was observed. The results of study indicate the important role of orexinergic mechanims underlying production of theta rhythm in HPC.

11. Direct action of relaxin-3 receptor (RXFP3) agonist on hypothalamic paraventricular nucleus neurons in the rat - in vitro patch clamp study

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Relaxin-3 is an ancestral member of relaxin peptide family. Along with its cognate receptor RXFP3, this signalling system is conserved in vertebrates. Previous studies have shown that acute injections of relaxin-3 into the paraventricular nucleus of the hypothalamus (PVN), which neurons are characterised by high density of RXFP3, promotes feeding in rats; and chronic RXFP3 activation in PVN leads to weight gain. The strong responsiveness of

relaxin-3 neurons to neurogenic stressors and their potential involvement in feeding behaviour suggests this system as a possible bridge between chronic stress and obesity. It is hypothesized that RXFP3 activation exerts its orexigenic effect through inhibition of PVN neurons activity. In studies using brain slices from 5-6-week old Wistar male rats, we performed whole cell patch clamp experiments in the presence of tetrodotoxin (1 μM) to investigate direct actions of RXFP3 agonist (RXFP3-A2, 600 nM) on PVN neurons. Characterization of the recorded cells was based on their electrophysiological properties and neurochemical content. Our preliminary data show a direct, postsynaptic hyperpolarising effect of the RXFP3 agonist on magnocellular PVN neurons. Our study reveals possible mechanism of RXFP3 activation in PVN neurons that may underlie the central orexigenic effect of relaxin-3/RXFP3 signalling.

12. Modulation of pacemaker channel activity by the auxiliary subunit TRIP8b in the thalamocortical system

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We aimed to determine how dysregulation of hyperpolarization-activated cyclic nucleotide-gated cation (HCN) channels due to the lack of expression of the tetratricopetide repeat-containing Rab8b-interacting protein (TRIP8b; an auxiliary subunit of HCN channels) alters the basic properties of hyperpolarization-activated inward currents (Ih) in thalamic and cortical neurons. Ih was measured in whole cell patch clamp recordings from thalamocortical (TC) neurons of different thalamic nuclei (ventrobasal thalamic complex, VB; posterior nucleus, PO; centro-median nucleus, CM and doso-lateral geniculate nucleus, dLGN), as well as neurons in layer V of the somatosensory cortex (S1) of epileptic TRIP8b-deficient (TRIP8b-/-) and non-epileptic control (C57Bl/6J) mice (p14 – p25). In all investigated brain regions, Ih amplitudes were significantly lower in TRIP8b-/- as compared to control mice. Analysis of the half-maximal activation (Vh) of Ih revealed that steady states activation curves were significantly shifted towards more hyperpolarized values in TRIP8b-/- in comparison to control mice. In addition, the resting membrane potential (RMP) of both TC neurons and cortex were more hyperpolarized in TRIP8b-/- when compared to control mice. The alterations in Ih properties and RMP in thalamic and cortical neurons may contribute to the epileptic phenotype of TRIP8b-/- mice.

13. The comparison of posterior hypothalamic and hippocampal theta rhythm redorded in vitro

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Hippocampal formation (HPC) theta rhythm is one of the finest examples of neural synchrony in mammalian brain. HPC theta field potentials, well-documented in rodents, consist of high-amplitude, almost sinusoidal waves in 3-13 Hz frequency range. It is known that the pathway of theta generation in HPC originates from the nucleus reticularis pontis oralis (RPO), then RPO projects to supramammillary nuclei (SuM), and finally through the medial septal area (MS) to HPC and other limbic structures. This tract is called the ascending brainstem-hippocampal synchronizing pathway. Recently, we have shown for the first time that the administration of cholinergic agent - carbachol, induces local theta rhythm in in vitro maintained posterior hypothalamic region, specifically SuM. So far, our data provides evidence that posterior hypothalamic in vitro theta shares many similarities with theta recorded from the hippocampal formation. The aim of this study was to present a comparison between the basic physiological and pharmacological properties of theta rhtyhm recorded in vitro in hippocampal formation and posterior hypothalamic area, respectively. Results of this comparison as well as mechanisms underlying theta generation in posterior hypothalamus are discussed. Supported by NCN grant 2011/01/B/N24/00373.

14. Effects of meclofenamic acid the retinal gap junction blocker on slow oscillatory activity in the rat olivary pretectal nucleus (OPN)

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The olivary pretectal nucleus (OPN) is a midbrain structure densely innervated by the retina. The characteristic feature of some OPN neurons is capability to generate spikes in an oscillatory mode with the period of approximately two minutes (slow oscillatory activity – SOA). We have previously showed that SOA depends on the contralateral retina, which inactivation causes its disappearance. Since cells within the retina are extensively coupled, not only by chemical

but also electrical synapses, we investigated effects of retina desynchronization, due to the blockade of gap junctions, on SOA in the OPN. We performed extracellular in vivo recordings on urethane anesthetised Wistar rats combined with intraocular injections of meclofenamic acid (MFA; 20mM; 5µL). The injection of MFA abolished SOA in all neurons tested (n=8) and caused a decrease in mean firing rate (from 14.35 ± 3.06 to 9.86 ± 3.68 Hz). In four neurons the effect was reversible and SOA recovered approximately 54 ± 8 minutes after the injection. All neurons stayed prone to light stimulation during the time when they did not generate spikes in oscillatory mode. Presented results suggest that spontaneous rhythmic retina activity is probably required for SOA generation in the OPN.

15. The impact of ghrelin on nucleus incertus activity in vitro: possible causal link between two feeding control circuits

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Ghrelin is an orexigenic peptide involved in regulating food intake, stress, arousal and neuroendocrine functions. Produced primarily in the stomach, with limited expression in the brain, ghrelin acts on various brain regions through the growth hormone secretagogue receptor (GHS-R). This generally leads to neural membrane depolarization and increased spiking frequency. Earlier studies [1] found GHS-R mRNA in the nucleus incertus (NI), a group of GABAergic brainstem projection neurons and a source of the orexigenic neuropeptide relaxin-3. Recent evidence suggests NI/relaxin-3 involvement in appetite control, arousal and stress responses. We investigated the effects of ghrelin on single NI neuron activity using whole-cell patch clamp recordings in brain slices from 14-21 day old Wistar rats. Ghrelin (200 nM) depolarized a subset of NI neurons and this effect persisted in the presence of tetrodotoxin (TTX), suggesting a postsynaptic mechanism of action. Our results show that NI neurons are activated by ghrelin in vitro. Given the orexigenic nature of both peptide systems, this suggests their functional cooperation in regulating feeding behavior. Further research is needed to specify the physiological source of ghrelin in the NI. [1. Zigman JM, Jones JE, Lee CE, Saper CB, Elmquist JK. (2006) J Comp Neurol 494, 528-548].

16. Impact of matrix metalloprotease inhibitor NNGH on long-term plasticity of NMDARs- mediated synaptic transmission in mouse CA1 hippocampal region

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The matrix metalloproteinases (MMPs) play a pivotal role in synaptic plasticity, learning and memory. However, mechanisms underlying their impact on neuronal plasticity remain poorly understood. We have previously shown that broad spectrum MMPs inhibitor FN439 (180um) abolished tetanization (4x100Hz) induced potentiation of isolated NMDAR-mediated synaptic transmission in CA3 hippocampal network (Wójtowicz and Mozrzymas, 2014). To address this phenomenon in more detail we sought to determine the role of more specific MMPs inhibitor NNGH (10uM) in shaping NMDAR-component during long-term synaptic potentiation (LTP) by recording field potentials in Sch-CA1 hippocampal synapses. NMDAR-mediated signals were isolated with AMPA/kainate receptors antagonist DNQX (20uM) in Mg2+-free solutions in mice (P30-P45) acute brain slices. We found that in the presence of bath applied NNGH, potentiation of NMDAR-mediated fEPSPs was completely abolished (178.7±12% vs 75.8±2.9% of baseline at 1 hour post 4x100Hz stimulation, n=5 slices, $p<0.05$). In addition, leftward shift in the input-output curves recorded before and 1h post LTP was absent upon NNGH treatment. In conclusion, MMPs, and in particular MMP-3, may interfere with NMDARs function upon episodes of increased synaptic activity and thus may affect the level of postsynaptic calcium influx in Sch-CA1 synapses. Supported by MNiSW grants NN401541540 and partially by 3/Pbmn grant.

17. Spatial variability of cortical ripples in humans

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Based on animal and human research ripple oscillations (80-300Hz) participate in physiological processes and epileptiform transformations in the brain. The cortical generators of such fast oscillations were demonstrated to have generators limited to a small cortical area. The purpose of this study is to describe the spatial variability of ripple oscillations and demonstrate that wide cortical area can contribute to their generation. Epilepsy patients undergoing

invasive preoperative evaluation were selected in this study. Two patient, (Pat1, Pat2) data were analyzed. The right frontal area (Pat1) and the left temporo-central area (Pat2) was covered by subdural grid electrodes. Ripple oscillations were detected on slow wave sleep EEG segments using automated method, detecting group of peaks (25 ms maximal within time) as putative ripple events (PR) exceeding 5 standard deviation (SD) of band pass and root mean square filtered data. The majority of PRs appeared on 1 or 2 channels, but there was a significant proportion of the events presented on various number of channels, in some cases almost all channels. Wide range ripples were found more often in the proximity of the seizures. In this case long-tailed distribution was observed in the involved channel number histogram. We demonstrated that relatively large cortical areas may contribute to the genesis of ripple oscillations that area might vary significantly. Two populations of small and wide range ripples were demonstrated. We hypothesize that the cortical extent of the ripples may be a factor of its epileptogenic nature. Supported by OTKA PD101754, TÁMOP-4.2.1./B-11/2/KMR-2011-002,T ÁMOP-4.2.2./B-10/1-2010-0014, TÉT-Multisca, TÉT-Neurogen, FP7-Neuroseeker, OTKA K81354.

18. Delayed hemodynamic response at 48 hours following global cerebral ischemia in rat

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Modern functional brain imaging techniques rely on the constancy of the neurovascular coupling process, measured by its hemodynamic response function (HRF). Nevertheless, brain pathology may alter the HRF confounding the interpretation of imaging studies. We have recently proposed a method to investigate the HRF by taking advantage of the discontinuous burst-suppression (BS) electrocorticographic (ECoG) pattern induced by anesthesia. The aim of this study was to analyze in rats whether the HRF is altered at 48 hours after a minimally injuring global cerebral ischemia (GCI). In 6 male Wistar rats (control), BS patterns were induced by an overdose of chloral-hydrate (CHL). In other 5 rats, a 5-minute GCI was performed, using a variation of the 4-vessel occlusion model. 48 hours post-GCI, the anesthetic BS was induced. Simultaneous ECoG activity and Laser Doppler (LD) signal were recorded from the left hemisphere. Post-GCI, with decreasing bursting frequency there was a progressive increase of HRF latency (time to HRF peak) that could be reasonably described by a linear regression ($R2=0.21$; slope $F=13$, $P<0.01$). The HRF latency also seemed to increase at lower bursting frequencies in control rats, with a similar slope. The Y-intercept was, however, about half than after GCI ($F=81$, $P<0.01$). The delayed hemodynamic response after GCI could not be attributed either to cardiovascular changes (heart rate remained normal) or to changes in electrical activity patterns (intra-burst ECoG was similar to that during anesthetic coma). Our data suggests that the process of neurovascular coupling itself is altered following GCI in rats.

EPILEPSY

19. Between-litter variations in susceptibility to electroshock-induced seizures

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According to clinical and experimental data, dysplastic brains display an increased susceptibility to spontaneous or evoked seizures. Electrostimulation lacks functional preference to any neuronal subsystem in contrast to chemically-induced seizure models. Here, we assessed individual as well as between-litter variations in seizure susceptibility in normal rats and rats with irradiation-induced brain dysplasia. Pregnant Wistar rats were exposed to a single 1Gy dose of gamma rays on gestation days: 13, 15, 17 or 19. Their male offspring as well as age-matched controls were subjected from postnatal day 60 to a series of 21 daily electrical stimulations to evoke seizures. After each stimulation, animals were placed in individual cages and observed until electroshock-induced behavioral symptoms disappeared. Evaluation of tonic seizures was done according to a previously established severity index scale. Significant differences were seen between litters in all experimental and non-irradiated control groups except for that irradiated on E17. The latter, however, showed seizures of minimal intensity which apparently might not be sufficient for expression of the between-litter variations at the level of statistical significance. We hypothesize that genetic diversity among animals and maternal effect could be responsible for these findings. Supported by NCN grant:2011/01/B/NZ4/00586.

20. Early manipulation of the endogenous cannabinoid system in WAG/Rij rats. The long term effects of chronic manipulation of the endogenous cannabinoid system with R(+)WIN55,212-2 on absence epilepsy, anxiety and pain

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Endocannabinoids play a role in signalling pathways. They act pre-synaptically, inhibiting the release of neurotransmitters. Cannabinoids are found to reduce pain and anxiety. Furthermore there is a connection between cannabinoids and epilepsy. To study the effects of CB1 receptor agonist R(+)WIN55,212-2 on pain, anxiety and absence epilepsy, 30 male WAG/Rij rats were used. At the age of 30 days 10 animals received 12 subcutaneous injections, within four weeks, with R(+)WIN55,212-2. The control group received the same amount of injections with vehicle. A third group did not receive injections. During adulthood two behavioural tests were conducted: the Elevated Plus Maze for anxiety and the Von Frey Hair test to evaluate the pain threshold. A 24 hour EEG was recorded. The study was blinded. R(+)WIN55,212-2 enhances the stress-induced reduction in SWD incidence and duration of the experimental procedure itself. No differences were found in the Von Frey hair test. R(+)WIN55,212-2 treated animals and controls are more anxious than rats who did not receive treatment. The likely cause is the pain of the injections. Manipulation of the endogenous cannabinoid system during early adolescence causes a reduction in the number of absence epileptic seizures per hour and the total duration of absence epileptic seizures.

21. Increased mRNA stability is a mechanism controlling Matrix Metalloproteinase-9 upregulation during epileptogenesis in the rat hippocampus

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Hippocampus is a brain structure crucial for a pathomechanism of epilepsy. MMP-9 is a pro-epileptic protein involved in a formation of aberrant brain neuronal networks during epileptogenesis, what finally leads to a development of seizures. Despite of its essential role in etiology of epilepsy, regulation of MMP-9 expression during epileptogenesis is unknown. Similarly, a dependence of MMP-9 expression on mRNA stabilization mechanisms in the brain is completely obscured. Our goal is to determine the existence of these mechanisms and to reveal their molecular machinery. As a model of rat epileptogenesis, we have applied repeated administration of GABA-A receptor antagonist – pentylenotetrazole at a subthreshold doses. Using RNA degradation assay, we have found significant stabilization of MMP-9 mRNA occurring duringepileptogenesis in the rat hippocampus, and corresponding to the phenomenon, a gradual upregulation of its hippocampal mRNA expression. Additionally, applying RNA electrophoretic mobility shift assay, we have detected changes in bindings of mRNA stabilizing proteins to the 3'UTR of MMP-9 mRNA during epileptogenesis in the rat hippocampus. Altogether, our results suggest that mRNA stabilizing mechanisms play an important role in a regulation of MMP-9 mRNA levels during epileptogenesis in the rat hippocampus. This work was supported by NCN grant No.2012/05/B/N23/01943.

22. The Role of Serum Response Factor in development of epilepsy in the adult brain

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Serum Response Factor (SRF) is thought to play a role in activity-dependent gene expression and in epilepsy, a chronic neurological disorder. An inducible Cre/loxP system was used to delete Srf gene in mice forebrain neurons. To test if lack of SRF in adult brain leads to spontaneous aberrant neuronal activity we recorded and analyzed EEG from freely behaving animals after injection of kainic acid into CA1 field. Mice with SRF deficiency had more seizures (increased seizures frequency), their seizures were more severe and duration of status epilepticus was longer. To investigate the role of SRF in epileptogenesis we checked if SRF deletion results in increase of seizures evoken by chemical kindling with PTZ (pentylenetetrazole). Kindling was performed by repeated intraperitoneal injections of subconvulsive (34mg/kg) doses of PTZ for several weeks in WT and SRF KO animals every other day. In SRF KO mice increased seizures severity in response to PTZ-induced kindling over time was observed. SRF KO mice have gradually become hypersensitive in response to prolonged stimulation probably due to the lack of important SRF-dependent genes activity.

23. GABA exerts opposite actions in cortex and thalamus in a genetic absence epilepsy model

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Recent signal analytical and pharmacological studies in rodents have paved the way for new theories on absence epilepsy. It is now established that spike-wave discharges (SWDs) originate in the somatosensory cortex and from there propagate through the Cortico-Thalamo-Cortical network to the thalamus and back. It has been shown that astrocytic GAT-1 functioning is impaired in the thalamus of genetic models of absence epilepsy, leading to increased tonic GABA-A inhibition and the presence of SWDs. Tiagabine, a GABA agonist, blocking the reuptake of GABA via GAT-1, increases SWDs when administered systemically. Here we investigate whether this GABA-ergic mechanism is similar in cortex and thalamus in WAG/Rij rats by comparing the response to local microinjections of tiagabine in both regions. Tiagabine showed opposite effects depending on the brain site of administration: SWD occurrence time and dose dependently increased when administered in thalamus but decreased when injected in the cortex. This is in line with the view that tonic inhibition is enhanced in the thalamus, but is reduced in the cortex. Different and opposite GABA-ergic mechanisms might be responsible for the initiation of the spontaneous seizures in cortex and the resonance of thalamic neurons.

24. Seizures contribute to their reoccurrence: open and closed loop stimulation compared

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Spike-wave discharges (SWDs) are the hallmark of absence epilepsy. This study investigated if the timing of stimulation related to SWD occurrence (closed loop: seizure contingent vs open loop: non-contingent) contributes to number and duration of SWDs later on. 15 WAG/Rij rats went through 5 days of 24h EEG and locomotor activity recording. A baseline was done, followed by two stimulation sessions, closed and open loop stimulation (counterbalanced). Stimulation sessions were followed by postmeasures. A day effect for both stimulation sessions on number and duration of SWDs was found: rats had less SWDs during stimulation than on baseline. Duration of SWDs during stimulation session was shorter than on baseline and postmeasure. A day*hour interaction for closed loop stimulation was found: during the last eight hours of the post measure less SWDs were generated compared to baseline. Absences seizures can be successfully interrupted by closed loop cortical stimulation, and the suppressive effects persisted during the postmeasure day. In contrast, open loop stimulation was less effective and seizures returned to baseline level. Closed loop stimulation has lasting seizure suppressive effects compared to open loop stimulation. This new finding suggests that seizures themselves are involved in their reoccurrence.

NEUROGENETICS

25. Involvement of TOR signaling pathway in the regulation of circadian rhythms

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Drosophila melanogaster is a valued model used in neurobiology and chronobiology and clock mutants have been isolated for the first time in this species. In the present study we examined an involvement of TOR signaling pathway in the regulation of the circadian rhythm in locomotor activity of D. melanogaster. Wild type CantonS flies and transgenic lines with silenced expression of tor, TSC, atg5 and atg7 genes in cells expressing per gene were used in this study. The expression of tor, atg5 and atg7 genes was examined by means of Real-Time PCR technique. Flies with silenced expression of above mentioned genes were used for locomotor activity analysis. The obtained results showed, that mRNAs of tor, atg5 and atg7 genes cycle in the brain of D. melanogaster. Moreover in flies with silenced expression of TSC gene in clock cells expressing per, the period of the locomotor activity rhythm was slightly longer and their activity level was higher when compared with the control. Our results showed, that TOR signaling pathway in clock cells maintains the period of the circadian rhythm in locomotor activity and regulates activity level of D. melanogaster. This work was supported by NCN grant No. UMO-2011/03/N/NZ3/01250 to EK.

26. Mutation in GBA gene involved in Gaucher disease in the eye of D. melanogaster affects circadian plasticity and lifespan

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Gaucher disease (GD) is one of the most common lysosomal storage disorders, caused by defects in the GBA gene encoding glucocerebrosidase. The aim of our study was to investigate how this mutation in photoreceptors affects lifespan, behaviour and the circadian rhythm in the level of synaptic protein Bruchpilot (BRP) in the first optic neuropil (lamina). The following lines were used in the experiments to express GBA mutation in photoreceptors driven by GMR promotor: w; GMR-GAL4/Cy0; UAS – GBA – RecNciI01, w; GMR-GAL4/Cy0; UAS – GBA- RecNciI04 and w; GMR-GAL4/Cy0;UAS-GBA-R120W21. The obtained results showed that the rhythm in BRP abundance was disrupted in two of three of examined GD model lines when compared with the control. The BRP rhythm changed from bimodal in control into unimodal, with a peak at the beginning of the night in w; GMR-GAL4/Cy0;UAS-GBA-R120W21 line. In w; GMR-GAL4/Cy0; UAS – GBA – RecNciI01 flies the rhythm was absent. Lifespan of investigated lines was longer with comparison to wild-type flies. In conclusion the mutation in GBA gene affects lifespan and circadian synaptic plasticity of flies, though it is present only in GMR expressing cells.

27. Small non-coding RNA regulates directly expression of synaptic plasticity related protease MMP-9 in activated hippocampal neurons

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Matrix Metalloproteinase-9 (MMP-9) is an extracellular enzyme stimulating development of synaptic plasticity. Its expression is neuronal-activity dependent, complex and regulated mainly on mRNA level. Our previous published and non-published data has showed that neuronal depolarization-dependent MMP-9 mRNA expression in the brain neurons is regulated by some epigenetic mechanisms, like histone modifications and DNA methylation. Thus, here we have studied miRNA dependence of MMP-9 expression after neuronal depolarization in the rat hippocampal neurons in vivo and in vitro. In silico analyses have selected miRNAs which can potentially bind to MMP-9 mRNA. We have evaluated their expression after neuronal depolarization in the rat hippocampus in vivo and in the hippocampal neurons in vitro showing that changes in their expression are inversely correlated to MMP-9 mRNA expression changes. Moreover, using luciferase reporter assay we have confirmed that these selected miRNAs silence MMP-9 mRNA expression via its 3\'UTR region in hippocampal neurons. Finally, we have demonstrated by gel zymography that overexpression of these miRNA molecules block native MMP-9 expression in the hippocampus. These results strongly suggest an involvement of RNA interference mechanisms in the complex regulation of MMP-9 expression after neuronal depolarization in the rat hippocampal neurons.

28. Selected gene polymorphisms in patients with brain tumors

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Brain tumors create a heterogeneous group with various biological behavior, therapy management and differing prognosis. Their etiology is multifactorial. The tumors take their origin as a result of an accumulation of various genetic alterations which allow the cells to escape physiological regulatory mechanisms and their destruction by the immune system cells. Various genetic alterations have been studied in connection to brain tumors. Glutathion S-transferases (GSTs) are enzymes that function on the detoxification of a wide range of exogenous agents including carcinogens. GSTs polymorphisms have been associated with brain tumor risk, survival rate in cancer patients and drug resistance and response of patients to therapy. Polymorphisms of epidermal growth factor (EGF) and insulin-like growth factor (IGF) are connected with poor survival of patients. TP53 is a critical tumor suppressor thatrestricts proliferation and cell

growth following stress. It is one of the most frequently mutated genes in human cancer cells. Patients with brain tumors (n= 33) who underwent surgery were included into this study. Patients were taken the venous blood sample. The sample of brain tumor tissue was obtained during open surgery. Using PCR method we evaluated the presence of polymorphisms of GSTs, TP53, EGF and IGF binding protein 3 (IGFB3) in obtained samples. We compared the results between samples of blood of the patients, samples of brain tumor tissue and venous blood samples from volunteers without any anamnesis of tumor. We observed significant ($p \geq 0,05$) differences in distibution of polymorphic allele C of TP53 gene between blood and tumor tissue of brain tumor patients. Significant difference was also observed in distribution of allele A and heterozygous and polymorphic genotype of IGFB3 gene between blood of controls and blood of tumor patients. No other significant differences were observed. Our preliminary results on small group of patients show higher incidence of TP53 and IGFB3 polymorphisms in patients with brain tumors. However, there is a need for more data before definitive conclusion could be made.

29. Regulation of MMP-9 mRNA by miR-132 in neurons

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The matrix metalloproteinase-9 (MMP-9) is an endopeptidase which plays an important role in synaptic plasticity. MMP-9 mRNA is transported to dendritic spines where it is locally translated and released to the extracellular environment in the activity-dependent manner. The active MMP-9 is involved in the reorganization of dendritic spine morphology through the cleavage of protein components of the extracellular matrix. Mir-132 is an neuronal-activity regulated micro RNA whose role in synaptic plasticity have been reported. Particularly it influences the morphology of dendritic spines having an opposite effect to MMP-9. The putative miR-132 binding site was predicted in the 3'UTR of MMP-9 mRNA. Therefore we investigated whether miR-132 regulates MMP-9 mRNA in neurons. To determine whether miR-132 binds to the 3' UTR of MMP-9 mRNA and inhibit translation, mir-132 was cotransfected with a luciferase reporter containing the 3'UTR of MMP-9. Overexpression of miR-132 in cortical neurons reduced the luciferase activity of the reporter construct. In the same time miR-132 failed to regulate the mutated MMP-9 3'UTR luciferase reporter, suggesting that it binds to the predicted seed sequence. The overexpression of miR-132 in neurons leads to the decrease of the level of secreted MMP-9 protein but do not affect the MMP-9 mRNA level. We hypothesize that miR-132 negatively regulates the level of MMP-9 in neurons through the inhibition of MMP-9 mRNA translation.

METHODS – NEUROBIOLOGICAL PERSPECTIVE

30. High-performance and reliable site-directed in vivo genetic manipulation of rodent brain by in utero electroporation with a triple-electrode probe

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In utero electroporation is a powerful tool to manipulate neural-precursor cells of the parietal cortex and their progeny in vivo. The standard method entails a quick and easy surgical procedure to inject DNA in the embryonic brain, followed by exposure to an electric field by a bipolar electrode. Here, we validate a new in utero electroporation design based on the use of three electrodes. This enables a more suitable positioning of the electrodes and overcomes the physical limitations of the common bipolar configuration. By simply adjusting the relative positions and polarities of the three electrodes, hippocampus, and motor, visual as well as prefrontal cortices were targeted with extremely high consistency, in comparison to standard bipolar configuration. Finally, the tripolar configuration, in virtue of the increased efficacy of the electrical field distribution, demonstrated here by a mathematical simulation, allowed extension of the developmental timeframe for reliable electroporation, succeeding for the first time in transfection of Purkinje cells in the cerebellum. Thus, the tripolar configuration offers a conceptual advance in the in utero electroporation technique that will further thrust the experimental frontiers paving the way to targeting new brain areas by simply varying the number, together with the polarities of the electrodes.

31. Generation of transgenic mice with selective inactivation of opioid receptors in the brain's reward system

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Opioid receptors are ubiquitous in the central nervous system and are best described for their roles in analgesia and processing of rewards. The activation of opioid receptors leads to inhibition of the neuron's activity, which indirectly may cause disinhibition of other cells and an increase in activity. The aim of this project is to create transgenic animals carrying miRNA selectively targeting opioid receptors in different brain regions. miRNAs targeting Oprm1, Oprd1 and Oprk1 receptors were designed with the BLOCK-iT RNAi Designer and cloned into pcDNA™6.2-GW/EmGFP-miR plasmids. For each opioid receptor we have chained two miRNAs targeting various regions of a single exon. miRNA silencing efficiency was validated in the CHO-K1 cell line co-transfected with the plasmids encoding opioid receptors and miRNA cassettes. Transfection of CHO-K1 cells resulted in at least 50% reduction in the transcript abundance. Validated miRNAs were recombined with D1, Dbh and DAT promoter carrying bacterial artificial chromosomes using the Red-ET recombination system. Purified transgenes were transferred by pronuclear injection to generate transgenic mice with selective inhibition of Oprm1 and Oprd1 in dopaminoceptive, Oprm1 in noradrenergic and Oprk1 in dopaminergic neurons. The methodology developed here may simplify generation of transgenic mice for studies on brain function.

32. Different precipitation methods in sample preparation for 1D and 2D electrophoresis

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Two-dimensional electrophoresis is still the most applied separation technique in proteomics. One of the difficulties in 2D electrophoresis is the presence of different sample impurities. There are several methods for sample precipitation to remove disturbing compounds. However, precipitation is prone to protein loss and it is necessary to improve sample preparation methods. Our aim was to evaluate different precipitation methods before electrophoresis of rat brain mitochondria and their impact on sample purity. We carried out three precipitation procedures – 2D Clean up kit, acetone/TCA precipitation and acetone precipitation. At 1-D SDS-PAGE precipitation with Clean up kit and acetone/TCA resulted in protein loss. Acetone precipitation seems to be an efficient sample concentration and desalting method. We also evaluated duration of isoelectric focusation (IEF) during 2D electrophoresis. Our results suggest that precipitation method does not affect the IEF. There were no significant differences in 2D gels between untreated and treated samples. Our study suggests that sample precipitation with acetone is the most efficient and does not affect IEF.
This work was supported by VEGA 1/0129/14; 1/0213/12 and project "Identification of novel markers in the diagnostic panel of neurological disease", ITMS: 26220220114, co-founded from EU sources and European Regional Development Fund.

33. A model of morphine addiction using group-housed mice

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Commonly used approaches for modeling morphine dependence involve the use of conditioned place preference, which lacks voluntary intake of the drug, and morphine self-administration, which requires isolating the animals. We wanted to create a model of opiate addiction under more natural conditions. Here, we describe a new model of voluntary morphine drinking by group-housed mice. We decided to use Intellicage system to observe group-housed animals without unnecessary experimental intervention. The animals were allowed free access to sweetened morphine or saccharine for 3 executive months. Then, we behaviorally challenged animals to Background: Commonly used approaches for modeling morphine dependence involve the use of conditioned place preference, which lacks voluntary intake of the drug, and morphine self-administration, which requires isolating the animals. We wanted to create a model of opiate addiction under more natural conditions. Here, we describe a new model of voluntary morphine drinking by group-housed mice.We aimed to test for symptoms of compulsive morphine drinking (saccharin reduction, progressive ratio schedule and schedule involving a risk of punishment). Sweetened morphine preference was 80-90 %, and maintained stable at 70-80 % even after complete removal of sweetener, that is despite the bitter taste of the drug. The animals performed significantly increased number of instrumental responses to obtain access to the bottle with morphine (progressive ratio schedule), when compared to saccharin. The risk of punishment resulted in significant reduction of drinking saccharin solution, whereas drinking of morphine solution remained stable. In conclusion, the model we describe avoids the limitations associated with testing isolated animals and reliably leads to stable morphine

drinking. Therefore, this model may be well suited to screening for the effects of genetic mutations or pharmacological treatments on morphine-induced behaviors.

34. Through the looking glass - are transfering data between animal and human really so simple?

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Animals (like mice) are a popular model for various studies, there are about 47,7% ongoing researches in the nervous system area conducted using various animal in the last year. This selectively bred, transgenic animals are used in wide branch of tests, such as drugs screening, testing new therapy, finding candidate genes for human brain disorders. Human neurological disorders could be modelled by procedures which recreates specific pathogenic conditions and their behavioral outcomes but there is a doubt about the degree to which complex neurological deficits can be productively studied in lower species.Only within the last year a few of novel drugs for human diseases (like Bapineuzumab, Semagacestat or LY2886721 for Alzheimer; Bitpertin and Bl-120 for Schizophrenia)*failed into Phase II or III of clinical trials as a potentially dangerous or ineffective. Inter-species diferencies and possibility of false similarities complicate translation of animal tests into human treatment. We examine methodological constraints on the animal models. We use complex clinical data to corroborate or falsify criteria of validating animal models. In animal model of diseases focus is on analogous behavioral and physiological phenotypes, functional polymorphisms and conservation of gene functions. We carefully analyse those justifications. Most of the tested research in our hypothesis are burdened with"false-positive effect. We propose a list of things which seems to be mostly problematic in prediction (and possibly a reason of) tests failure. Further analysis is recommended, but preliminary results indicated that that ethical and methodological issues needs to be raised while designing the research. Furthermore, we propose some remarks to improve existed methodology used to evaluation of animal model used in research.

35. A comparative analysis using four selected R classification packages

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The paper compares the effectiveness of four algorithms written in R, which have been used to classify a few selected datasets. For this comparison the paper uses four R packages: the maptree package, the randomForest package, one of the versions of the boosting algorithm written using raw R commands, the adabag package and the nnet R neural network package. By using these packages the paper compares the abilities of four algorithms written in R to classify data, i.e. the classification tree algorithm, the random forest algorithm, the boosting algorithm and the back-propagation neural network algorithm. All these algorithms have been tuned up by modifying their available entry arguments to increase the possible results. More valuable intermediate outcomes obtained for various input options of these four packages have been compared with the final results and visualized using the R shiny package. Additionally the paper presents the contents of the scripts with R commands used for this comparison and analysis.

DEVELOPMENT / APOPTOSIS / NEUROTOXICITY

36. Impact of Triclosan on activation of aryl hydrocarbon receptor (AhR) in mouse neocortical cells

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Triclosan is an antimicrobial component commonly used in personal care and sanitizing products, as well as in household items. Triclosan has been detected in human breast milk, blood samples and as metabolites in the urine. The aim of the present study was to investigate the effect of Triclosan on the activation of AhR in cultured neocortical mouse neurons. Aryl hydrocarbon receptor is well known to be involved in the neural development and apoptosis. The cultures of neocortical neurons were prepared from Swiss mouse embryos on 15/16 days of gestation. The cells were cultured in phenol red-free Neurobasal medium with B27. To study the involvement of AhR in the action of Triclosan, the specific AhR agonist beta-Naphthoflavone and antagonist alpha-Naphthoflavone were used. The release of lactate dehydrogenase (LDH) and caspase-3 activity were measured after 6 and 24 hours of cells exposure to Triclosan and AhR agonist or antagonist. Our experiments have shown that Triclosan induces caspase-3 activity, apoptotic body formation, and LDH release. Co-treatment with both, AhR agonist and antagonist potentiate the neurotoxic effects of

Triclosan. In summary, our preliminary data demonstrate that AhR is involved in the mechanism of Triclosan action in neuronal cells.

37. The effect of DEHP on viability and apoptosis in mouse hippocampal neuron cells

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Di-2-ethylhexyl phthalate (DEHP) is one of the most popular plasticizers used in a large variety of products including flexible PVC materials, enteric coatings of pharmaceutical tablets and household products such as paint and glues. There has been a growing concern regarding potential toxicity and endocrine disrupting effect to human associated with DEHP. The aim of this research was to investigated the cytotoxicity of DEHP and its impact on apoptosis in mouse hippocampal cells. The cultures of hippocampal neurons were prepared from Swiss mouse embryos on 18/19 days of gestation. The cells were cultured in phenol red-free Neurobasal medium supplemented with B27 in the presence of rising concentration of DEHP for 6, 24 and 48h. Afterwards, lactate dehydrogenase (LDH) releases, caspase-3 activity and apoptotic bodies formation were studied. The results showed that after 24 and 48 hours of exposition to DEHP the decrease in LDH release was observed. However, the caspase-3 activity as well as the amount of apoptotic bodies were increased. To conclude, DEHP enhance hippocampal neurons apoptosis in dose dependent manners. Support by NCN grant 2012/07/B/NZ4/00238

38. Analysis of acetylcholinesterase (ACHE) activity in selected brain structures of mice after intra-peritoneal injection of Acrylamide

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Acetylcholinesterase is a key enzyme in central and peripheral nervous systems. Acrylamide is a good example of such toxic ingredients of human diet. It is present in numerous popular food products. International Agency for research on Cancer classified acrylamide as probable human carcinogen (Chico et al., 2006; Mustafa et al., 2008). The aim of our work was to estimate activity of acetylcholinesterase in selected brain structures after acrylamide: the right hemisphere, the left hemisphere, cerebellum and brainstem. The experiment was carried out on 24 male mice of Swiss strain, average body weight 25 to 26 g, fed standard diet with unlimited access to water. The measurements were performed after 48, 72 and 192 hours after acrylamide injection in two doses – 20 mg/kg and 40 mg/kg. Statistical analysis was performed using analysis of variances ANOVA. Homogoneity of variances was estimates using Dunnett test. We noticed influence of acrylamide on acetylcholinesterase activity in selected brain structures. There were significant changes in the activity of acetylcholinesterase in each structure after 48, 72 and 192 hours. This changes were after both doses of acrylamide (20 mg/kg and 40 mg/kg). Both doses of acrylamide caused decreased activity of acetylcholinesterase. In most of the structures the significance level was at p=0,001. It seems that the decrease of acetylcholinesterase activity was associated with toxic properties of acrylamide.

39. Biochemical change in blood, activity and cognitive function in rats on high fat diet

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Recent studies have shown that fat and caloric intake is associated with not only development of obesity and metabolic disease but also with impaired cognitive performance, in particular learning and memory in humans and in laboratory animals. The biochemical relationship between high fat diet and cognitive decline is still unclear. In our experiment we used fifty male Wistar rats and divided them into two groups (n=25). Animals were fed standard laboratory chow or high-fat diet (HFD) with high level of sucrose (40%fat, 40% sucrose) for a year. Body weight, blood levels of glucose and ketone bodies were measured every two weeks. Spatial learning was assessed with radial 8-arm maze at 3-, 6-, 9- and 12-months. Blood levels of glucose and ketone bodies were significantly elevated in the experimental group. Furthermore, rats on HFD diet were finding a prize significantly faster and were more active than control group. Our results are not in line with previous studies and suggest that high level of fat and sugar in the diet do not directly lead to deterioration in learning. Supported by a grant from the Polish National Science Center (2011/03/B/NZ4/03771).

40. Effect of homocystein and its metabolites on the viability of human glial cells

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Hyperhomocysteinemia is considered to be a risk factor for neurodegenerative disorders and is associated with cognitive and memory decline as well as brain atrophy in humans. Several molecular mechanisms underlying the detrimental effect of homocysteine (Hcy) on neuronal cells were suggested and their role in impairing the physiological functions of animal neural cells was tested. The effect of Hcy and its metabolites (2-oxo-butyrate and cysteine) on survival of human glioblastoma cell line, T98G, was tested by biochemical methods, MTT test and LDH assay. Decreased cell viability induced by Hcy was partially observed after short term (24 hrs) and strongly in long term (72 hrs) administration. It indicated a cumulative toxic effect of Hcy on human glial cells. However, cytotoxicity was also induced by 2-oxo-butyrate, but only in long term (72 hrs) administration. Cysteine had no effect on survival of T98G cells. Our results indicate that neurodegeneration assotiated with hyperhomocysteinemia can be consequenced on damage processes not only in neurons but in glial cells too. This work was supported by projects VEGA grant 1/0242/13;\"Competence Center for Research and Development in the diagnosis and therapy of oncological diseases“ code ITMS 26220220153; The increasing of opportunities for career growth in research and development in the medical sciences“, code ITMS: 26110230067; “Identification of novel markers in diagnostic panel of neurological diseases, code ITMS: 26220220114.

41. Duration of incubation of SK-N-SH and U-87MG cells in presence of oxytocin modulates levels of cytoskeletal proteins associated with neuronal growth

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Neuropeptide oxytocin potentially modulates growth of neuronal cell processes by stimulation of oxytocin receptor and cytoskeletal proteins. The aim of present study was to evaluate effect of different durations of incubation (2, 6, 12, 48h) with 1 μM oxytocin on mRNA and protein levels of cytoskeletal proteins nestin, microtubule-associated protein 2 (MAP-2) and oxytocin receptor (OXTR) in neuroblastoma SK-N-SH and glioblastoma U-87MG cells. After 12 hours, levels of mRNA for nestin significantly increased in both cell types, but after 48 hours changes disappeared. We did not find any major changes in protein levels of nestin in SK-N-SH cells, but they were elevated after 48 hours in U-87MG cells. Levels of mRNA for MAP-2 increased after 12 hours and decreased after 48 hours in U-87MG cells. After 12 hours levels of mRNA for OXTR increased in both cell types and protein levels increased in U-87MG cells after 48 hours. Our results indicate that time effect of oxytocin could be important for growth of neuronal cones and regulation of microtubule stability. Growth and differentiation of neuronal cells might be modulated by fluctuations in quantity and activity of oxytocin receptors. Supported by grants of APVV-0253-10, VEGA 2/0132/12.

42. The assessment of the level of ghrelin in animal model of obesity

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Binge eating is defined as overconsumption of food in a short time (about 2 hours). The potential explanation of this phenomenon is based on deregulation of dopaminergic neuronal pathway (reward circuits). The aim of this study was to determine the level of ghrelin, the hormone that stimulates the reward system and willingness to eat. Male Wistar rats (300 ± 20g) were kept in separate cages at room temperature 22º C and humidity of 40-50% under reverse 12h light-dark cycle. Animals were divided into four groups according to food exposure: (I) control (standard diet), (II) high/fat/sugar diet continuously, (III) high fat/sugar diet daily with 2-h access from 8 to 10 a.m. and (IV) high fat/sugar diet access every two days. The level of ghrelin was assessed by means of the Elisa test (Merck Milipore TM). The data obtained was evaluated by one-way Anova and T-student test with Benferroni correction. The results revealed the statistically significant difference only in sucrose fed animals [$F(3,28)=8,795$; $p=0,001$]. It could mean that in this group both diet and eating schedule influenced the level of aforementioned hormone.

43. Lack of differences in size of pituitary adenomas in Eker rats subjected to ketogenic diet

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Ketogenic diet is already used in tuberous sclerosis (TS) patients, however its influence on tumor growth is still not clear. Eighty two Eker rats, an animal model of TS, were used in the experiment. 62 have been maintained on high fat, low carbohydrate ketogenic diet for 8 (KD8, n=26), 6 (KD6, n=19) and 4 (KD4, n=17) months, while 20 (control group) – received a standard diet. At the age of 14 months, all rats were sacrificed, pituitary adenomas were collected and their volume was measured. Immunohistochemistry for MMP-9, p53, VEGF and PCNA was prepared. Average level of ketone bodies in ketogenic groups was 1.6 mM, while in control it was 0.63 mM. Glucose level in animals on ketogenic diet was lower (4,4 mM) in comparison with control (8,4 mM). Mean tumor volume in ketogenic groups was 89 mm3 (KD8), 143 mm3 (KD6) and 163 (KD4) vs 217 mm3 in control. Size of tumors does not differentiate statistically between groups, thus ketogenic diet has no influence on volume of pituitary adenomas. Pituitary adenomas show a positive staining for MMP-9, p53, VEGF and PCNA. Presence of these markers characteristic for invasive tumors confirms an aggressive potential of pituitary adenomas in Eker rats.

44. Effect of body temperature on the level of lipid peroxidation products in newborn rats exposed to an anoxia

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Anoxia is a common cause of damage in the neonatal brain. The important process responsible for the severity of brain injury as a result of anoxia and reoxygenation is excessive free radicals formation, lipid peroxidation and ultimate neuronal cell death. Because body temperature maintained during anoxia and reoxygenation is very important factor that affects the extent of the brain lesions we decided to test effect of body temperature on the level of lipid peroxidation products in newborn rats exposed to a critical anoxia. Two days old newborn rats were subjected to 10 min anoxia in 100% nitrogen atmosphere followed by 120 min resuscitation period. Their body temperature was kept at different levels: 31°C (hypothermic conditions), 33°C (typical of rat neonates) or 39°C (elevated to the level typical of febrile adults). Control rats were exposed to atmospheric air in the respective thermal conditions. The concentration of thiobarbituric acid reactive substances, conjugated dienes and concentration of free malondialdehyde were determinated in brain homogenates. These preliminary data showed that simulated perinatal anoxia in rats with elevated body temperature to 39°C, as well as, at hypothermic conditions 31°C induces oxidative changes in the brain, whereas physiological body temperature of neonates protects them from such disturbances.

45. High-fat high-carbohydrate diet is surprisingly good for hippocampus in an animal model

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Obesity was associated with accelerated aging and elevated risk of neurodegenerative diseases. In animal models, high-fat high-carbohydrate diet (HFCD) is commonly used to induce obesity. We hypothesized that HFCD will lead to lower concentrations of brain metabolites in hippocampi, which are predictors of neurodegenerative diseases both in humans and in laboratory animals. Twenty five male Wistar rats were put on HFCD (~40% fat, ~40% carbohydrates) on their 55th day of life, while 25 control male rats (CON) remained on chow. At one year, all animals 1H magnetic resonance spectroscopy at 7T. HFCD rats consumed slightly more calories than CON, but less proteins. However, their protein intake was within recommended amounts. Contrary to our hypotheses, HFCD rats had 8% larger concentration of N-acetylo-aspartate, marker of neuronal viability, p=0.01), .6% larger concentrations of both glutamate (neurotransmitter playing a role in long-term potentiation), as well as creatine containing compounds (p=0.02 and p=0.001, respectively) than CON. The results do not support the thesis that HFCD per se leads to degeneration of the nervous system. On the contrary, it lead to improved markers of neuronal viability. More research is needed to pinpoint the mediating factors. Supported by Polish National Science Centre (2011/03/B/NZ4/03771) to S. Gazdzinski.

46. Autophagy inhibition reduces cell viability and influences apoptosis in astrocytes exposed to oxygen and glucose deprivation

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Recent studies have implicated important role of autophagy in cerebral ischemia pathophysiology. It remains unclear whether autophagy activation is protective or detrimental for cells suffering from ischemic insult. The present study evaluates contribution of autophagy activation to cell death in rat primary astrocyte cultures subjected to combined oxygen glucose deprivation (OGD) for 1, 4, 8 and 24 h. The role of autophagy in OGD-induced death of astrocytes was assessed by pharmacological inhibition of autophagy with 3 - methyladenine (1mM). The levels of autophagy- and apoptosis- related proteins were examined with immunoblotting. Cell viability was determined with alamarBlue Assay (Invitrogen) and LDH assay. To evaluate ischemia-induced mitochondrial damage, mitochondrial membrane potential was determined with JC-1. Autophagy inhibition was confirmed by reduced number of monodansylcadaverine (MDC)-labeled vesicles and p62 accumulation. The results showed that autophagy inhibition reduces cell viability and worsens ischemia -induced mitochondrial damage. Moreover, autophagy inhibition enhances stress-induced cytochrome C release as well as caspase 9 and caspase 3 activation. Our results suggest that autophagy activation during ischemia may be a protective mechanism that helps astrocytes to survive in stress conditions and delays apoptosis activation.

47. Human glioblastoma cells response to combined treatment with biologically active phospholipids and cytostatics in vitro

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Glioblastoma is the most common primary brain tumor in adults. Chemoradiotherapy is the standard care for newly diagnosed glioblastoma. Resistance to chemotherapy is a major obstacle to successful treatment. Biologically active phospholipids derivates has adjunctive beneficial effects in tumor and metastasis inhibition, although mechanism of their influence is still unknown. We study human glioblastoma cell line (T98G) response to combined treatment with biologically active phospholipids (BAF®) and cytostatics. Viability of cells was assayed biochemically by cytotoxic methyl-thiazol tetrazolium (MTT) assay and cytologically by cellular nuclei staining with DAPI and by histological staining with May-Grünwald/Giemsa. Results of our study confirm that cultivation of T98G cells with active form of BAF® induces cell death while cultivation with inactive form of BAF® or without BAF® has no inhibition effect on cells growth. Cultivation with cytostatics alone shows different responses of glioblastoma cells to specific cytostatics. Temozolomide is commonly used in clinical practice. We confirm that glioblastoma cells are sensitive to temozolomide in treatment level doses in vitro. Combination of pre-culturing with active form of BAF® and following treatment with temozolomide leads to higher effectiveness of cytostatic also in lower doses and inhibition of T98G cells growth in vitro. This work was supported from APVV-0224-12 and company Areko Praha.

48. Ghrelin meets the nucleus incertus - the behavioural effect in the rat

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The nucleus incertus (NI) in the dorsal midline pons is the main site of brain neurons producing relaxin-3 (RLN3), which plays an important role in regulating feeding and stress responses in rodents. Ghrelin is a 28aa peptide expressed in the stomach and brain (in hypothalamus) as an endogenous ligand for the growth-hormone secretagogue receptor (GHS-R). In situ hybridization studies showed that GHS-R is expressed in the rat NI [1], but the action of ghrelin in this structure remains obscure. The aim of our study was to describe the effect of NI ghrelin injection (1μg/0,5μl) on feeding behavior and locomotor activity in adult, male rats. The home-cage food intake test revealed that ghrelin-treated rats, despite of satiety, consumed significantly more chow than the control group. Subsequent locomotor cell tests showed that ghrelin-injected rats were less active than the controls. Based on in situ hybridization studies [1] and our behavioral data, we suggest that ghrelin signaling conveys the information about the "energetic status of the organism to a major RLN3 containing neural network in the hindbrain, which further influences brain structures controlling animal's feeding behaviour. [1. Zigman JM, Jones JE, Lee CE, Saper CB, Elmquist JK. (2006) J Comp Neurol 494, 528-548].

PAIN

49. Minocycline influences the anti-inflammatory interleukins and enhances the effectiveness of morphine under mice diabetic neuropathy

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We have demonstrated that a single streptozotocin(STZ)-injection in mice can induce significant neuropathic pain along with an increase in plasma glucose levels and a decrease in body weight. To analyze the inflammatory factors that may be involved in these effects, we used RT-qPCR, western blotting and antibody array techniques. Seven days after the administration of STZ, an upregulation of C1q-positive cells was observed. Additionally, interleukins (IL-1beta, IL-3, IL-4, IL-6, IL-9, IL12p70, IL-17); proteins of the tumor necrosis factor (TNF) family, e.g., IFNgamma and sTNF RII, were upregulated. These STZ-induced changes are modulated by the chronic administration of minocycline, an inhibitor of microglial activation that is also an inhibitor of MMP-9 and p38 MAP kinase. Chronic administration of minocycline increases antinociceptive factors (IL-1alpha, IL-2, IL-10, sTNFRII) in diabetic mice. In addition to the biochemical effects described above, minocycline reduces the occurrence of neuropathic pain and significantly potentiates the antiallodynic and antihyperalgesic effects of morphine. In summary, this study describes a decrease in neuropathic pain symptoms along with an increase in morphine effectiveness following the administration of minocycline in diabetic neuropathy. Supported by 2011/03/B/NZ4/00042, 2012/05/N/NZ4/02416, KNOW and statutory funds.

50. The designed opioid agonist–NK1 antagonist hybrid as an effective analgesic in neuropathic pain

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Opioids are important in treatment of pain, although their prolonged use leads to various undesired side effects. Multiple designed hybrid ligands designed opioid agonist–NK1 antagonist hybrid are thought to eliminate negative side effects. In this study, one hybrid was tested together with its parent compound containing only opioid agonist pharmacophore and their effects were compared with morphine in naive rats and in a neuropathic pain model. The compounds were injected intrathecally through chronically implanted cannulas and neuropathic pain was induced by sciatic nerve injury. In the experiment on naive rats, both tested compounds showed strong analgesic effects significantly stronger than after morphine. In a neuropathic pain model, the effect of the parent compound seemed to be much weaker but the antiallodynic effect of the hybrid was more pronounced than after morphine. The above effects were also confirmed by ED50 value. Interestingly, the parent compound loses its efficacy in neuropathic pain model, the phenomena known for opioid analgesics in the clinic. The results supported the idea of new analgesics composed with opioid agonist and NK1 receptor antagonist. Acknowledgements: 1. MAESTRO NCN2012/06/A/NZ4/00028; KNOW; statutory funds. 2. Research Foundation Flanders (FWO-Vlaanderen) and the Ministère du Développement Economique, de l'Innovation et de l'Exportation du Québec.

51. Minocycline modulates nociceptin efficacy under neuropathic pain

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Nociceptin plays an important role in the pathophysiology of neuropathic pain acting as an agonist of nociceptin-opioid receptor (NOR). The goal of our studies was to examine the influence of minocycline on microglia cell activation and nociceptin efficacy under neuropathy. The Wistar rats were implanted with intrathecal catheters and 7 days later chronic constriction injury (CCI) of the sciatic nerve was performed. Allodynia (von Frey) and hyperalgesia (cold plate) were measured. NOR mRNA and protein levels were measured in the rat spinal cord tissue and rat primary microglia cell cultures using qRT-PCR, Western blot and [35S]GTP□S binding. Chronic intraperitoneal administration of minocycline attenuated the neuropathic pain symptoms and enhance nociceptin (2.5-5 μg) analgesia. Minocycline diminished nerve injury-induced NOR down-regulation in the spinal cord. Minocycline treatment in CCI-exposed rats

increased NOR coupling to Gi proteins in the spinal cord. Interestingly, the in vitro study on microglial cell cultures using qRT-PCR, Western blot and immunocytochemistry showed the down-regulation of NOR by minocycline. Our results suggest that microglia inhibition enhances nociceptin effectiveness under neuropathic pain. Acknowledgments: Supported by grant 2011/03/B/NZ4/00042 and statutory founds. Agnieszka Jurga is a Ph.D. student from the KNOW.

52. The inhibitor of NF-kappaB, parthenolide, enhances morphine analgesia under neuropathic pain

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The nuclear factor κB (NF-κB), which is a key regulator of inflammation, has been suggested to be involved in neuropathic pain. In the present study, we examined the effect of parthenolide (PTL), an inhibitor of NF-κB, on nociception in a rat model of neuropathy (chronic constriction injury, CCI). The rats were implanted intrathecally (i.t.) with catheters and then CCI was performed. Parthenolide (5μg, i.t.) was dissolved in 50% DMSO and preemptively administered 16h and 1h before CCI and then once daily for 7 days. Vehicle-treated and PTL-treated rats received a single morphine (5μg, i.t.) injection 7 days post-CCI. Two behavioral tests were conducted to measure allodynia (von Frey) and hyperalgesia (cold plate). MOR, DOR and KOR mRNA were measured in the rat spinal cord using qRT-PCR. The experiments were carried out according to IASP rules. Chronic i.t. administration of PTL attenuated the allodynia and hyperalgesia. In PTL-treated rats, we observed enhancement of morphine analgesia. In response to chronic injections of parthenolide, we observed the spinal up-regulation of MOR, DOR and KOR mRNAs. Summing up, the inhibition of NF-κB by PTL enhanced morphine efficacy under neuropathy, possibly by up-regulation of opioid receptors. Supported by NCN2011/03/B/NZ4/00042 and statutory funds.

53. The effects of minocycline on pro- and anti-inflammatory factors after LPS stimulation in primary cultures of rat microglia

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In neuropathic pain, microglial cells are strongly activated and release many factors. e.g. cytokines, MMPs, which are implicated in the development of hyperalgesia and allodynia. The aim of our study was to examine the influence of minocycline on pro- and anti-inflammatory factors secreted from microglia in unstimulated and LPS-treated primary cell cultures. Primary cultures of microglial cells were prepared from cerebral cortices of 1-day-old Wistar rat pups. Microglial cells were resuspended in culture medium and plated at a final density of 20 x 104 cells onto 24-wells plates. Cells were treated with minocycline [10 μM] for 30 min and then with LPS [100 ng/ml] for 6h. RNA was extracted according to Chomczynski and Sacci, 1987. The mRNA levels for the selected cytokines and TIMP-1 were significantly up-regulated and the level of TIMP-2 was down-regulated after LPS treatment. Minocycline alone down-regulated TIMP-2 mRNA level but did not influence LPS effect, however, it potentiated the level of IL-1β and IL-10 after LPS and down-regulated TIMP-1. Summing up, minocycline change the levels of pro- and anti-inflammatory factors. Acknowledgments: grants NCN 2011/03/B/NZ4/00042, NCN 2012/07/N/NZ3/00379, KNOW and statutory funds.

54. The role of chemokine receptors CCR2 and CCR5 in neuropathic pain

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Chemokines seem to play an important role in the pathophysiology of neuropathic pain. Pronociceptive properties of chemokines were recently identified, however, only the role of a few of them was studied. It was documented in a neuropathic pain model that the expression of CCR2 and CCR5 receptors increased as a result of nerve injury. The goal of our studies was to examine the influence of antagonists of CCR2-RS504393 and CCR5-maraviroc receptors on allodynia and hyperalgesia under neuropathy. Wistar rats were implanted with intrathecal catheters according to Yaksh and Rudy (1976). Seven days later chronic constriction injury (CCI) of the sciatic nerve was performed according to Bennett and Xie (1988). Three behavioral tests were conducted to measure allodynia (von Frey test) hyperalgesia (cold plate test) and nociceptive threshold (tail-flick). The experiments were carried out according to IASP rules (Zimmermann, 1983). We provide evidence that chronic i.th. administration of RS504393 and maraviroc attenuated the allodynia and hyperalgesia on day 3 and 7 in CCI-exposed rats. Interestingly, maraviroc, in contrast to RS504393, diminished also spinal nociception as measured by the tail-flick test. Our results suggest that CCR2 and CCR5 are a

potential novel target for neuropathic pain drug development. Supported by NCN2011/03/B/NZ4/00042.

55. Action of N-arachidonyol-serotonin, dual fatty acid amide hydrolase (FAAH)/ vanilloid receptor 1 (TRPV1) bloker, in animal model of neuropathic pain

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Neuropathic pain is a chronic condition caused by a damage or impaired functioning of the nervous system. Commonly used drugs turned out to be ineffective, therefore there is strong need of new therapeutic strategies. It has been proven, that targeting more than one molecule may serve wider analgesic effect. Endovanilloid and endocannabinoid systems play crucial role in neuropathic pain conductivity, therefore in our studies, we examined effect of dual-targeting molecule AA-5-HT in a rat model of neuropathic pain. Chronic constriction injury of the sciatic nerve was used as a neuropathic pain model in male Wistar rats. The effectiveness of intrathaecal administration of drugs was assessed 7 days after injury in behavioral tests: von Frey's, Hargreaves' and cold plate. We found that treatment with AA-5-HT led to decrease in pain threshold to non noxiuous mechanical and thermal stimuli, but we observed no effect in response to peripherally mediated response to thermal stimulation. These data suggests a different responsiveness of heat responive C-fibers, cold-responsive Aδ-fibers and mechano-responsive Aβ-fibers to the tested compound. Summarizing, AA-5-HT may held great efficiency in the treatment of allodynia, one of the most undesirable and difficult to treat component of neuropathic pain. Supported by the LIDER/29/60/L-2/10/NCBiR/2011 grant.

56. Anandamide metabolism alterations in the development of neuropathic pain

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There is a strong evidence showing involvement of CB1/TRPV1 receptors system in pathophysiology of neuropathic pain. Our studies focused on metabolism pathways of anandamide (AEA), an CB1/TRPV1 agonist, which is involved in development of pain and inflammation. Chronic constriction injury of the sciatic nerve was used as a neuropathic pain model in Wistar male rats. The sciatic nerve injury was performed 3, 7 and 14 days before spinal cord (SC) and dorsal root ganglia (DRGs) samples dissection. Gene expression analysis was performed using Assay-On-Demand Taqman probes. Levels of enzymes of PLC/SHIP1 pathway were elevated in both analyzed structure in all time points. The highest expression levels were observed on day 7 and 14 for DRGs and SC respectively. Moreover PLA2 was up regulated in DRGs especially on day 3. Expression levels of all tested enzymes involved in AEA degradation were significantly upgraded in particular on ipsilateral side. Our data shown up regulation of PLC/SHIP1 pathway which might be responsible for elevated level of AEA in neuropathic pain development. The specific lateralization of the enzymes involved in AEA degradation may identify a new approach for neuropathic pain treatment.

57. Neurochemical changes in opioid systems activity in adult mice as consequences of neonatal painful stimulation

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An increased focus on the neurobiology of pain pathways highlighted the importance of pain experience in infancy which influences pain sensitivity in adult life. The objective of the present study was to determine the consequences of neonatal injection of carrageenan (CARR) into the hind paw on post-natal day 1, on pain modulation by endogenous opioid systems. Biochemical studies using RT PCR measured the changes in mRNA level of proopiomelanocortin, proenkephalin, prodynorphin and in mu- delta- and kappa-opioid receptors (MOR, DOR, KOR, respectively) in the spinal cord and PAG of naïve and CARR-injected 90 days old male and female mice. Results show that CARR administration causes the differences in the spinal cord between males and females in proopiomelanocortin, proenkephalin and all receptors. The proopiomelanocortin system is much impaired in females because it has a simultaneous decrease of both, peptides and MOR receptor level. Opposite regulation is observed in the PAG, where level of proopiomelanocortin is increased in female mice. The pain stimulus in post-natal day 1 seems to change the functioning of the descending antinociceptive system by lowering opioidergic tone especially in female mice. Supported by grant MAESTRO NCN2012/06/A/NZ4/00028 and statutory funds and The Joint Research Project between PAS-Poland /CNR-Italy

58. Antinociceptive effects of either intrathecally or intraperitoneally administered amitriptyline and fluoxetine in neuropathic rats

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The antidepressants have antinociceptive effects and they are widely used for the treatment of neuropathic pain. We tested the analgesic efficacy of drugs belonging to TCA and SSRI, and their impact on the levels of neuroimmune factors which are thought to be involved in antidepressants' analgesic properties. One group of male Wistar rats was implanted with an intrathecal (i.th.) catheter and subsequently subjected to CCI procedure, the other group underwent only CCI. We tested the analgesic effect depending on the different routes of administration of amitriptyline and fluoxetine. Both antidepressants were administered chronically (10µg i.th., 7 days) or as single intraperitoneal injection (amitriptyline 10mg/kg and fluoxetine 20mg/kg). Western Blot analysis of microglia (IBA1) and astroglia (GFAP) activation in the lumbar spinal cord and DRG were performed. Amitriptyline and fluoxetine significantly attenuated both allodynia and hyperalgesia. Western blot analyses showed that i.p. and i.th. injection of amitriptyline caused IBA1 up-regulation, whereas i.p. and i.th. injection of fluoxetine decreased the level of this protein in the spinal cord and DRG. Our results suggest that nerve injury-induced pain is associated with microglia activation, which is diminished by fluoxetine treatment, therefore, this antidepressant is recommended for the treatment of neuropathic pain. Acknowledgements: grant-POIG.01.01.02-12-004/09

59. Painful thoughts – a preliminary EEG study on electrophysiological correlates of pain catastrophizing

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Pain catastrophizing, defined as a tendency to exaggerate the threat value or seriousness of the experienced pain, has been shown to be a risk factor for pain chronification. The neural basis of pain catastrophizing remains, however, unclear and requires intensive investigation. This preliminary study was aimed at exploring the electrophysiological correlates of pain catastrophizing in healthy subjects. EEG data were collected during induced state of pain-related negative, depressive, positive and neutral rumination conditions. Catastrophizing was measured using the Pain Catastrophizing Scale (PCS) developed by Sullivan. This scale is used for measuring catastrophic thinking related to pain and has been shown to predict subjective pain intensity of an individual with chronic pain. It was hypothesized that differences between individuals on the PCS scale can be evident in activity of the regions involved in cognitive and emotional modulation of pain, measured by spectral power. EEG source localization method with the use of DIPFIT2 was performed and followed by K-means cluster analysis. It was revealed that pain catastrophizers can be differentiated from non-catastrophizers on the basis of alpha power spectrum characteristics in the parietal regions and beta power in the prefrontal and anterior cingulate cortex clusters especially during depressive and pain-related conditions. The results of the study will contribute to the better understanding of chronic pain syndromes development.

60. Intra-rater reliability of a new method of determining pressure-pain threshold by using algometer of authorial construction

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Previous methods applied to determine the pressure-pain threshold (PPT) do not eliminate interference of researcher in reading data raised from the research. Therefore in the following paperwork, proposition of a new, authorial approach to outlining PPT with its reliability's appraisal will be presented. 15 volunteers took part in this research. Measurement was made by algometer of one own's construction on forefingers of both arms. Three measurements were made in three series among which there were 5 minute breaks. These measurements were being recorded and saved as short films. Pressure's value appearing in given film on recorded algometer's screen, at the time of sound signal generation by investigated person, was treated like PPT. Reliability was appointed through intraclass correlation coefficient (ICC). Received coefficients ICC among first series and the second one amounted to 0.74 for one measurement, 0.90 for average of two, 0.94 for average of three measurements. ICC among first and third series amounted to: 0.74, 0.90, 0.95, and between second and the third one: 0.80, 0.93, 0.95 respectively. A proposed new

method of appointing PPT is characterized by moderate and good reliability for a single measurement, whereas for an average of two or three measurements, it accepts the good or excellent.

IMAGINERY, REPRESENTATIONS, INTENTIONS

61. The influence of motor imagery on the learning of a motor skill

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Motor imagery has been argued to affect motor skill acquisition and to improve performance in sports disciplines and rehabilitation. The present study examined whether motor imagery induces motor learning. A modified discrete sequence production (DSP) task was used: the Go/Nogo DSP task. Sequences of five stimuli signaling a specific response sequence were presented, and after an informative cue signaled by a specific color, the cued response sequence had to be executed, imagined or withheld. To measure the effect of motor learning, the experiment was divided into a practice phase and a test phase. In the latter phase we compared mean response times during the execution of new sequences, old only imagined sequences and old executed sequences. The electroencephalogram (EEG) was measured from 128 channels, to compare activity between motor imagery and motor execution. The analysis from the event-related potentials and the lateralized readiness potentials in the practice phase showed more similarities between motor imagery and motor execution relative to the trials in which the response sequence should be withheld. Behavioral results in the test phase, however, could not confirm that motor imagery resulted in motor learning.

62. Effectiveness of visual half-field paradigms in assessing the asymmetries of object representations

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Numerous studies on the lateralization of cognitive functions have taken advantage of the segregation of information from the left and right visual field in the primary visual cortex. The aim of our study was to investigate whether or not behavioral visual half-field (VHF) tasks can be utilized to assess the asymmetries associated with the processing of man-made objects that can be distinguished on the basis of higher-order characteristics (e.g., tools or non-tools). To this end, 17 left-handed participants (9 women) took part in two VHF experiments. In Experiment 1, the task was to categorize the object presented for 200 ms in one of the VHFs, whereas in Experiment 2 it was to categorize the central object preceded by 35ms prime presented in one of the VHFs. The results of reaction times analyses revealed that only given enough time to direct attention (but not to initiate a saccade), participants demonstrated the expected VHF advantage for the processing of more specific ob jects (i.e., tools). These findings suggest that the VHF paradigms can be a reliable behavioral measure for the asymmetries of object representations, but the parameters of the procedure should be carefully adjusted to the categories in question.

63. Short-term kinesthetic training for sensorimotor rhythms (SMR): effects in experts and amateurs

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The aim of this study was to examine a differences in the power of sensorimotor waves (SMR) in different frequency ranges : alpha (8-12 Hz), lower beta (12,5-16 Hz) and beta (16-20 Hz) during imagery movements of left and right hand. We compared two groups of subjects: experts (jugglers, casual exercisers similar movement) and amateurs (no-active in any sports). Additionally, we examined the impact of using short-term kinaesthetic training (ie. referring to feelings flowing from the body during performing proper motor acts) on the level of sensorimotor wave activity. As a result of analysis, it was observed that performing simple kinesthetic exercises significantly increased ($p < .01$) power in the range of alpha waves during motor imagery task in the case of a group of amateurs (recording in EEG from C3 and C4 position according 10-20 standard). However, this effect was not present in the group of people involved in juggling. The effects may be an argument for the possibility of using kinesthetic training as a method to support the clarity of motor representations, for example to used in control of brain-computer interfaces based on sensorimotor rhythms (SMR and Motor Imagery BCI).

64. The neural basis of task-reward associations

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In dynamic environments, a rewarding task (e.g. selling stocks) can quickly become unrewarding. In order to adapt to such changes in the environment, we need to first represent and update the association of specific tasks and rewards ("If task A, then high reward). Although there is a growing body of evidence implicating a fronto-parietal network in task representation, and a large literature on the role of striatal and orbitofrontal regions in reward processing, it is unknown which brain areas represent associations between both. We conducted an experiment explicitly addressing this issue. Subjects performed one of two tasks for a low or a high reward in each trial, while we acquired functional MRI data. We orthogonalized tasks and rewards and extracted the neural response to different task-reward associations (TRAs). Using time-resolved multivariate pattern analysis, we were able to extract the time-course of TRA information, as well as reward and task information. Results indicate that the inferior parietal cortex represents TRAs, and flexibly switches within a trial from representing TRAs to representing rewards. This finding is in line with the multiple-demand framework and emphasizes the role of parietal cortex in reward-guided behavior.

65. Movement related cortical potentials on corticography

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Knowledge of sensorimotor integration is essential to plan brain computer interfaces (BCI). Movement related cortical potentials (MRCP) have been studied for long, but intracranial sources have not been evaluated in details. Patients with epilepsy implanted with subdural macro electrodes (MAE) over the left central region was included in this study. Self-paced finger tapping (FT), and n. medianus somatosensory evoked potentials (SSEP) were recorded. Surface voltage maps were drawn. MRCP was averaged to the button press event. FT induced peri-movement motor potential (MP) was visualized on the MAE array. The low amplitude dipole lasted from -10ms to 50ms, and had the peak negativity postcentrally, positivity precentrally. The surface dipole configuration resembled the N20 component of intracranial SSEP. The low amplitude MP negativity seems to localize to the postcentral region despite previous data provided in the literature. We plan to further investigate the sensory-motor integration, and try to compare it to preoperative high-density EEG results and time frequency analysis. The findings could be translated for BCI applications as the investigated MP can be used as a control signal.

EMOTIONS & AFFECTIVE NEUROSCIENCE

66. On Emotion Specificity in Decision Making: Emotions as a Factor Behind the Direction of the Discounting Process

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The present study attempts to combine the decision-making process with tradition of one of the fields within the psychology of individual differences – emotions, by examining the relationship between emotions with the discounting process. Discounting refers to a decrease in the subjective value of a reward (or loss) as its delay increases. Steep discounting of delayed outcomes is of growing interest because of its relation to a number of socially important problems (e.g. drug abuse). Both theoretical models and functional imaging studies implicate the involvement of emotions within the delay discounting process. However, defining this role has been difficult to establish with neuroimaging techniques given the automaticity of emotional responses. To address this, the current study examined electrophysiological correlates involved in the detection and evaluation of immediate and delayed monetary outcomes. The results showed that modulation of both early and later ERP components previously associated with affective stimuli processing are sensitive to the signaling of delayed rewards. The assumed reason for the change of the direction in the amount effect is an anticipation of possible disappointment and regret, when the chosen uncertain or shared alternative is not actually obtained, and, at the same time, a smaller, sure reward – missed.

67. Categorisation of discrete emotions in a new emotional picture database – the Nencki Affective Picture System (NAPS)

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Selection of static visual stimuli inducing emotional states in affective research is mostly based on valence and arousal ratings gathered according to dimensional theories of emotion. However, it was shown, using neuroimaging methods that neuronal mechanisms underlying processing of emotionally charged stimuli differ between discrete emotional categories. So far, only the International Affective Picture System (IAPS; Lang et al., 1997) provides behavioural norms (Mikels et al., 2005) which allow scientists to appropriately select stimuli for research aimed to modulate discrete emotions. The purpose of this project was to evaluate the subjective emotional experience induced by pictorial materials included in the Nencki Affective Picture System database (NAPS; Marchewka et al., 2013) using discrete emotional categories (happiness, surprise, fear, sadness, disgust and anger). 510 images of the NAPS database were rated by English-speaking European subjects (N=76) using computerized valence and arousal scales as well as discrete emotions scales of happiness, surprise, fear, sadness, disgust and anger. In the second step, images were classified on the basis of confidence intervals overlap of discrete emotions ratings (Mikels et al., 2005). The preliminary data allowed distinguishing 360 images inducing one basic emotion, 55 images inducing several basic emotions and 95 images with undifferentiated emotional content. Provided data on dimensional and discrete emotional content of NAPS images will allow scientific community to select appropriate visual stimuli for affective research. The ratings freely available at http://naps.nencki.gov.pl/.

68. Basic emotions characteristics of Polish words from the Nencki Affective Word List

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Recently the Nencki Affective Word List (NAWL, Riegel et al., 2014, in press) has been introduced as a standardized database of Polish words suitable to study various aspects of emotion. While NAWL was constructed within the most common framework of valence and arousal dimensions, it is clearly not the only perspective of investigating emotions. Another approach is based on discrete categories of emotions (Briesemeister et al., 2011; Stevenson et al., 2007). Since both perspectives are recognized as complementary, the present study is aimed at supplementing the NAWL database with basic emotions categories. In the present study we applied the rating procedure previously introduced in the literature (Briesemeister et al., 2011; Stevenson et al., 2007), in which participants evaluated Polish words according to the basic emotion intensities. As a result, each of the 2902 NAWL stimuli was assigned to the categories of: happiness, anger, sadness, fear and disgust. The investigation of the affective characteristics of the present database revealed that Polish words may be successfully used to induce different types of basic emotions. Using NAWL databases will allow Polish researchers to study affect from both perspectives: dimensional and discrete, providing them with highly controlled experimental verbal material.

69. The assessment of basic emotions in Polish word database: The Nencki Affective Word List

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Using word stimuli in studies of emotional processing requires providing normative data. To date, a number of databases has offered affective norms for words in different languages, yet not in Polish. To facilitate investigations of verbal emotional processing, we introduce the Nencki Affective Word List (NAWL), being the cultural adaptation of the German database Berlin Affective Word List-Reloaded (BAWL-R; Võ et al., 2009). It consists of 2902 emotional and neutral words with the controlled psycholinguistic parameters, such as: frequency of use, number of letters and grammatical form. All the words have been standardized on the population of 266 subjects (130 men, 136 women) aged 20-52 years (M=23,7; SD=4,99) and mostly of Polish origins, on the dimensions of emotions such as valence and arousal, as well as imageability. Arousal was rated on a 5-point scale using the Self-Assessment Manikin (SAM; Lang,

1980), whereas valence and imageability were rated on 7-point scales. The obtained ratings formed the boomerang-shaped affective space, in which emotionally valenced words are characterized by higher arousal. The standardized NAWL database is suitable for a wide range of experimental studies on the Polish population, as well as for the cross-cultural studies.

70. The relationship between the Emotional Intelligence Questionnaire (PKIE), Toronto Alexithymia Scale (TAS) and Autism Spectrum Quotient (AQ). Emotion recognition in eye tracking task

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Empathy and emotion recognition are an important part of life and is what helps us to understand the attitudes and feeling of others. Autism impairs these attributes, so a study was carried out with students (N=123) who completed questionnaires using PKIE and TAS and their relationship to AQ with an eye tracking task to assess emotion recognition. In the first part of the study, a strong, negative correlation was found between PKIE and TAS ($p<0.01$) and moderate negative correlation between PKIE and AQ ($p<0.01$). This part of the study also shows the different level of Emotional Intelligence between the sexes. For the second part of the study, the subject group was divided to check if there is any difference between the groups that had high and low scores on AQ. People from these groups were invited to complete the Emotional Recognition Task from CANTAB. The final part was based on eye tracking examination, where 70 photos of seven emotions from the Karolinska Directed Emotional Faces Task was used to see if the pattern of emotion recognition was the same. The time in this task was not limited, but subjects were informed to pick one of the answers as quickly as it is possible. The number of correct answers and response latencies was measured in both tasks.

71. Saliency of and attention to words with a negative (sensory, emotional) component

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Perception of the world around us is modulated by attention; an insect walking across our desk draws our attention immediately, making us abandon our previous task. The same issue is found in the perception of pain and negative concepts; these seem to either capture or hold attention. This has far-reaching consequences for the way humans, and especially the sub-group of patients, deal with pain and negative concepts. There has been quite a bit of research on the perception of words, where saliency and emotional processing are often key outcomes. However, these outcomes are an indirect measure, and are subject to a multitude of confounding elements. To investigate the issues more directly, we have set up an experiment where we use several methods to determine saliency, arousal, and attentional effects. Primarily, EEG will be used to compare deflections associated with attention, with specific focus on the P4PC. Additionally, we will use EMG to estimate motor onset, which may correlate with per-word saliency. A more complete measure of saliency will be determined by the use of eye-tracking (through timing and gaze, amongst others), and a self-report saliency questionnaire. These methods will be used to extract as much outcomes as possible, which we will then try to correlate with self-report measures, with specific focus on mental state (such as depression), personality profile (through the EPQ - RSS), coping strategies (such as 'catastrophizing'), and sensory amplification.

72. Which 'faces' are in fact faces? Evidence from the N170 component

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Recent findings suggest highly specialized brain module critically involved in the face processing, located in the fusiform gyrus. Activity of this module can be reflected in the amplitude of the face-sensitive N170 component. Typically, larger amplitude of the N170 can be obtained to faces when compared to non-face objects. In our experiment we compared the amplitudes and latencies of N170 recorded in response to several different categories of visual stimuli (non-face objects, face-like-objects, animal faces, primates faces and human faces) presented in the upright and inverted position. We found significantly larger amplitude and shorter latency of the N170 when elicited by human faces when compared to other stimuli. We also noticed that the N170 response to face-like-objects, animal faces and primate faces was larger in amplitude in comparison to non-face objects, while its latency was comparable for all these stimuli. Moreover, we found a typical effect of face inversion (higher amplitude and longer latency of the N170), but this effect was restricted to human faces and was virtually absent for other stimuli. These findings let us suggest that human faces activate brain module specialized in the face processing differently than all other objects,

including face-like-objects and animal faces. This research has been supported by a grant from the National Science Centre of Poland (2011/03/B/HS6/01640).

73. Trait anxiety alters early stages of emotional expression processing – an investigation with ERP components

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There is growing evidence that trait anxiety influences the processing of threat-related information, and therefore can alter brain responses to facial emotions (fearful or angry faces). To test this hypothesis we recorded ERPs in response to various facial emotions in low- and high-anxious individuals (STAI scores). We found increased amplitude of the N170 elicited by emotional faces in comparison to neutral stimuli. We also found the anxiety-specific effect reflected in the enhanced positivity observed for high-anxious subjects between 100 and 150ms after the stimulus onset. This effect was restricted to right hemisphere, and was evident irrespective of the emotional expression. Additionally, the anxiety-related effect was also obtained at right parieto-occipital electrodes for the latency window of 170 – 400 ms poststimulus where the enhanced negativity for subjects scoring higher on STAI was observed. Our findings indicate that anxiety level modulates early stages of information processing, as reflected in the P1 component. This can lead to anxiety-related differences in processing of emotional expression at later stages. This research has been supported by a grant from the National Science Centre of Poland (2011/03/B/HS6/01640).

74. Emotional content of an image attracts attention more than visually salient features in various signal-to-noise ratio conditions

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Emotional images are processed in a prioritized manner, attracting attention almost immediately. In the present study we used eye tracking to reveal what type of features within neutral, positive and negative images attract early visual attention: semantics, visual saliency or their interaction. Semantic regions of interest were selected by observers, while visual saliency was determined using the Graph Based Visual Saliency model. Images were transformed by adding pink noise in several proportions to be presented in a sequence of increasing and decreasing clarity. Locations of the first two fixations were analyzed. The results showed dominance of semantic features over visual saliency in attracting attention. This dominance was linearly related to the signal-to-noise ratio. Semantic regions were fixated more often in emotional images than in neutral ones, if signal-to-noise ratio was high enough to allow participants to comprehend the gist of a scene. Visual saliency on its own did not attract attention above chance, even in the case of pure noise images. Regions both visually salient and semantically relevant attracted a similar amount of fixation compared to semantic regions alone, or even more in the case of neutral pictures. Results provide evidence for ultra-fast and robust detection of semantically relevant features.

AUDITORY PROCESSING

75. Synchronization of movements with sounds in autistic children in comparison with other disorders

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The purpose of this study was to check if there are any significant differences in temporal processing between children with ASD and children with other disorder, for example: ADHD, dyslexia etc. The research included 21 children who were 8 years to 9 years. They were diagnosed before participating the study. The subjects were assigned to one of two groups according to psychological diagnosis (ASD vs other disorders). Two groups were pretested using Interactive Metronome® and received 18 session of this training. After Interactive Metronome® training all children were tested again. The study show a significant pattern of improvement. The results indicate the differences between 2 groups in temporal processing (pretests) which has got a huge impact on cognitive functions as: motor coordination, fluency of speech etc. Additionally the Interactive Metronome® training caused the error correction measured in milliseconds in

both groups. Interactive Metronome® allows to precisely estimate the millisecond error. What is more important this training causes the error correction in many clinical groups of patients. It is very important to use it in practical way.

76. Pure deficits of vocal performance in the general population

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Singing proficiency is widespread in the general population. A few recent studies indicate that almost everybody can carry a tune when producing a well-known melody with lyrics at a slow tempo. Nevertheless, there are still some individuals who sing inaccurately (tone deaf). The main goal of the study was to find those participants who have problems with singing whithout problems with perception (pure vocal tone deaf). One hundred and twenty eight occasional singers sung two well-known melodies ("Panie Janie" and "Sto lat") with lyrics and on the syllable /la/ in the short screening test. Moreover, we used Discrimination task to check their perception abilities. Based on the obtained results we selected ten participants with singing deficits and examined them using MBEA, the battery measuring perceptional abilities, to exclude individuals with potential amusia. Preliminary results suggests that tone deafness might be more remarkable in performance than in perception. Deficits of sung performance can be very specific, selectively affecting particular musical abilities, involving perceptual and motor planning components, memory retrieval, auditory–motor mapping, and complex feedback mechanisms. There is a need for further research in this area which will ultimately provide useful information for understanding the beneficial effect of vocal performance in rehabilitation.

77. Distribution of rhythm deafness in the general population

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Despite the fact that so far been published a lot of studies on the rhythm production and perception in professional musicians, much less is known about connections between rhythm perception and production in the general population. Recent Recent studies indicate that some individuals (so-called "rhythm deaf) may exhibit impaired rhythm perception and inaccurate sensorimotor synchronization (SMS), while showing spared pitch processing. In our study we examined perception and SMS in the general population. In a first screening experiment, 99 non-musicians synchronized with musical and non-musical stimuli in a hand-tapping task. Synchronization accuracy and consistency were analyzed with Circular Statistics. The results allowed to select 16 participants revealing difficulties in the SMS task (Poor Synchronizers). In a second experiment, 10 of the Poor Synchronizers and 23 Controls underwent various SMS tasks (e.g., with different pacing stimuli and using different tempos), and to rhythm perceptron tasks. The analyses confirmed that 7 participants were poor synchronizers. In particular, 2 of them exhibited normal rhythm perception. These findings represent the original source of knowledge and points to a possible mismatch between perception and action in the rhythm domain, similar to what previously observed in the pitch domain.

LANGUAGE PROCESSING

78. Where brain "sees" words - functional Visual Word Form Area localizer study

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Visual Word Form Area (VWFA) is a functionally specific subregion of the fusiform gyrus known to be involved in reading and word recognition (e.g.http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2706007/). The activation of the left VWFA when word-stimuli is presented was observed regardless of the culture or subjects native language. Exact

nature and function of this region are under special investigations. Interaction between meaningful string of letters exposition and VWFA activation is intensively studied, as the topic comprises both scientific and social issues. Here we present results from the functional Visual Word Form Area localizer (which is a part of the greater experiment). We expect to find activation in VWFA accompanying words presentation. Eight adult (aged 20-26) subjects (both men and women) participated in the study. Our procedure comprised of short (2 min) block-designed scanning session. During the scanning participants were asked to look at the presented visual stimuli which were words and non words (23 strings per block, 6 block per condition). 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 analysis. Our analysis of the contrast between words and non-words reveled a robust activation in the left ventrolateral occipital cortex, covering the region known as a Visual Word Form Area. This result stays in line with previous findings showing the selective properties of this brain region.

79. Sign or signed? Neural basis of natural and artificial communication systems in the deaf

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Natural sign languages that evolve spontaneously in deaf communities (e.g. Polish Sign Language, abbreviated as PJM) should not be confused with artificially created manual variants of spoken languages (e.g. Signed Polish, SJM). Classifier constructions (CCs), i.e. complex three-dimensional structures that replace typical verbs to transmit spatial or movement information, could be viewed as yet another mode of manual communication. The aim of our study was to compare the neural basis of these 3 signing forms. 15 congenitally deaf signers and 14 hearing non-signers underwent functional magnetic resonance imaging (fMRI) while viewing either PJM, SJM or CC-type sentences. The sentences were matched for meaning so that only the grammar differed across the 3 conditions. Perisylvian regions were activated in deaf signers when watching any of the 3 forms of sign communication. PJM activated the left posterior superior temporal gyrus to a greater extent than SJM. CCs compared to either PJM or SJM activated superior and inferior parietal lobules and precentral gyrus bilaterally. Our study demonstrates that based on the activity of the left posterior superior temporal region one can distinguish natural from artificial sign communication systems. Furthermore, our results highlight the special status of CCs in the communication of native signers.

80. Can visual attention span increase with reading acquisition?

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Visual attention span (VAS) is defined as the number of individual visual elements that can be processed in parallel (Bosse, Tainturier & Vadlois, 2007), it increases with age and predicts single-word reading speed in both: normal reading and dyslexic children (Lobier, Dubois & Valdois, 2013). We wanted to investigate whether VAS abilities would increase with reading aquisition. We know that reading acquisition enhances an early visual process of contour integration (Szwed et al., 2012). Contour integration performance is lower in illiterates than in both ex-illiterate and literate controls. In our study we tested three groups: illiterates, ex-illiterates and literates by VAS test and Attention Network Test (ANT) as control experiment. Our results did not show statistically significant differences between groups in VAS test. There were no statistically significant differences in ANT test effects (conflict and orienting). Visual attention span does not increases with reading acquisition.

81. Parafoveal information processing during reading: A registration study with eye movements - methodological issues

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By using the moving window technique developed by McConkie and Rayner (1975) we utilised the display change after crossing an invisible boundary technique (Kliegl et al. 2012). When the eye tracker detects one of the eye crossing a horizontal line on the screen the display is changed. We used manipulation where was a random timer inserted between the boundary crossing and the display change, which delayed the display change by a random number between 0 and 100ms. Participants had been reading from left to right. Our results indicate that display change latency (DCL) and different preview condition have significant impact on fixation duration (FD) in the current moving window paradigm with display change manipulation. This experiment showed how important variable in parafoveal information processing during reading researches is display change latency and how it affects the length of fixation.

82. Does the McGurk stimulus evoke the Mismatch Negativity?

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It has been shown that the mismatch negativity (MMN) event-related potential component can be evoked by the stimuli that integrate auditory and visual modalities, such as the McGurk stimulus (e.g., Colin et al., 2002, 2004; Saint-Amour et al., 2007). Current study utilized the event-related paradigm and consisted of two experiments. The first one included an audiovisual deviant stimulus (a syllable) that differed from the standard one only in the visual component, and resulted in the perception of a different syllable. In the second experiment, the deviant stimuli were changed in both auditory and visual channel; however, both kinds of stimuli were coherent due to the illusory percepts. The aim of our study was to investigate whether or not such changes in the stimuli might affect the bimodal processing and still evoke the MMN. The results do not support those reported in the previous studies (Colin et al., 2002, 2004). Moreover, we found that the McGurk stimulus has induced a positive component, the P600. These outcomes require further investigation.

GENERAL PSYCHOLOGY & PSYCHOLOGY OF INDIVIDUAL DIFFERENCES – NEURAL BASIS

83. Neurobiology of time

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Psychology of time is very important and interesting, but - for many years - underestimated field of research. Nowadays this state is changing: we can observe an increasing number of research projects, aimed at explaining human thinking about time. One of the more interesting theories was developed by Philip Zimbardo, who described five temporal perspectives, which are related to the emotional and cognitive processes. Depending on the dominant time perspective, people can focus on the past, present or future - in positive or negative affective dimension. As a consequence, the way of thinking about the world always occurs in the temporal context. This theory became basis of study, which is part of doctoral research about the children's perception of time, conducted at the Faculty of Education, University of Warsaw. Previous research reports in this area allow to conclude that the perception of time changes with age. Study of the temporal perspectives of youth and adolescents, conducted in Warsaw high schools, colleges and universities and described in this material, seems to confirm this thesis. The main conclusion from this research is that future time perspective (FTP) increases with age of the subject. This effect is mainly related to the maturation of the brain

structures responsible for abstract thinking, planning, or delaying gratification. This material is a discussion of the results of the study in the neurobiological context.

84. The intrinsic-complexity of the spontaneous brain activity reflects the personality traits

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Despite researcher's efforts, it is still unclear how the personality is encoded in the brain. The aim of our study was to investigate whether the Big Five personality traits are reflected in the intrinsic-complexity of the spontaneous bioelectrical activity of selected brain areas or in their functional connectivity. Thirty-six young, right-handed healthy subjects (50% females) participated in our study. Personality traits were measured using a Revised NEO Personality Inventory. Subjects were asked to relax with their eyes closed while EEG signal was recorded from 64 scalp electrodes. The Higuchi's fractal dimension was used as an indicator of the level of complexity of the EEG signal. Functional connectivity between selected brain regions was evaluated using the phase-locking algorithm. We found that subjects' sex moderated the relationship between the particular personality traits and both: complexity of the EEG signal and phase locking values. We conclude that the Big Five personality traits are reflected in the intrinsic complexity of the spontaneous activity of brain. The study was supported by Dean of Faculty of Humanities and Rector of Nicolaus Copernicus University in Torun.

85. Electrophysiological correlates of intelligence – evidence from the analysis of the intrinsic-complexity of the EEG signal

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Existing studies provide inconsistent or even contradictory empirical findings regarding the relationship between the intelligence and EEG signal characteristics. Analytic methods derived from of deterministic chaos theory and fractal geometry can advance our understanding of the associations between neurophysiological and cognitive phenomena. Dynamic changes of the EEG intrinsic-complexity can be quantified by evaluation of fractal dimension using Higuchi's method (HFD). The aim of the study was to verify association between the complexity of the EEG signal and the intelligence level. Intelligence level was assessed using Raven's Advanced Progressive Matrices (RAPM) in thirty-six young, right-handed, healthy subjects (18 females). Subsequently, subjects were asked to relax with eyes closed while the EEG signal was acquired from 64 electrodes. HFD was calculated for individual electrodes and as subject's average. Strong negative correlation between the performance on RAPM and HFD of the EEG signal was revealed. Sex has been found to act as a moderator variable for intelligence-complexity relationship. Subjects performing better on RAPM also have brains that exhibit bio-electrical activity that is relatively richer in self-similar patterns (less stochastic or more deterministic). Neuronal correlates of intelligence vary between sexes. Study supported by Nicolaus Copernicus University (Faculty of Humanities, Rector).

86. The right hemisphere bias in false memory does not depend on modality

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The aim of the present study was to investigate hemispheric asymmetry in false memory with pictorial and auditory variants of the popular Deese-Roediger-McDermott paradigm. It was inspired by Phelps & Gazzaniga (1992) demonstration of left-sided bias in a pictorial false memory task, conforming with the postulate of the left-hemispheric "interpreter mechanism. We used lateral presentation of sets of categorically related pictures and simultaneous dichotic presentation of word-lists in the memory tasks. We compared the false recognition rates for the lures categorically related to the left-side and the right-side stimuli. We also looked for possible relations of false memory asymmetries with

lateral preferences and brain laterality as indicated by asymmetries of performance in language, attention, and manual tasks. The results suggest that the right hemisphere was less able than the left to reject semantically related distractors in both modalities. The false recognition asymmetries in both tasks were correlated. They showed no significant correlations with laterality measures. The findings of the present study contradict the predictions of the left-hemisphere interpreter explanation of false memory. They rather conform with the Jung-Beeman's coarse semantic coding proposition.

FUNCTIONAL NEUROANATOMY

87. Basal ganglia volume – reference ranges and lateralization indices

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Basal ganglia asymmetries in healthy individuals have been described in prior studies. According to this study, right caudate nucleus was larger than left while right putamen and right globus pallidus were smaller than left. The purpose of this study was to estimate reference ranges for basal ganglia asymmetry based on large cohort of healthy individuals (n=1087). MRI brain scans from 1087 participants (Male=734, Female=335) using 3T acquisitions included in ADHD-200 and ABIDE datasets. Volumetric measurements of basal ganglia were obtained using automated segmentation (FreeSurfer). Statistical analysis was performed by utilizing a R-CRAN. Asymmetries were calculated used two lateralization indices: (L-R)/(L+R) and Right/Left ratio. Tolerance interval estimates were used to calculate reference ranges. Reference ranges of lateralization index (L-R)/(L+R) for caudate nucleus -0.08-0.04, for putamen -0.04-0.07, for globus pallidus -0.07-0.14. Reference ranges of lateralization index (R/L ratio) for caudate nucleus 0.9-1.2, for putamen 0.8-1.1, for globus pallidus 0.7-1.2. Both lateralization indices show R&L asymmetry of caudate nucleus, L&R asymmetry of putamen and L& R asymmetry of globus pallidus. As expected, there are asymmetries of basal ganglia in healthy controls. The results confirmed the rightward asymmetry of caudate nucleus, leftward asymmetry of putamen and leftward asymmetry of globus pallidus.

88. Increased size of posterior ventral cingulate cortex is related to better creativity

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Present study investigates the role of cingulate cortex regions in various verbal creativity characteristics. 15 right-handed females (59-85 years old). We performed magnetic resonance morphometric analysis of T1 images in order to measure absolute square surfaces (in mm2) of three cingulate cortex regions – anterior (BA 24 and 33), posterior ventral (BA 23), posterior dorsal (BA 31) areas of both hemispheres. Overall creativity, originality, fluency and flexibility were measured with the Russian adaptation of Guilford's Alternate Uses test. We calculated non-parametric correlations ($p<0.01$) between creativity characteristics and morphometrical data. Originality correlates positively with the size of posterior ventral cingulate cortex area ($r=0.71$). Overall creativity also correlates positively with the same cingulate cortex region ($r=0.68$). No significant correlations between other cingulate cortex regions and creativity characteristics were revealed. It is known that posterior ventral cingulate cortex is connected to hippocampus (associative memory), anterior cingulate cortex (cognitive evaluation) and precuneus (emotional evaluation). This can explain the relation of this brain region to the originality, which involves all of those processes. Correlation between originality and the right hemisphere can be related to the fact that producing original answers may require imagination, rather than verbal thinking.

METHODS – COGNITIVE PERSPECTIVE

89. Averaging in analysis of electrophysiological data

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Common method in analysing signals correlated in time with a stimulus is averaging. It is based on three main assumptions: 1.The reaction always have the same latency, 2.The morphology of the signal is always the same, 3.The background, present in each biological signal, can be treated like a white noise. To investigate the shape of bioelectric signal we can use several procedures, for example Woody's averaging, averaging in subsets, averaging in blocks. Each of them examines slightly different features of the response and requires data collected in property way. They find use in electroencephalography by analysis of Evoked Potentials. To compare qualities not directly connected with the morphology of the signal, we can average amplitude spectra or even complex Fourier transforms. This method is characteristic for analysis of Steady State Evoked Potentials. In my presentation I'm going to show and explain the differences between presented methods, using simulated and real EEG recordings.

90. Large-Scale Modeling of Resting-State Activity

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Brain activity at rest is not random, but well organized in characteristic slow-fluctuating spatiotemporal patterns called Resting State Networks (RSNs). RSNs relate to the underlying neuronal activity and are likely shaped by structural connectivity. Nevertheless, there still is a link missing in order to understand how RSNs are formed – the dynamics. In this study we investigate the dynamics of resting state activity based on the model of Deco and Jirsa (2012). Additionally, we use the dynamic mean field model technique and the feedback inhibition control approach. We aim to understand the origins of resting state activity through modeling it via a large-scale cortical dynamic mean field model. Functional magnetic resonance imaging and diffusion spectrum imaging were used to obtain global functional and structural connectivity matrices of healthy people. By integrating the biologically realistic neuroanatomical connectivity into the model, we observed emerging resting state functional connectivity of the brain network that fits very well both the empirical functional connectivity and temporal aspects of signal oscillations during resting state in humans. This work provides a new way of investigating resting state activity, based on theoretical approaches, which can serve as fertile test ground for basic neuroscience, especially for clinical applications.

91. Measure Projection Toolbox as an alternative to standard ICA clustering: application to memory related EEG study

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Independent Component Analysis (ICA) has been widely used in research using Electroencephalography (EEG). One problem connected with this method is how to group components gained from different subjects into clusters representing similar (location- or task-wise) activity. Here, we use Measure Projection Toolbox (MPT) to group components of EEG activity registered during maintenance period in Sternberg Task (78 participants). This EEGLAB toolbox uses measures such as power spectrum or event -related spectral perturbations (ERSP) to gather ICs in domains that have similar dipole location and activity pattern. We compare domains of activity obtained via MPT from all subjects taken together with MPT results taking into account information about which groups/conditions subjects belong to. Moreover, we investigate how data preparation influences the quality of MPT results.

92. Wavelet-neural detection of induction motor drive's faults

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The paper presents a method of a fault identification of induction motor drive by means of the application of a wavelet analysis of a tested signal and a supervised learning neural network model, and also a model of a neural network processed in the next epochs by means of an algorithm, which makes essential changes to parameters of this network. Wavelet decomposition's coefficients related to chosen state variables were applied in identification simulations to the training of the first neural network and also processing in the next epochs of the second neural network. The tests which were executed on three important state variables, describing physical quantities of the chosen induction motor drive model confirmed the usefulness of the method used for diagnostic purposes. In particular the method is allowing for the identification of the fault type occurring in the induction motor drive in the initial phase of formation. This formation is usually described by nonlinear characteristics of elements with discontinuity in the zero of physical quantity's signal having target slope of absorption's characteristics in experiment. The results of executed simulations confirmed that information contained in wavelet decomposition's coefficients can be used in the process of reasoning the type and localization of fault's occurring of this model's elements.