



# NEURONUS 2013

IBRO & IRUN NEUROSCIENCE FORUM

MAY 9-11 2013, KRAKOW, POLAND

## BOOK OF ABSTRACTS

## **ORAL PRESENTATIONS**

May 9 <sup>th</sup> 2013 (Thursday) .....	3
May 10 <sup>th</sup> 2013 (Friday).....	6
May 11 <sup>th</sup> 2013 (Saturday).....	18

<b>POSTER PRESENTATIONS.....</b>	<b>33</b>
----------------------------------	-----------

**14.00 – 15.30: ADOLF BECK'S MEMORIAL SESSION**

---

***Adolf Beck - discovery of the brain electrical activity***

**Andrzej Trzebski**

Department of Experimental and Clinical Physiology, Warsaw Medical University, Poland

On 20 October 1890 Adolf Beck submitted for publication a short version of his doctoral thesis on the electrical potentials on the distinct areas of the brain cortex in dogs and rabbits, evoked by visual, auditory and limb sensory stimulations and observed spontaneously as a waxing and waning rhythmical electrical activity (Centralblatt Physiol., 1890; vol.4: 473-476). The subject of his thesis was proposed by his teacher and mentor Napoleon Cybulski, the professor and chairman of the Department of Physiology at the Medical Faculty of the Jagiellonian University in Cracow. The response to Beck's publication was immediate. Several claims to the priority of discovery and some critical remarks were raised and published. Beck (Centralblatt Physiol. 1890; vol.4: 571-573) and Beck with Cybulski (Centralblatt Physiol. 1892; vol.6: 1-6) discussed and rejected them after additional testing experiments. Only an early publication of Richard Caton, a Liverpool physician (Br. Med. J. 1875, vol. 2: 278), unknown to Beck and to physiologists at that time, reported the findings similar to that discovered independently by Beck. The importance of the discovery is clear. In the last decades of the XIX century neuroscience was at its beginning. General view on the microstructure of the cerebral cortex was based on the theory of protoplasmic reticular theory unable to generate action potentials and on work of Golgi on thin interconnecting nerve filaments in the cortex. Recognition of nerve cells as independent units in cerebral cortex by Ramon y Cajal and the term neuron (von Waldeyer) were ahead. Debates on holistic function versus specific localized function of the brain cortex were going on. Discovery of Richard Caton, and independently of Adolf Beck was in the mainstream of emerging modern neuroscience in XIX century.

***Napoleon Cybulski and Adolf Beck – the most prominent Polish physiologists at the Department of Physiology at the Faculty of Medicine of the Jagiellonian University between 1885 and 1895***

**Wiesław W. Pawlik, Tomasz Brzozowski, Stanisław Konturek**

Department of Physiology, Jagiellonian University Medical College, Poland

When Gustaw Piotrowski, for many years a professor of physiology at the Jagiellonian University Faculty of Medicine, died on the last day of 1884, the Faculty Council initiated the search for the most suitable candidate for the vacant position. The decision was made very soon and turned out to be extremely accurate. The faculty offered the position to a young 31-year-old researcher Napoleon Cybulski, a most promising student of Professor Ivan Tarchanov who was recognized as a prominent physiologist at the Military Surgical-Medical Academy in St Petersburg. Under Tarchanov's supervision Cybulski gained experience in physiology and experimental studies. After his graduation in 1880 with a medical diploma, Cybulski continued to work for Prof. Tarchanov until leaving for Kraków in 1885. During his work at St. Petersburg he had a scientific contact with Ivan Pavlov, because of the fact that they both worked on blood circulation at that time. One of his greatest achievements was the construction of a device for precise measurements of blood movement in the vessels - the photohemotachometer. In the field of endocrinology Cybulski together with Szymonowicz, found out that adrenal extracts contain biologically active substances that elevate blood pressure. He applied for the first time the device called condensator discharges, to stimulate nerves and in using this device, he analyzed changes in the excitability of tissues depending on the electrical energy and the time of its duration. In 1890 Adolf Beck received a doctor's degree in all medical sciences after completing his medical studies at the Jagiellonian University in Kraków. As early as during his studies in 1886, he started working at the Department of Physiology of this university under the guidance of Napoleon Cybulski. On Cybulski's recommendation, Beck

performed the research on the sensory centers in the central nervous system by means of the observations of electrical phenomena. In 1891 he published his famous doctoral thesis "The determination of localizations in the brain and spinal cord with the aid of electrical phenomena". In the following years Beck continued research related to neurophysiology and electrical activity of the brain, but he also carried out a number of studies using the photohemotachometer. Beck studied blood flow in the portal vein. Oscillations in blood flow velocity in this important vein were rather moderate in normal conditions, but an increase in the velocity was observed during digestion, with an elevation of blood pressure and the increased heart rate. He also studied the blood pressure in peripheral veins and published the results in 1895. In 1895 Adolf Beck was appointed as the Chair in the newly organized Department of Physiology at the University in Lwów. From this extraordinary moment in Beck's life the scientific collaboration of both outstanding scientists was strengthened and continued until Cybulski's death on 26 April 1919.

### ***Beck's place in the history of electroencephalography***

**Anton M.L. Coenen**

Department of Biological Psychology, Donders Centre for Cognition, Radboud University Nijmegen, the Netherlands

A cornerstone in the history of electroencephalography formed a paper of Adolf Beck from Poland in the 'Centralblatt für Physiologie' in 1890. This was about the recording of electrical waves from the brains of animals. This was the start of a polemic arose between physiologists concerning the discovery of electrical brain activity. The discussion was ended by the Englishman Richard Caton referring to a, completely ignored, abstract from 1875, in which he described the spontaneous waxing and waning of the electrical waves recorded from the brains of animals. Caton's claim was convincing, and it is now accepted that this abstract contained the first description of the electroencephalogram. Beck was not aware of Caton's work, but he explored the electrical brain activity much more detailed and extensively. Beck described the localization of sensory modalities on the cerebral cortex by electrical and sensory stimulation and by recording the electrical activities with clay electrodes and a string galvanometer. Beck explored, in frogs, dogs and rabbits, the parts of the cortex that reacted upon stimulation with electronegativity. This was done for several sensory modalities and this was the first description of 'evoked potentials'. Beck also found the spontaneous fluctuations of brain potentials, and brought up the potential decrease upon sensory stimulation. He observed a cessation in the fluctuations of the electrical waves after afferent stimulation. Thus, he was the first to describe the desynchronisation in the EEG following stimulation. Much later in 1929, the German Hans Berger published a lengthy paper about the recordings of electrical activity from the surface of the human brain, and promoted so the technique into a non-invasive one for humans. Berger described the conditions under which the two rhythms, alpha and beta rhythm, appeared. After seeing the changes in the electrical wave pattern during sleep and narcosis, and the aberrant activities during epileptic attacks, Berger came to the conclusion that the discovery of the EEG was a main breakthrough in neurophysiology, and highly important for its diagnostic value. This makes that he is now considered as the father of electroencephalography. Nevertheless, but in looking back it seems best to attribute the discovery of electroencephalography to the trio Richard Caton, for his brief description of brain waves, to Adolf Beck, for his extensive and innovative brain work in animals, and to Hans Berger, for making the recording technique applicable for humans.

### ***Life and work of Adolf Beck in Lemberg/Lwów***

**Oksana Zayachkivska**

Physiology Department, Lviv National Medical University, Ukraine

On the 28<sup>th</sup> of May 1895 at an age of 32 Adolf Beck accepted the offer to take the chair and to be appointed professor at the Physiology Department in the Medical Faculty at the University in Lemberg, where he worked till 1935. This department in nowadays known as the Lviv National Medical University at Lviv in the Ukraine, a city formerly known as Lemberg (1772–1919) or Lwów (1340–1772; 1920–1939). Beck also spent the rest of his life in this city where he, despite political discrimination and racism, became one of the XX century's leading scientist, but unknown in the XXI century to a wide audience.

Beck served the university as Dean in 1904/1905 and in 1916/1917, as a Rector in the period 1912/1913, and as a Pro-rector in the turbulent period 1914/1915. The whole scientific portrait of Adolf Beck is not only related to the development and use of electrophysiological and neurophysiological methods to investigate the cerebral cortex, but also to his work in the field of general physiology, such as visceral, sensory functions, and laboratory medicine. He achieved investigations into complicated, interdisciplinary problems, ranging from basic science to clinical problems. Beck's scientific creativity involved a synthesis of concepts and methods from diverse disciplines. Beck's influence on the growth of the fields of electrophysiology, neuroscience and human physiology is much greater than is apparent from his publications. During the First World War Beck was speaking on behalf of science with political opponents and developed lines of communication with them. As professor at the Medical Faculty, Adolf Beck emphasized that the science and education must be seen to bridge the political and social antitheses in public society. After the Second World War Adolf Beck was mainly disregarded, until Mary Brazier (1904–1995) from the Harvard Medical School, and the Massachusetts Institute of Technology (1940-1960), of the Brain Research Institute at the University of California at Los Angeles (1961-1988), neuroscientist, author and editor par excellence, international organizer, and the prominent expert in the history of neuroscience, translated Beck's dissertation into English (Beck, 1973). Despite the efforts of Dr. Brazier the name of Prof. Beck, important scientist, innovator, teacher, and great person, is still hidden in the world of global medical history, science and culture.

---

## 16.30 – 17.30: OPENING LECTURE

---

### *Kainate receptors and their interactome in neuron plasticity*

**Juan Lerma**

Instituto de Neurociencias de Alicante, CSIC-UMH, San Juan de Alicante, Spain

Of the known ionotropic glutamate receptors, kainate receptors (KARs) are ubiquitous in the CNS and are present at both sides of the synapse. Pre- and postsynaptic KARs regulate both transmission of information and excitability in a synapse-specific manner. The involvement of KARs in synaptic plasticity is now clear and they play a fundamental role in epilepsy through the strategic control of network excitability. Proteins interacting with KARs subunits are being identified and functional studies have evidenced the existence of a dual signalling system. Indeed, KARs may signal through ion flux or by activation of G-proteins. The latter was first observed in the hippocampus and later confirmed in other preparations. An essential aspect for neurotransmitter receptors function is the appropriate localization and cell surface expression. Differential subunit trafficking, targeting and assembly tightly regulates the physiological roles of glutamate receptors and these events are controlled through interactions with proteins that bind to cytoplasmic domains of receptor subunits. The knowledge of these aspects from KARs lags far behind that for other receptors, and only lately has our understanding of KARs trafficking and targeting grown. To get insights into these aspects, our lab recently started a project with the aim of identifying proteins involved in KARs signalling and/or trafficking. As a result, we have identified a number of proteins that seems to be important for the KARs function. Two instances of this are the following. 1- We have found that SNAP25, a protein classically involved in transmitter release, is critical for the synaptic removal of KARs, specifically acting via GluK5 subunits. SNAP25/PICK1/GluK5 interactions are dynamically regulated by protein kinase C resulting in the activity-dependent long-term depression of KAR-mediated synaptic responses, which provides a mechanism for both rapid and chronic changes in the number of synaptic KARs. 2-We have also identified CRMP2 and CRMP4 as interactors of GluK5 subunits. These proteins are highly expressed in the developing nervous system and are known to control neurite outgrowth, neuronal polarity and axon guidance. To assess how KARs could modulate neuronal development, mice DRG neurons were used as a model. We found that KARs modulate neuronal maturation and neurite outgrowth in a bidirectional manner. Data indicate that these actions were mediated by the control of CRMP2 phosphorylation sites after the kainate receptor activation of PKC. These facts document roles from KARs interacting proteins and further unveil a number of unexpected roles for KARs, some of them triggered through their non-canonical signalling.

**9.00 – 10.30: BASIC NEUROSCIENCE**

chaired by: **Matthew Holt** (VIB Center for the Biology of Disease, KU Leuven, Belgium)

---

***Fundamental Mechanics of Membrane Trafficking: Lessons from the Central Nervous System***

**Matthew Holt**

VIB Center for the Biology of Disease, KU Leuven, Belgium

Membrane fusion is absolutely fundamental to maintain the complex organization of eukaryotic cells, in which biochemically distinct processes occur in discrete membrane-bound organelles. These organelles need to communicate with each other, a process that usually involves specialized trafficking vesicles, which bud from the precursor compartment and are transported to the target compartment, where they dock and fuse. However, there are many problems inherent to such a system. For instance, how does one form a fully functional transport vesicle containing all the relevant lipids and proteins? How can it be ensured that this transport vesicle fuses with the correct target? How can you actually force together two negatively charged phospholipid membranes packed with protein? In this talk I will attempt to give an overview of our current understanding of mechanisms involved in membrane trafficking, using the best characterized example – the release of neurotransmitter from neurons in response to action potential stimulation – a process which requires the constant trafficking of small synaptic vesicles in the presynaptic terminal.

***A novel tangential neurons in the peripheral visual system of the *Drosophila melanogaster****

**Agata Kołodziejczyk**

Institute of Environmental Sciences, Jagiellonian University, Poland

The morphology of the visual system in the fruitfly, *Drosophila melanogaster*, is very well described. However tangential neurons communicating in paracrine fashion are only partially known. Using transgenic fly lines combined with immunocytochemistry we discovered four new types of efferent tangential neurons branching distally to the lamina which express respectively: myoinhibitory peptide, acetylcholine and two types of serotonin receptors: 5-HT1A and 5-HT7. We speculate, that discovered tangential 'plexus' may function as an internal eyelid of the *Drosophila* eye.

***Different availability of potassium currents determines two functionally distinct populations of CCK-expressing neurons in the CA3 region***

**Viktor Oláh, Janos Szabadics**

Experimental Medicine, Hungarian Academy of Sciences, Hungary

Specific functions of various voltage-dependent ionic channels contribute to the functional divergence of GABAergic cell types by resulting in different excitability properties. We distinguished two populations of CCK-expressing GABAergic cells (CCK-IN) in the CA3 region of the hippocampus based on the presence or the absence of a potassium current that leads to state-dependent firing properties using recordings from anatomically identified GABAergic cells in acute slices. We found that in a large subset of CCK-INs action potentials are inhibited at the onset when the firing patterns were recorded from hyperpolarized membrane potentials. However, this transient outward rectification (TOR) was absent in

the same cells at depolarized membrane potentials. Interestingly, the second subset of morphologically indistinguishable CCK-INs did not show state-dependent inhibition of action potential generation (non-TOR cells). Voltage-clamp recordings revealed that TOR CCK-INs have substantial A-type potassium currents at lower membrane potentials than their action potential threshold, whereas in non-TOR cells potassium currents are activated only above the threshold. Importantly, the data suggested that the left-shifted voltage-dependency of this potassium current can underlie the state-dependent firing patterns. Altogether, the results revealed that different availability of inactivating potassium conductances distinguishes two functionally different populations among anatomically homogeneous CCK-INs in the CA3 region.

***Mutation of  $\alpha 64$  residue at GABAA receptor binding-site influences not only agonist binding but also conformational transitions between bound states of the receptor***

**Marta M. Czyżewska**, Magdalena Kisiel, Marcin Szczot, Jerzy W. Mozrzymas

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

GABAA receptor (GABAAR) is a ligand-gated ion channel belonging to cys-loop receptors family and mediate fast inhibitory transmission in adult nervous system. It consists of 5 subunits, usually 2  $\alpha$ , 2  $\beta$  and  $\gamma$ , and the ligand-binding site is localized at the interface between  $\beta(+)$  and  $\alpha(-)$  subunit. In the present study we asked how mutations of  $\alpha 64$  residue (agonist binding pocket) in the  $\alpha 1\beta 1\gamma 2$  receptors affected the agonist binding and conformational transitions of bound receptors (gating). We used patch-clamp technique with ultrafast perfusion system and numerous protocols of agonist application. Not surprisingly, this mutation right-shifted the dose-response suggesting a weaker binding. However, this mutation also affected activation rate and desensitization of currents evoked by saturating agonist, suggesting profound changes in gating. Moreover, our analysis indicated that mutation dramatically decreased the maximum open channel probability, further indicating altered gating. Altogether, these experiments show that mutation at the binding site affects not only agonist binding but also the receptor gating. This seems interesting as the binding sites are particularly distant (ca. 60 angstroms) from the channel's pore, suggesting thus that the  $\alpha 64$  residue might be involved in initiating the energy transfer from the binding site to the activation gate.

---

## **9.00 – 10.30: VISUAL ATTENTION**

chaired by: **Rolf Verleger** (Department of Neurology, University of Lübeck, Germany)

---

***How Can We See Things in the Middle Without a Middle Brain?***

**Rolf Verleger**, Marie Dittmer, Kamila Śmigasiewicz

Department of Neurology, University of Lübeck, Germany

Little is known about how the hemispheres interact in processing of stimuli presented at vertical midline. Processing might be mutually independent or cooperative. Here we measured target identification and visually evoked EEG potentials while stimulus streams containing two targets, T1 and T2, were either presented at vertical midline above and below fixation, or laterally, left and right. With left and right streams, potentials evoked by filler stimuli and by T2 were earlier at the right than the left visual cortex, and T2 was better identified left than right, confirming earlier results and suggesting better capabilities of the right hemisphere in this task. With streams above and below fixation, EEG potentials evoked by filler stimuli and by T2 were likewise earlier at the right than the left hemisphere, and T2 was generally identified as well as, but not better than left T2. These results suggest right-hemisphere preference for this task even with stimuli at vertical midline, and no added value through hemispheric cooperation.

Lacking asymmetry for T1 amidst asymmetries for filler stimuli and for T2 might indicate alternating access of the hemispheres to midline stimuli as one means of hemispheric division of labor.

### ***Exogenous cuing of visual spatial attention during dual-stream rapid serial visual presentation***

**Kamila Śmigasiewicz** (1), Dariusz Asanowicz (2), Nicole Westphal (1), Rolf Verleger (1)

(1) Department of Neurology, University of Lübeck, Germany

(2) Jagiellonian University, Poland

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 might reveal easier attraction of attention to the LVF. We introduced the visual cue shortly before T2 onset in order to exogenously attract attention to valid or invalid target location. If right-T2 is often missed because it draws attention less effectively than left-T2, then it should profit more from the valid cue, because attention shifting will be already initiated by the cue. 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 detecting the relevant events outside the focus of attention.

### ***The Simon effect towards memorized locations: EEG support for the involvement of attention***

**Rob H.J. van der Lubbe** (1,2), Carsten Bundt (1), Elger L. Abrahamse (1,3)

(1) Cognitive Psychology and Ergonomics, University of Twente, Enschede, the Netherlands

(2) Department of Cognitive Psychology, University of Finance and Management in Warsaw, Poland

(3) Department of Experimental Psychology, Ghent University, Belgium

About a decade ago it was shown that the Simon effect, the tendency to react towards the side of a stimulus when its location is irrelevant, also occurs when stimuli have to be retrieved from memory. Recently, it was proposed that spatial attention may be responsible for this effect as it might select the relevant object in spatial working memory. An experiment employing the electroencephalogram (EEG) was carried out in which a colored frame (blue, yellow, green, or red) indicated what colored stimulus, one out of four presented in separate quadrants, was the target. The frame occurred either before, simultaneously with, or after the stimuli. In the latter case, the stimuli were first masked and were no longer visible, implying that they had to be retrieved from memory. Simon effects were observed in all conditions, implying that responses were also faster when the side of the to-be-memorized stimulus and the required response side corresponded. Importantly, determination of a newly derived EEG measure, the lateralized power spectra (LPS) in this condition revealed increased ipsilateral occipito-parietal power at around 500 ms after frame onset in the alpha band, supporting the view that attention was directed towards the location of the to-be-memorized item.

### ***Neural networks related to pro-saccades and anti-saccades revealed by independent component analysis***

**Ewa Beldzik**

Department of Neuroergonomics, Institute of Applied Psychology, Jagiellonian University & Neurobiology Department, Malopolska Centre of Biotechnology, Jagiellonian University, Poland

The saccadic eye movement system provides an excellent model for investigating basic cognitive processes. While the mechanism of pro-saccades (PS) is well known, in the case of the antisaccade task (AS) it is still not clear which brain regions play a role in the inhibition of reflexive saccade to the target, nor what is the exact mechanism of vector inversion (i.e. orienting in the opposite direction).

Independent component analysis (ICA) is one of the methods being used to establish temporally coherent brain regions, i.e. neural networks related to the task. In the present study ICA was applied to fMRI data from PS and AS experiments. The study revealed separate networks responsible for saccade generation into the desired direction, the inhibition of automatic responses, as well as vector inversion. The first function is accomplished by the eye fields network. The inhibition of automatic responses is associated with the executive control network. Vector inversion is accomplished by the network comprising: intraparietal sulcus, precuneus cingulate cortices, retrosplenial and parahippocampal. Those regions are associated with the parieto-medial temporal pathway, so far linked only to navigation. These results provide a new insight into understanding of the processes of the inhibition and vector inversion.

---

## **11.00 – 12.30: NEUROPHYSIOLOGY**

chaired by: **Inna Slutsky** (Department of Physiology & Pharmacology, Tel Aviv University, Israel)

---

### ***Hippocampal Plasticity: From synaptic dynamics to Alzheimer's Disease***

**Inna Slutsky**

Department of Physiology & Pharmacology, Tel Aviv University, Israel

It is widely believed that memories are encoded and stored in the pattern and strength of synaptic connections. Individual synapses, the elementary units of information transfer, encode and store new information in response to the environmental changes through structural and functional reorganization. The number and plasticity of synapses are largely maintained through adulthood, but slowly decline during ageing and rapidly deteriorate in a variety of neurodegenerative diseases including Alzheimer's disease. However, the key mechanisms that normally maintain plasticity of synapses during adulthood or initiate synapse loss in neurodegenerative diseases remain elusive. A persistent challenge in unraveling mechanisms that regulate memory function is how to bridge the gap between inter-molecular dynamics of single proteins, activity of individual synapses and emerging properties of neuronal circuits. To target this question, we developed an integrative approach to correlate structure and function at the level of single synapses in hippocampal circuits. Utilizing FRET spectroscopy, optical imaging, electrophysiology and molecular biology we explore the casual relationship between the pattern of ongoing neuronal activity, structural rearrangements within the synaptic signaling complexes and plasticity of single synapses and whole networks. Our results suggest a critical role for ongoing spiking patterns in shaping the function and transition to dysfunction in hippocampal circuits.

### ***Differential effects of MMP-9 and MMP-3 on synaptic plasticity in mossy fiber-CA3 and CA3-CA1 hippocampal projections***

**Grzegorz Wiera** (1), Jerzy W. Mozrzymas (2)

(1) Laboratory of Cellular Neuroscience, Wroclaw Univeristy, Poland

(2) Biophysics Department, Wroclaw Medical University, Poland

Matrix metalloproteinases (MMPs) are enzymes that reorganize the architecture of perisynaptic environment and regulate signaling pathways by proteolysis of extracellular and membrane proteins. It is known, that in the hippocampus, expression and activity of MMP-3 and MMP-9 is involved in the synaptic plasticity and cognitive processes. Interestingly, in spite of different plasticity mechanisms in three hippocampal projections: perforant path-dentate gyrus, mossy fiber-CA3 (MF-CA3) and CA3-CA1, application of a broad spectrum MMP inhibitor impairs long-term potentiation (LTP) in all of them. This result raise a question whether the roles of particular MMPs in LTP induction are universal. Using acute

brain slices from transgenic animals and field potential recordings, we have shown that in mice lacking functional mmp-9 gene, LTP is almost abolished in MF-CA3 pathway but not in CA3-CA1. Oppositely, in slices from rats overexpressing mmp-9 LTP is impaired in both projections. To elucidate the role of MMP-3 protease in LTP, we used highly specific inhibitor (UK356618) and found that MMP-3 inhibition impairs LTP in CA3-CA1 projection but not in the MF-CA3 pathway. In conclusion, we provide the first evidence that LTP induction and consolidation in the MF-CA3 and CA3-CA1 pathways is differentially regulated by MMP-3 and MMP-9.

### ***Oscillations within the amygdalo-prefronto-striatal network as correlates of prospective timing in rats***

**Jeroen M.J. Knippenberg** (1), M. Graupner (2), V. Doyère (1,2)

(1) Centre de Neurosciences Paris-Sud, CNRS-UMR8195, Université Paris-Sud, Orsay, 91405, France

(2) Center for Neural Science, New York University, New York, NY 10003, USA

In Pavlovian conditioning procedures an organism not only learns that stimulus A predicts stimulus B, it also learns when stimulus B is presented. Recent evidence suggests that the amygdala might be involved in this kind of temporal encoding. On the other hand, prefrontal cortex and dorsal striatum have traditionally thought to be involved in time perception. We recorded local field potentials (LFPs) from these three structures during auditory fear conditioning in rats, in which a tone conditioned stimulus (CS) predicted the delivery of a footshock unconditioned stimulus (US) at a specific time during the CS. Using a conditioned suppression paradigm (with lever pressing for food as instrumental basis), we demonstrated that rats acquired precise temporal knowledge regarding the arrival time of the US. Analysis of oscillations in LFPs showed that within prefrontal cortex and striatum spectral power in the theta range (4-9Hz) gradually increased towards, and peaked at, the expected time of the US. At the same time, beta power (13-20Hz) decreased during the CS, reaching its minimum during the expected US time. In addition, increases in coherence between oscillations in different structures were present in the theta band, while decreases were observed in the beta band.

### ***How particular photoreceptors contribute to infra slow oscillatory activity generation in the rat olivary pretectal nucleus?***

**Patrycja Orłowska**, Szkudlarek H.J., Lewandowski M.H.

Department of Neurophysiology and Chronobiology, Jagiellonian University, Poland

The olivary pretectal nucleus (OPN) is a midbrain structure which plays a crucial role in pupil constriction and circadian entrainment. It is also one of few structures within the Circadian Visual System, which generate spikes in an infra slow oscillatory mode (ISO) with a period of approximately two minutes. We have previously shown that ISO in the OPN depends on functional, contralateral, retinal input and due to that we decided to verify the role of particular photoreceptors and general retinal desynchronization in ISO generation. Experiments were performed on urethane anaesthetized Wistar rats by using extracellular recordings combined with contralateral, intraocular injections. L-(+)-2-amino-4-phosphonobutyric acid (10 mM), DL-2-amino-5-phosphonopentanoic acid (5 mM) and 6,7-dinitroquinoxaline-2,3-dione (5 mM) were used to eliminate rod-cone input; 2-aminoethoxydiphenylborane (1mM) - melanopsin, carbenoxolone (1mM) to desynchronize the retina. The results have shown that only activity of melanopsin cells is crucial for SOA generation in the OPN. Inactivation of melanopsin cells caused disappearance of oscillations in 91% of inspected neurons. Chemical blockade of 'classic' photoreceptors neither changed firing pattern nor the period of oscillations. Similar results were obtained for retinal desynchronization. Presented data suggest that oscillatory activity in the OPN is driven or strongly modulated by melanopsin ganglion cells.

---

## 11.00 – 12.30: AFFECTIVE NEUROSCIENCE

chaired by: **Gilles Pourtois** (Psychopathology & Affective Neuroscience Laboratory, Department of Experimental Clinical & Health Psychology, Ghent University, Belgium)

---

### ***Variety of affective state-dependent modulations of attention control and early gain control effects in primary visual cortex***

**Gilles Pourtois**

Psychopathology & Affective Neuroscience Laboratory, Department of Experimental Clinical & Health Psychology, Ghent University, Ghent, Belgium

In this paper, I will review recent neurophysiological data showing that early visual stimulus processing and attention gating effects are not only determined by the amount of resources available at a given moment in time, but also by the current affective state of the participant. Noteworthy, different affective states can trigger qualitatively different changes in early sensory processing and attention control. For example, whereas positive emotion appears to broaden up the attention focus, by comparison, negative emotion narrows down this attentional focus, with early traceable effects in the primary visual cortex. Moreover, depending on the type of dread induced and sustained, negative affect can also sometimes lead to effects that eventually look like a broadening of the attentional breadth. These results will be discussed in light of a new theoretical framework that posits that multiple attention control systems dynamically gate sensory processing, early on following stimulus onset along the visual processing hierarchy. Moreover, these new findings emphasize an extraordinary flexibility in the ability of healthy adult participants to easily switch from one mode of exploration to another one, depending on the specific needs and goals imposed by the actual task demands and affective state.

### ***Time-course of attention-emotion resource competition in early visual cortex is related to the latency of emotional cue extraction***

**Valeria Bekhtereva, Matthias M. Müller**

University of Leipzig, Germany

We have previously investigated competitive interactions for processing resources in early visual cortex between a flickering foreground task that elicited steady state visual evoked potentials (SSVEPs) and task-irrelevant emotional background images from the IAPS set. Affective images withdrew more attentional resources from the foreground task than neutral images, causing a greater reduction in SSVEP amplitudes. This reduction was preceded by the extraction of emotional content as indexed by the early posterior negativity (EPN; ~240 ms). Here, we tested whether the time-course of biased competition differs between task-irrelevant emotional faces and IAPS images. Emotional cue extraction for faces precedes emotional cue extraction for IAPS images: the N170 (~170 ms) to faces is sensitive to emotional content. We therefore predicted an earlier reduction in SSVEP amplitudes with emotional background faces than emotional IAPS images. We found more negative deflections for emotional stimuli in both the EPN (330 ms) to IAPS images and the N170 (175 ms) to faces. As predicted, the SSVEP showed a significant decrease earlier (~200 ms) with emotional background faces than with emotional IAPS images (~500ms). Thus, the time course of competition bias seems to be linked to the latency of emotional cue extraction, rather than to a time-invariant switching process.

## ***Asymmetry of the conflict adaptation effect for the positive and negative incongruent stimuli in the face-word Stroop task***

**Filip Gęsiarz**

University of Amsterdam, the Netherlands

It is well established that the resolution of conflict in one trial in classical Stroop task speeds up the resolution of conflict on the subsequent trial. This phenomenon, known as conflict adaptation effect, has been recently also demonstrated for the novel emotional face-word Stroop task, in which participants categorize face expressions, while ignoring congruent or incongruent labels superimposed on them. The aim of the current study was to investigate if this version induces similar effects at the neuronal level as its cognitive equivalent. EEG recordings were used to examine if emotional Stroop modulates conflict related N450 component and face related N170 component. In the light of the studies showing that the experience of conflict facilitates processing of negative and impairs processing of positive stimuli, it was hypothesized that the conflict adaptation will be seen only for the incongruent negative expressions. Consistently with these predictions, it was shown that conflict speeded up reaction times to subsequent negative incongruent stimuli, simultaneously increasing the amplitude of N170 and decreasing the amplitude of N450 components. The opposite tendency was seen for the positive stimuli. Overall, this asymmetry of conflict adaptation for different expressions suggests engagement of some additional processes to cognitive control during the experience of emotional conflict.

## ***Electrophysiological evidences for increased vigilance and selective attention effects in fear and anxiety***

**Jarosław Michałowski (1), Christiane Pané-Farré (2), Alfons Hamm (2)**

(1) University of Warsaw, Poland

(2) University of Greifswald, Germany

Previous ERP studies consistently demonstrated the preferential processing of threat-relevant stimuli in fear/anxiety (Kolassa et al., 2006, Miltner et al., 2005, Michalowski et al., 2009; Walentowska & Wronka, 2012). Moreover, some of these data also suggest that increased fear and anxiety are associated with a greater hypervigilance in a threatening context (Kolassa et al., 2006; Michalowski et al., 2009; Walentowska & Wronka, 2012). We investigated these issues in several ERP studies in participants with high and low fear and anxiety during viewing of aversive (threat-relevant and threat-irrelevant) as well as non-aversive pictures. In contexts in which threat-relevant aversive materials were likely, high fear and anxiety individuals responded with larger P1 amplitudes than controls, an effect that was not observed in a context in which aversive pictures were not expected. Furthermore, high fear and anxiety participants showed an increased selective attention towards threat-relevant aversive pictures when compared to controls. These increased selective attention effects appeared specific for the threat-relevant materials. They were also observed for simple cues associated with threat. These results demonstrate a temporal unfolding in perceptual processing from unspecific vigilance occurring in the aversive context (P1) to increased threat-specific perceptual and evaluative analysis in high fear and high anxiety individuals.

---

## **12.40 – 13.40: PLENARY LECTURE**

---

## ***Compound mechanisms for sensory map plasticity in the mouse barrel cortex***

**Anthony Holtmaat**

University of Geneva, Switzerland

Experience-dependent cortical plasticity is based on activity-dependent strengthening and weakening of pre-established synapses and may even include synapse formation and elimination. Some of the most compelling evidence for experience-dependent remodeling of adult cortical circuits has come from studies in the mouse somatosensory barrel cortex. Individual infra and supragranular cells, which become highly tuned to a single whisker on the mouse's snout during development, retain the capacity to alter their receptive fields in adulthood. The interplay between functional and structural types of synaptic plasticity in the somatosensory cortex is poorly understood. We study both types of plasticity over short and long time frames *in vivo*. First, using whole cell recordings of L2/3 cells *in vivo* we have monitored forms of experience-dependent metaplasticity that may set the stage for long-term changes in circuit function. We found that a brief period of whisker sensory deprivation caused disinhibition of spared (sparing) whisker sensory inputs, which in turn facilitated spike-time dependent LTP. The deprivation also augmented inputs of a non-specific paralemniscal pathway that is relayed in the posterior medial (POM) thalamic nucleus. Second, we used *in vivo* optical imaging techniques to investigate the relationship between the relatively slow structural modifications in synaptic circuits and alterations in receptive fields upon long-lasting imbalances of sensory input. We tested the hypothesis that peripheral nerve deafferentation causes large-scale dendritic reorganization in the cortex. We repeatedly imaged whisker-evoked intrinsic optical signals as well as L2/3 and L5 pyramidal dendritic structures in the mouse barrel cortex over months after the removal of a subset of the whisker follicles. Although this procedure caused the expansion of spared whisker responses, it failed to induce large-scale sprouting of dendrites. Changes remained limited to increased dendritic spine stabilization. This suggests that large map shifts do not depend on large-scale restructuring of dendritic arbors but are associated with and might be caused by local changes in synaptic connectivity only.

---

## 15.00 – 17.00: NEUROIMAGING

chaired by: **Grzegorz Wilczyński** (Laboratory of Molecular and Systematic Neuromorphology, Nencki Institute of Experimental Biology, Warsaw, Poland) & **Vincent Bonin** (Neuro-Electronics Research Flanders, Leuven, Belgium)

---

### ***Activity-dependent architectural remodeling of the neuronal cell nucleus***

**Grzegorz Wilczyński**

Laboratory of Molecular and Systematic Neuromorphology, Nencki Institute of Experimental Biology,  
Warsaw, Poland

Studies in cultured non-neuronal cell types have demonstrated the existence of higher-order epigenetic mechanisms, determining the relationship between expression of the gene and its positioning within the architectural framework of the cell nucleus. It is unknown, however, whether such mechanisms operate *in vivo*, in post-mitotic, highly differentiated cell types, such as neurons. Recently, we have examined whether the intranuclear positions of *Bdnf* and *Trkb* genes, encoding the major neurotrophin and its receptor respectively, change upon neuronal activation, and whether there are functional consequences of such movements. Using fluorescent *in situ* hybridization with confocal detection, and an innovative three-dimensional image analysis software, we found, in a rat model of *status epilepticus*, that the elevated neuronal expression of *Bdnf* gene after seizures is associated with its detachment from the nuclear lamina, and its translocation toward the nucleus center. In contrast, the position of stably expressed *Trkb* gene remains unchanged after seizures. Our study demonstrates that activation-dependent architectural remodeling of the neuronal cell nucleus *in vivo* contributes to activity-dependent changes in gene expression in the brain.

## ***Large-scale physiology and imaging of targeted neuronal populations in behaving mice***

**Vincent Bonin**

Neuro-Electronics Research Flanders & KU Leuven, Belgium

The brain is made of billions of neurons organized in dispersed yet highly interconnected local networks whose activity forms the basis for our sensations, emotions, memories and actions. How large-scale and local network activity is coordinated during behaviour however, remains poorly understood. In this talk I will describe an experimental infrastructure we have developed to address this question in the visual system of behaving mice. Like that of primates, the mouse visual system consists of anatomically and functionally specialized areas showing distinct patterns of connections and performing specific visual computations. The mouse's small brain and its amenability to genetic manipulations allow for chronic large-scale electrical and optical recordings of targeted cell populations across multiple brain areas. Combined with recently developed rodent behavioural assays, these tools yield an unprecedentedly detailed view of brain function during behaviour. In the future we envision a similar approach to study the neural basis of learning both in the healthy and dysfunctional brain.

### ***Effect of MMP-9 activity on dendritic spine turnover and morphology***

**Marta Pyskaty, Z. Szepesi, M. Bijata, L. Kaczmarek, J. Wlodarczyk**

Nencki Institute of Experimental Biology, Warsaw, Poland

MMP-9 is a member of matrix metalloproteinases (MMPs) family, secreted and activated in the extracellular space in response to enhanced neuronal activity. MMP-9 can cleave and release signaling molecules from extracellular matrix (ECM) which affects morphology and turnover of dendritic spines. Recently, we have shown that enzymatic activity of recombinant autoactivating MMP-9 influences spine morphology. To investigate the impact of endogenous MMP-9 on dendritic spines morphology and turnover we employed a chemically induced long-term potentiation (cLTP) model. We have demonstrated that cLTP increases activity of endogenous MMP-9 localized to the dendritic spines and drives the formation of spine head protrusions in cultured neurons. Furthermore, the quantitative analysis of spine turnover shows that MMP-9 is engaged in spine elimination mechanism.

### ***Optimization of 3D segmentation of neuronal cell nuclei in the mouse brain***

**Iwona Czaban, Małgorzata Broszkiewicz, Adriana Magalska, Błażej Ruszczycki, Grzegorz M. Wilczyński**

Nencki Institute of Experimental Biology, Warsaw, Poland

Little is known about the relationship between neuronal gene expression and the architecture of the neuronal cell nucleus. We wanted to study the cell nuclei in neurons of the mouse cerebral cortex, using confocal microscopic immunocytochemistry. We used a segmentation algorithm, based on continuous boundary tracing, able to reconstruct the nucleus surface and to separate adjacent nuclei (Walczak et al. J Neurosci 33:2507, 2013). The algorithm did not use a rigid threshold what made it robust against variations in image intensity and poor contrast. However, when we analyzed mouse, but not rat, neuronal nuclei there have occurred a considerable problem with an appropriate segmentation. This problem was related to the presence of the discrete chromocenters, which are much more prominent in the mouse than in other species. Therefore, in order to assure the proper segmentation, we used sections co-immunostained for the lamin protein. Our refined program is an efficient segmentation tool for crowded and overlapping objects in 3D space, regardless of the particular species. It allows us to study quantitatively the architecture of the neuronal nucleus using confocal-microscopic approach.

---

## **15.00 – 17.00: EPILEPSY & SOMATOSENSORY PROCESSING IN ANIMAL AND HUMAN STUDIES**

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

---

### ***Altered properties of thalamic pacemaker channels in a rat model of human absence epilepsy***

**Thomas Budde**

Institute of Physiology I, University of Münster, Germany

Rats of the WAG/Rij strain represent an accepted rodent model of human childhood absence epilepsy. EEG recordings revealed that sleep-related delta activity precedes the occurrence of epileptic spike-and-wave discharges (SWDs). Hyperpolarization-activated cyclic nucleotide-gated cation (HCN) channels are the molecular substrate of the pacemaker current  $I_h$  and act as critical pacemakers for intrinsic delta oscillations in thalamocortical (TC) neurons. Alterations in the electrophysiological properties of  $I_h$  in WAG/Rij rats seem to contribute to epileptogenesis. HCN channels in TC neurons are characterized by an increased HCN1 expression, a negative shift in  $I_h$  activation curve, and an altered responsiveness of  $I_h$  to cAMP. These changes in HCN channel properties are accompanied by an increased expression of the  $\beta$ -subunit TRIP8b. Furthermore we cloned HCN1 channels from WAG/Rij rat thalamic cDNA libraries (WAG-HCN1), and found an N-terminal deletion of 37 amino acids. Heterologous expression in *Xenopus* oocytes revealed 2.1-fold increased current amplitude of WAG-HCN1 compared to rat HCN1. Fluorescence imaging demonstrated stronger surface expression of WAG-HCN1. Our findings indicate that the observed alterations in WAG/Rij TC neurons may be based on an enhanced  $\beta$ -subunit interaction in combination with the expression of the WAG-HCN1 variant which may facilitate the switch from physiological oscillations to SWDs.

### ***Unraveling brain networks in absence epilepsy***

**Annika Lüttjohann, Gilles van Luijtelaar**

Donders Institute for Brain, Cognition and Behaviour, Radboud University Nijmegen, the Netherlands

Purpose Spike and Wave discharges (SWD), the electrophysiological hallmark of absence epilepsy are generated within the cortico-thalamo-cortical system, but the network interactions between cortex and thalamic nuclei remain enigmatic. WAG/Rij rats were equipped with multiple electrodes targeting layer 4 to 6 of the somatosensory-cortex, rostral and caudal RTN, VPM, anterior- (ATN) and posterior- (Po) thalamic nucleus. Six-seconds lasting pre-ictal  $\rightarrow$  ictal transition-periods were analyzed by pairwise-phase-consistency (PPC) and nonlinear-association analysis. A decrease in PPC was found between the caudal-RTN and the deep somatosensory-cortex, VPM and Po 2.5 sec before SWD generation, strong increases in coupling-strength were seen between cortical layer 5/6 and Po 1.25 sec before SWD onset. Other thalamic nuclei became only later involved in seizure activity. The cortex guided most thalamic nuclei during the first 500ms of a seizure, in contrast cortex and Po kept a bidirectional crosstalk throughout SWD. The disattachment of the caudal-RTN sets the cortico-thalamo-cortical system in a pro-epileptic state. This lack of control allows the cortical epileptic focus to increase its communication with the thalamus and ultimately entrain it in SWD activity. The Po is the primary thalamic counterpart for SWD generation given its strong and early involvement. The bidirectional coupling provides an initial reverberation-circuit.

## ***The effects of responsive and scheduled subicular high frequency stimulation in a seizure model of TLE***

**Lili Huang, Gilles van Luijtelaa**r

Department of Biological Psychology, Donders Center for Cognition, Donders Institute for Brain, Cognition and Behaviour, Radboud University Nijmegen, the Netherlands

Responsive deep brain stimulation (rDBS) is a promising and newly emerging treatment for refractory temporal lobe epilepsy in which current is delivered to target areas dependent of occurrence of seizures. We compared responsive and scheduled subicular high frequency stimulation (HFS) with a sham control group on acute seizures and seizure sensitivity 2 weeks later and the role of status epilepticus (SE) on efficacy of both types of stimulation. Adult Wistar rats received kainic acid (KA) injections intrahippocampally until they reached Stage V (Racine scale) on Day1. Responsive, scheduled or sham HFS (125 Hz, 100  $\mu$ s) was delivered in three groups while EEG were recorded. The sensitivity to KA-induced seizures was established again on Day15. All rats reached Stage V and 60% reached SE on Day1. Focal seizures were suppressed in both stimulated groups (the scheduled groups was slightly more effective) on both days in only non-SE rats, also generalized seizures in non-SE rats but only on Day15. Both types of stimulation suppressed focal and generalized seizures, albeit differently. Beneficial effects of DBS were restricted to non-SE rats. Responsive stimulation is effective, despite the small amount, supporting it as a new stimulation approach for epilepsy treatment.

### ***Together but apart: relationship between absence seizures and motor activity***

**Magdalena K. Smyk** (1), A. Coenen A. (2), M.H. Lewandowski (1), G. van Luijtelaar (2)

(1) Department of Neurophysiology and Chronobiology, Chair of Animal Physiology, Institute of Zoology, Jagiellonian University, Poland

(2) Department of Biological Psychology, Donders Centre for Cognition, Donders Institute for Brain, Cognition and Behaviour, Radboud University Nijmegen, the Netherlands

7-11 Hz spike-wave discharges (SWDs) are electroencephalographic manifestation of absence seizures in WAG/Rij rats, a well characterized model of absence epilepsy. Both SWDs and activity occur rhythmically, predominantly in the dark phase, since they are controlled by the circadian timing system. However, in a short-time scale, active wakefulness is the least probable to precede SWDs. Here it is investigated whether this negative coupling is due to the presence of the photoperiod or remained present after a phase shift. EEG and motor activity were recorded simultaneously for min. 12 days in 8-12 WAG/Rij rats. Rats were subjected to 12:12 LD cycle, constant dim light or an 8 hour phase-shift. Results show that the rhythms of SWDs and activity are coupled to each other under 12:12 LD cycle, but they desynchronize in the free run and after a phase-shift. Those changes however, are not able to affect momentary relationship between SWDs and active wakefulness. It can be concluded that SWDs and activity are related on two different levels. Their circadian rhythms coupled under entrained circumstances, are controlled by two distinct oscillators. The momentary coupling of AW and SWDs however, was not affected by experimental circumstances.

### ***Altered resting state EEG in patients with chronic abdominal pain***

**Marjan de Vries** (1), Oliver HG Wilder-Smith (2), Emanuel N van den Broeke (1), Harry van Goor (1), Clementina M van Rijn (3)

(1) Department of Surgery, Radboud University Nijmegen Medical Centre, Nijmegen, the Netherlands

(2) Department of Anesthesiology, Pain and Palliative Care, Radboud University Nijmegen Medical Centre, Nijmegen, the Netherlands

(3) Donders Institute for Brain, Cognition and Behavior, Radboud University Nijmegen, the Netherlands

Electroencephalography (EEG) might be a promising method to detect alterations in brain activity accompanying chronic pain. Several studies in patients with chronic neuropathic pain observed slowed EEG rhythmicity and increased EEG power in the brain resting state. The aim of this study was to investigate the effects of chronic pancreatic pain on the spontaneous brain activity in the alpha band. Resting state EEG data from 16 patients with persistent abdominal pain due to chronic pancreatitis (CP) were compared to data from healthy controls (HC) matched for age, gender and education. The peak alpha frequency (PAF) and power amplitude in the alpha band (7.5-13 Hz) were compared between groups in four regions of interest (frontal, central, parietal, and occipital), and were correlated with pain duration. The average PAF was lowered in CP patients compared to HC, observed as a statistically significant between group effect ( $F= 4.20$ ;  $p= 0.049$ ). In addition, we observed a significant negative correlation between pain duration and PAF ( $r= -0.379$ ;  $p= 0.032$ ). No significant group differences were found in peak power amplitudes. Chronic pancreatitis pain is associated with alterations in the spontaneous brain activity, observed as a shift towards lower PAF. Accordingly, these findings could be helpful for assisting diagnosis, establishing optimal treatment and studying efficacy of new therapeutic agents in chronic pain patients.

### ***Intraoperative somatosensory evoked potential monitoring decreases EEG burst suppression ratio during general anesthesia***

**Alexandru Călin** (1,2), Vishakhadatta Mathur Kumaraswamy (2), Diana Braver (2), Dinesh G. Nair (2), Mihai Moldovan (3,1), Mirela V. Simon (2)

(1) Department for Functional Sciences, Division of Physiology and Neuroscience, „Carol Davila” University of Medicine and Pharmacy, Bucharest, Romania

(2) Intraoperative Neurophysiology Unit, Department of Neurology, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts, USA

(3) Neuroscience and Pharmacology, Panum, University of Copenhagen, Denmark

The burst-suppression (BS) electroencephalographic (EEG) patterns induced by general anesthesia can react to somatosensory stimuli. We investigated to which extent peripheral nerve stimulation used for routine intraoperative spinal cord monitoring by somatosensory evoked potentials affects BS patterns. The relative time spent in suppression expressed as BS ratio (BSR) and mean burst duration (BD) were measured pre (BSRPre), during (BSRStim) and post (BSRPost) a 60-second repetitive electrical ulnar nerve stimulation in 9 patients under total intravenous general anesthesia with propofol. The BS reactivity was measured as BSRPre- BSRStim. We included 27 trials with BSRPre up to 77%, indistinguishable from BSRPost. During stimulation, the mean BSR transiently dropped from 42% to 35%. For each 1 % increase in BSRPre the BS reactivity increased with 0.6 % whereas the BD remained about 3 s. For BSRPre below 30% the BS reactivity was negligible. Our data suggest that during deep general anesthesia SSEP monitoring can evoke bursts, altering the “spontaneous” BS patterns. Such changes in the level of somatosensory input should be accounted for when BSR is used to target the anesthetic concentration or to estimate the changes in cortical excitability for procedures like neurophysiologic motor mapping.

---

## **17.30 – 18.30: PLENARY LECTURE**

---

### ***When Thoughts Become Actions: Imaging Disorders of Consciousness***

**Adrian Owen**

Centre for Brain and Mind, University of Western Ontario, Canada

**9.00 – 10.30: NEUROPSYCHIATRY**

chaired by: **Karolina Skibicka** (Institute of Neuroscience and Physiology, University of Göteborg, Sweden)

---

***My gut made me do it! The story of how gut hormones influence food reward and motivation***

**Karolina Skibicka**

Institute of Neuroscience and Physiology, University of Göteborg, Sweden

Obesity is becoming a worldwide epidemic. The unhealthy body weight is contributing to development of many diseases including cardiovascular disease and diabetes. So why do we continue on overeating? Emerging research suggests that food might impact on brain circuits in a similar way to drugs of addiction or alcohol, creating an addiction like phenotype. The mesolimbic dopamine circuitry, already shown to be core in alcohol and substance abuse is now implicated in the reward derived from food. Therefore targeting this brain circuit might provide a novel effective therapy to reduce overeating behavior. Emerging results show that gut produced hormone, glucagon-like peptide 1 (GLP-1), can play a major role in regulating the mesolimbic circuitry and the food reward behavior. Indeed, exciting new data indicate that targeting the mesolimbic GLP-1 receptors may lead to a reduction in food reward behavior. These results potentially open up new avenues for treatment of obesity.

***Antidepressant-like activity of newly synthesized quinoline and isoquinoline analogues of aripiprazole***

**Dagmara Wróbel** (1), Magdalena Jastrzębska-Więsek (1), Anna Partyka (1), Anna Wasik (1), Paweł Zajdel (1), Grzegorz Satała (2), Andrzej Bojarski (2), Maciej Pawłowski (1), Anna Wesołowska (1)

(1) Jagiellonian University Medical College, Poland

(2) Institute of Pharmacology, Polish Academy of Sciences, Kraków, Poland

Aripiprazole is an atypical antipsychotic that has been recently registered for the treatment of mood disorders. Series of new quinoline- and isoquinoline-sulfonamides, aripiprazole analogues, was tested for their affinity for serotonin 5-HT<sub>1A</sub>, 5-HT<sub>2A</sub>, 5-HT<sub>6</sub>, 5-HT<sub>7</sub> receptors and serotonin transporter (5-HTT). Their antidepressant-like activity was investigated in the forced swim test (FST) in mice. Effective compounds, administered in sub-antidepressant doses, were tested toward possible interaction with antidepressant reference drugs, i.e. escitalopram and imipramine, and with a selective 5-HT<sub>1A</sub> receptor antagonist, WAY-100635, to clarify their mechanism of action. Two selected compounds, PZ-508 and PZ-549, with high affinity for 5-HT<sub>1A</sub> (K<sub>i</sub>=59 nM and 14 nM, respectively) and 5-HT<sub>7</sub> (K<sub>i</sub>=21 nM and 12 nM, respectively) receptors and relatively significant affinity for 5-HTT (K<sub>i</sub>=783 nM and 224 nM, respectively), demonstrated antidepressant-like activity, (PZ-508 in a dose of 10 mg/kg, PZ-549 in doses of 5 and 10 mg/kg). Active and non-active doses of both compounds show synergistic action with inactive doses of antidepressants used. Nevertheless, the antidepressant action of neither PZ-508 nor PZ-549 was significantly blocked by WAY-100635. Herein, antidepressant-like activity of both derivatives may be explained by their high affinity for 5-HT<sub>7</sub> receptors and relatively high affinity for 5-HTT in the case of PZ-549.

## ***Chronic psychosocial stress makes rats more pessimistic in the ambiguous-cue interpretation paradigm***

**Justyna Papciak, Rafał Ryguła**

Department of Behavioral Neuroscience and Drug Development, Institute of Pharmacology  
Polish Academy of Sciences, Kraków, Poland

Human decisions are often biased by emotions. Stressed and depressed individuals tend to make negative, pessimistic judgements while those in positive affective states are often more optimistic. Chronic psychosocial stress has been shown previously to induce in rats a spectrum of behavioural and physiological changes considered to be correlates of depressive symptoms in humans. In the present study we investigated whether chronic social defeat can make animals more pessimistic. To measure the changes in the cognitive judgement bias we applied the ambiguous-cue interpretation paradigm. In the operant boxes, the rats were trained to press one lever in response to one tone to receive a reward and to press another lever in response to a different tone to avoid punishment. Cognitive bias was tested by measuring the pattern of animals' responses to a tone of intermediate frequency (ambiguous-cue). To induce chronic psychosocial stress we subjected the animals to daily social defeat in the resident-intruder paradigm for 3 weeks. We report that chronic psycho-social stress that induces depressive symptoms in rats, makes them also more pessimistic. [This work was supported by the Foundation for Polish Science "Homing Plus" Programme co-financed by the European Regional Development Fund (Innovative Economy Operational Programme 2007–2013)].

## ***Role of Retinoid X receptors in control stress adaptation processes in social defeat model***

**Anna Podlesny (1), Agnieszka Krzyzosiak (2), Wojciech Krezel (2)**

(1) IITD PAN (Institute of Immunology and Experimental Therapy, Polish Academy of Science),  
Wrocław, Poland

(2) IGBMC (Institut de Génétique et de Biologie Moléculaire et Cellulaire), Illkirch, France; Inserm,  
U 596, Illkirch, France; CNRS, UMR 7104, Illkirch, France; Université Louis Pasteur, Strasbourg, France

Preclinical genetic and pharmacological studies indicated that compromised signaling through retinoid X receptor (Rxr) gamma in the nucleus accumbens (NAc) is associated with depressive-like behavior. In order to understand physiological functions of Rxr gamma in stress adaptation processes and its implication in the etiology of depressive-like behaviors we studied its signaling in mouse model of social defeat stress (SDS). The role of Rxrs in mechanisms of stress adaptation was studied by analysis of Rxr-specific pharmacological treated mice. Molecular studies were performed by RT-qPCR and DNA microarray analyses concerning transcripts with genetic ablation of Rxrg. We found that in wild type C57BL6N mice stress led to hyperactivity of NAc shell as monitored by enhanced expression of several early responsive genes which were also identified among Rxrg<sup>-/-</sup> mice. Absence of reduced expression of Rxrg in response to chronic stress suggests its up-stream position in the process of stress-related adaptive changes in the NAc. Here we showed a potential role of Rxrs in modulation of stress adaptation processes. It may be instrumental for understanding of clinical depression associated with abnormal signaling of isotretinoin or n-3 polyunsaturated fatty acids, the pharmacological modulators of transcriptional activities of Rxrs.

---

## 9.00 – 10.30: PSYCHOPHYSIOLOGY OF COGNITIVE & EMOTIONAL FUNCTIONING

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

---

### ***Rule application versus rule discovery: A cardiovascular perspective***

**Tytus Sosnowski**, Aleksandra Sobota, Andrzej Rynkiewicz

University of Warsaw, Poland

Our previous research showed that mental tasks that involve rule application (RA), e.g. performing arithmetic operations, cause greater tonic increase in cardiovascular activity than tasks that require a rule discovery (RD), e.g. logical completion of a series of digits. However, it was not clear what physiological mechanism was responsible for this difference. The aim of the experiment was to compare cardiac response patterns while solving three mental tasks matched for their duration and difficulty: a (control) simple RT task and RA and RD numeric tasks. Forty-eight males, university students, divided randomly into three groups (n = 16), participated in the experiment. Each group performed a different task. Task-evoked changes in heart rate (HR), stroke volume (SV), cardiac output (CO), pre-ejection period (PEP), and power of HF component of heart rate variability were subject of the analysis. The results showed a higher tonic HR increase during the RA task than the two other tasks and larger shortening of PEP during the RA than the RD task. The HF was larger during the RT than the RA task. The results support the hypothesis that higher cardiac responsiveness to RA than RD tasks is mainly due to the difference in sympathetic activation.

### ***The heart of emotions: understanding fear through left ventricular contractility***

**Javier R. Árbol**, I. González, J.L. Mata, J. Vila

University of Granada, Spain

Physiological changes involved in emotions may help us to better understand how brain structures coordinate our behavior and to build a comprehensive conceptual framework of the meaning of emotions and their implications in human health. Regarding to emotions, one of the most interesting neurophysiological aspects is the activity of neurovegetative tracts innervating the heart, since it determines the blood flow and therefore the level of energy mobilized for reacting properly in that very situation. The Pre-Ejection Period (PEP), an index of left ventricular contractility obtained by analysis of simultaneous recording of impedance cardiography and electrocardiography, shows with a great temporal resolution the influences of autonomic system on the heart. In order to elicit an affective and automatic psychophysiological response, participants underwent an experimental preparation of cardiac defense response, a well established paradigm of cardiovascular affective-mediated reactivity. Assessment of PEP in a sample of 40 young volunteers (20 women) subjected to this psychophysiological test, shows gender differences in the beta-adrenergic activation pattern elicited. These results provide support to the possible existence of neurovegetative differences in the experience of fear between men and women.

### ***Electrophysiological correlates of individual differences in tendency to ruminate***

**Magdalena Ferdek** (1), Mirosław Wyczesany (2)

(1) Jagiellonian University, Poland

(2) Psychophysiology Laboratory, Jagiellonian University, Poland

Ruminations are repetitive thoughts associated with symptoms, causes, and consequences of one's negative feelings. It has been shown that this maladaptive form of self-reflection is a good predictor of

major depression episodes. However, neuronal basis of depressive ruminations remains unclear and require further investigation. This study aimed to explore electrophysiological correlates of depressive ruminations in non-clinical subjects. Participants were selected based on their scores in Ruminative Responses Scale and divided into two groups: ruminators and non-ruminators. It was hypothesized that they would differ in prefrontal and medial cortex activity related to affective and cognitive modulatory mechanisms. The EEG data were collected during induced state of depressive ruminations and compared with positive and neutral control conditions. The EEG cluster analysis revealed locational specificity of valence and group effects: the former pronounced mostly in left temporal and left dorsolateral regions while the latter in prefrontal areas. Moreover, interactions of these factors were found in left dorsolateral as well as in left paralimbic areas. The data suggest that there are evident differences in the brain activity between ruminators and non-ruminators even in non-clinical population. The results will be discussed in terms of emotional control processes.

### ***The neural mechanisms of the non-specific digestive tract diseases. Preliminary report***

**Patrycja Naumczyk** (1), Sabisz, A. (1), Skrobisz, K. (2), Markiet, K. (2), Szurowska, E. (2), Piotrowicz, G. (3)

(1) University of Gdańsk, Poland

(2) Gdańsk Medical University, Poland

(3) 7th Navy Hospital, Gdańsk, Poland

The aim of the study is to explore the neural mechanisms underlying the differences in functioning of the patients with non-specific digestive tract diseases as compared with the healthy controls. The report summarizes the results of the nineteen subjects – twelve of whom (the study group) suffering from the non-specific digestive tract disease (the Functional Dyspepsia, the Inflammatory Bowel Disease or the Irritable Bowel Syndrome), seven of whom (the control group) without any medical problems. All of the participants underwent the psychological examination as well as the resting-state functional magnetic resonance imaging (fMRI) examination. The results of the both of the assessments are consistent. The psychological tests showed no heterogeneity within the study group together with significant differences in the field of the emotional functioning as compared with the control group. The fMRI examination showed significant alternations in the functioning of the anterior cingulate cortex (ACC) network between the groups covering the ACC, the insula and the amygdala. The results suggest different mechanism of emotional control in the study group as compared with the healthy control.

---

## **10.40 – 11.40: PLENARY LECTURE**

---

### ***The neurobiology of language beyond the information given***

**Peter Hagoort**

Donders Centre for Cognitive Neuroimaging & Max-Planck Institute for Psycholinguistics,  
Nijmegen, the Netherlands

---

## 12.00 – 13.30: NEUROGENETICS

chaired by: **Lora Heisler** (Department of Pharmacology, University of Cambridge, UK)

---

### ***Integration of Metabolic Signals by CNS Serotonin Pathways***

**Lora Heisler**

Department of Pharmacology, University of Cambridge, UK

The brain serotonin network has a long established involvement in regulating energy homeostasis, as demonstrated by successful obesity pharmacotherapies targeting this system. However, due to side effects, these compounds have since been withdrawn. An understanding of the precise mechanism through which serotonin modulates energy balance is therefore of intense interest. Pharmacological and genetic research implicates the Gq-coupled 5-HT<sub>2C</sub> receptor (5-HT<sub>2C</sub>R) and the Gi-coupled 5-HT<sub>1B</sub> receptor (5-HT<sub>1B</sub>R) specifically in these effects. We sought to further elucidate the specific mechanism through which serotonin modulates ingestive behaviour and investigated both downstream and upstream pathways employed. We observed that d-fenfluramine/serotonin activates neurons in the hypothalamic arcuate nucleus (ARC) expressing the endogenous anorectic melanocortin agonist proopiomelanocortin (POMC) via a dual mechanism (i) postsynaptic action at 5-HT<sub>2C</sub>R expressed on POMC neurons and (ii) presynaptic action at 5-HT<sub>1B</sub>R on GABAergic terminals that reduce an inhibitory input onto POMC neurons. Given this mechanism of action, we then determined that combined 5-HT<sub>2C</sub>R and 5-HT<sub>1B</sub>R agonists potentiates appetite suppression compared to single agonist treatment; an effect associated with increased POMC neuron activation on both the population and single cell level. These data further clarify the heterogeneity of ARC POMC neurons by revealing distinct subpopulations activated by 5-HT<sub>2C</sub>R, activated by 5-HT<sub>1B</sub>R *via* disinhibition and regulated by both receptors. Efforts to identify upstream mediators of central serotonin activity revealed histamine, noradrenaline and orexin, but not leptin, to be regulators of this appetitive microcircuit. Together, these data identify a critical microcircuit through which serotonin modulates appetite and reveal multiple points that may be amenable to pharmacological interrogation for future obesity treatment.

### ***How to make a schizophrenic mouse?***

**Dorota Badowska**, M.M. Brzozka, P. Falkai, M.J. Rossner

Max Planck Institute of Experimental Medicine, Göttingen & Clinics of Psychiatry and Psychotherapy, University of Göttingen, Germany

The human TCF4 gene encodes a bHLH transcription factor and has been identified in multiple Genome Wide Association Studies (GWAS) as a novel schizophrenia (SZ) susceptibility gene (Steffanson, et al., 2009, Li et al 2010, Steinberg et al 2011, Ripke, et al. 2011). Tcf4 plays an important role in brain development and in learning and memory in adult mice. A transgenic mouse model overexpressing Tcf4 in the adult forebrain (Tcf4tg) revealed cognitive and impairment of sensorimotor gating (Brzozka et al., 2010) which resembles phenotypes frequently observed in schizophrenic patients. It is generally accepted that the risk of schizophrenia is caused by interactions of genetic and environmental factors (GxE). Therefore, various environmental factors may either enhance or protect against disease outbreak in subjects carrying gene variants conferring an increased risk. Social stress as well as urbanization seems to enhance the risk to develop SZ while physical activity and social integration appears to be protective (Pajonk et al. 2010). In this study we analyzed behavioral phenotype of male Tcf4tg mice in a battery of behavioral tests monitoring cognitive and social behaviors to address the genetic risk factor and its interaction with different housing conditions. Four weeks old Tcf4tg mice and their wild-type littermates were housed in enriched environment (EE) or upon single cage housing (SH) until they reached 8 weeks of age. EE is known to improve cognition and may help to overcome stress, while SH mimics social isolation often observed in schizophrenic patients. Adult animals were subjected to

behavioral tests addressing the basic behavior and cognitive abilities (such as Morris water maze and fear conditioning). Tcf4tg mice show decreased freezing in cued fear conditioning compared to the control mice when housed in isolation. There are, however, no significant differences between genotypes in EE. In the Morris water maze in reversal learning phase single housed Tcf4tg mice learn the position of the hidden platform slower than the controls. Tcf4tg mice exhibit reduced fear memory and impaired flexibility in spatial learning. Manifestation of these potentially schizophrenia-relevant behaviours depends on the housing conditions. Social isolation worsens the phenotype of Tcf4tg mice and enrichment rescues it.

***Investigation of long-term effects of genetically evoked selective noradrenergic denervation on dopaminergic system functioning***

**Agnieszka M. Jurga** (1), Katarzyna Rafa-Zabłocka (1), Marta Kot (2), Władysława A. Daniel (2), Irena Nalepa (1), Grzegorz Kreiner (1)

(1) Department of Brain Biochemistry, Institute of Pharmacology PAS, Krakow, Poland

(2) Department of Pharmacokinetics & Drug Metabolism, Institute of Pharmacology PAS, Krakow, Poland

Neuronal cell death in Parkinson's Disease (PD) is restricted not only to dopaminergic cells of substantia nigra (SN) and ventral tegmental area (VTA) but affects noradrenergic system as well. Studies performed on toxin-induced animal models revealed that loss of noradrenaline worsens the dopamine nigrostriatal damage and its overexpression may have neuroprotective effects. The aim of this study was to determine whether genetically evoked, selective loss of noradrenergic neurons may have any long-term, negative impact on the dopaminergic system. We applied the conditional inactivation of gene encoding transcription factor TIF-1A by the Cre/loxP system to induce noradrenergic neurodegeneration by expressing Cre recombinase under dopamine beta-hydroxylase promoter. The selective loss of noradrenergic neurons in resulted TIF-1A<sup>Cre</sup> mice was confirmed by immunohistochemistry showing 77% reduction of TH<sup>+</sup> cells. The number of TH<sup>+</sup> cells was not changed in SN/VTA of 12-week TIF-1A<sup>Cre</sup> mutants. Nevertheless, our preliminary data revealed (a) 25% reduction of homovanillic acid (HVA, a dopamine metabolite regarded as an indicator of dopaminergic system activity) concentration in striatal tissue, (b) 1.4-fold upregulation of glial fibrillary acidic protein (GFAP) mRNA and (c) enhanced level of oxidative stress shown by immunoblot detection of carbonyl groups in SN/VTA of mutant mice. (Supported by grant 2011/03/B/NZ7/05949).

***Impaired corneal epithelial wound healing and innervations in SP and alpha-CGRP knockout mice***

**Kamila Mizerska** (1), Adolfo Aracil (1), Laura Fernández-Sánchez (2), Nicolás Cuenca (2), Carolina Luna (1), M.Carmen Acosta (1), Carlos Belmonte (1), Juana Gallar (1)

(1) Instituto de Neurociencias, Universidad Miguel Hernandez – CSIC, Spain

(2) Departamento de Fisiología, Genética y Microbiología, Universidad de Alicante, Spain

The morphology of corneal innervation and corneal epithelial wound healing were studied in knockout mice for pain neurotransmitters Substance P (Tac1 KO) and alpha calcitonin gene-related peptide (alpha-CGRP KO) and their corresponding wild type (WT) strain. Corneas of KO and WT mice were processed using the ABC staining technique, photographed and drawn. Chemical wounds were performed in the corneal epithelium of KO and WT animals in order to study the Epithelial Migration Rate (EMR) and the Estimated Time of Healing (ETH). The effect of exogenous CGRP on alpha-CGRP KO and WT on wound healing was also studied. Tac1 KO and alpha-CGRP KO mice showed reduction of the subbasal nerve density comparing to WT. KO animals exhibited impaired corneal epithelial wound healing and altered EMR and ETH. Exogenous application of alpha-CGRP delayed the healing in WT animals in comparison with vehicle-treated mice. The percentage of decrease in subbasal nerve density in KO is similar to the percentage of the SP and CGRP positive neurons previously described for control animals in the bibliography. The impairment of the wound healing process in KO may be related to the absence of the corresponding neuropeptides, as well as to the reduction of corneal sensory input.

---

## 12.00 – 13.30: PERCEPTION & BRAIN PLASTICITY

chaired by: **Gregory Kroliczak** (Institute of Psychology, Adam Mickiewicz University, Poznań, Poland)

---

### ***An fMRI study of perception and imitation of transitive and intransitive skills***

**Gregory Kroliczak**

Institute of Psychology, Adam Mickiewicz University, Poznań, Poland

Although recent clinical data show new cases of selective dissociations between impaired control of transitive and intransitive skills, neuroimaging evidence from healthy right- and left-handers indicates that planning these gestures engages a common left-lateralized network. What has not been assessed so far using functional magnetic resonance imaging (fMRI) is whether distinct representations support transitive versus intransitive skills when they are perceived with a view to imitating them. Twelve right-handed participants watched gestures shown in a video and repeated them with their right hands. Perception and imitation of these two gesture categories activated common networks, different between the tasks. Nevertheless, watching transitive gestures additionally modulated an unexpected network of areas, including the right caudal temporo-parietal cortex. Whereas imitation of transitive gestures resulted in greater recruitment of the left dorsal premotor and motor cortices, imitation of intransitive gestures led to additional near/below baseline modulations of the bilateral posterior insulae, medial prefrontal cortices, the right ventral precuneus, postcentral and intraparietal sulcus, and the left parietal operculum. These results support current proposals that transitive gestures are more demanding, both during visual processing and manual performance. Yet, they also indicate that imitation of intransitive skills depends on subtle modulations within a bilateral network of areas.

### ***Dejerines' reading area revisited with intracranial-EEG: selective responses to letter-strings***

**Marcin Szwed** (1,2,3,4,5), **Carlos Hamame** (1,6), **Philippe Kahane** (7), **Olivier Bertrand** (7),  
**Jean-Philippe Lachaux** (6)

(1) CNRS Research Center for Cognitive Psychology, Aix-Marseille University, Marseille, France

(2) Université Pierre et Marie Curie-Paris 6, Faculté de Médecine Pitié-Salpêtrière, IFR 70, Paris, France

(3) INSERM, ICM Research Center, UMRs 975, Paris, France

(4) INSERM, Cognitive Neuroimaging Unit U992, IFR 49, Gif sur Yvette, France

(5) Current Affiliation: Dept of Psychology, Jagiellonian University, Kraków, Poland

(6) INSERM U821, Dynamique Cérébrale et Cognition, Centre Hospitalier Le Vinatier, Lyon, France

(7) Department of Epilepsy, Grenoble University Hospital (Centre Hospital du Grenoble),  
Grenoble, France

The visual word form area (VWFA) is a region of the left ventral occipito-temporal cortex (vOT) that develops with acquisition of reading skills. It is debated whether this area is specialized for word recognition, or whether it is rather a general-purpose area that associates visual form (be it words or objects) with meaning. Non-invasive neuroimaging techniques have insufficient spatial resolution to resolve this issue. Here we recorded intracerebral-EEG signal from two epileptic patients undergoing surgical treatment which required implantation of one electrode in the VWFA (Hamame, Szwed et al., *Neurology*, 2013). The VWFA responded almost exclusively to written text, over ten times stronger than the strongest responses to other classes of stimuli (objects, faces and landscapes). With the exception of the fusiform face area, the observed level of specificity has never been described before in the human visual system. Our results thus constitute novel evidence in favor of the existence of strongly specialized human brain regions. Given the fact reading was invented only ~5400 years ago and there was no sufficient time or evolutionary pressure to evolve a brain system devoted to reading, these results also demonstrate that such strong specialization can be achieved through cultural learning.

***An EEG-rTMS study of the influence of rTMS over the left DLPFC: A comparison of different stimulation protocols in healthy subjects***

**Agata Woźniak-Kwaśniewska, David Szekely, Olivier David**

Brain Function and Neuromodulation, Grenoble Institute of Neuroscience, Inserm U836,  
Université Joseph Fourier, Grenoble, France

An EEG-rTMS co-registration allows to compare short-term plasticity induced by iTBS, cTBS, 10Hz, 1Hz and sham protocols. Twenty healthy subjects received stimulation during wakefulness with eyes-closed. EEG power was calculated using FFT and averaged within frequency bands: delta, theta, alpha, low/high beta, and gamma. Significant changes of EEG power between post- and pre-rTMS periods were estimated at the scalp and the cortex level. Results of ANOVA of active vs. sham rTMS showed spread decrease of power in delta frequency after active protocols as compared to sham. In theta band the significant response was observed in post 10Hz, iTBS and 1Hz. Significant changes in high beta oscillation were induced by 10Hz, iTBS and cTBS protocols, inhibiting frontal lobe, whereas an enhanced activity was found in the parieto-occipital cortex. Furthermore, in gamma frequency we observed wide decrease after 10Hz, where other protocols induced decrease of power in the left or right DLPFC, iTBS and 1Hz with cTBS, respectively. Additionally, all protocols except 10Hz enhanced gamma activity in temporal or parieto-occipital lobes. All significant results have  $p < 0.05$  (FWE). Moreover, the results of source localization showed that active protocols effected suppression of all cortical oscillations in the left and right region of interest.

---

**12.00 – 13.30: INTERACTIVE ORAL SESSION OF MEDICAL CASE REPORTS**

chaired by: **Krzysztof Banaszkiwicz** (Krakow Academy of Neurology, Poland)

---

***First Bite Syndrome***

**Brandon Michael Henry**

Jagiellonian University Collegium Medicum, Krakow, Poland

First Bite Syndrome is a rare neurological complication of parapharyngeal surgery that is characterized by excruciating pain upon the first sensation of taste or smell of food. The pain is often exacerbated by chewing, brushing teeth, or even the thought of eating. The symptoms are always worse with the first bite and may improve with subsequent bites only to return at the next meal. FBS is caused by damage to cervical sympathetics innervating the parotid gland, resulting in denervation supersensitivity of myoepithelial cells to parasympathetic neurotransmitters triggering a supramaximal contraction. The patient discussed in this case is a 59 year old female who underwent a deep neck dissection for excision of a vagal schwannoma. She presented with severe pain over the right parotid region, jaw, and ear, weight loss, fatigue, and dysphagia. Examination revealed no sign of ptosis, miosis, or anhidrosis of the face. The patient was treated with a series of intraglandular botulinum toxin injections and experienced moderate pain relief.

***Coincidence of dementia and ataxia – a challenge for clinician and pathologist.  
Consideration based upon unusual complex clinicopathological familial syndrome***

**Adrian Chrobak**

Jagiellonian University Medical College, Krakow, Poland

Overlap of different clinical syndromes like Parkinsonism, dementia and many others, create especially difficult challenge for neurologist, but they are also difficult for neuropathologists. The very basic issue is to decide whether there is incidental co-occurrence of two degeneration processes or there is common

causative factor. Case of 76 years old male patient is presented. Clinical data reveals 12 years history of declining dementia, ataxia, cataract, brain and cerebellar atrophy, with family history of unidentified dementia in first degree relatives – mother, and sister with involuntary movements. Clinical manifestation of patient suggested various genetic neurodegeneration disorders like SCA's 1, 2, 3, 17, DRPLA or HD which have been excluded by genetic screening. The following pathology have been noted, in macroscopic view: cortical brain and cerebellar atrophy; microscopic view: neurofibrillary tangles, beta amyloid plaques, nodular calcifications, unspecific ischemic neurodegeneration and cerebral and cerebellar amyloid angiopathy, loss of Purkinje cells, Bergmann gliosis, atrophy of the cerebellum, diffused and extensive granular ubiquitin deposits in white matter, syderocalcinosis of the vessels and TDP 43 + intracellular inclusions in midbrain. In case like this where there is apparently indisputable familial history it is much greater probability that co-occurrence of different symptoms is caused by common factor.

### ***Angiocentric glioma as a rare cause of drug-resistant focal seizures – case report***

**Grzegorz Siwek**

Pathology Students Club, Department of Pathomorphology and Neuropathology, CM-UJ,  
Krakow, Poland

Angiocentric glioma (AG) is a rare low grade neoplasm, occurring usually in children and young adults with only 59 patients reported to date. Here, we present a case of 10 -year-old girl, admitted to the hospital after an episode of generalized seizures. MRI imaging showed T2 non-enhancing mass in left fronto-parietal lobe. Due to close proximity to sensory and motor cortex, surgery was preceded by tractography. Girl has undergone left-side frontal craniectomy with complete resection of the tumor. Histopathological examination of the resected tissue revealed a tumor composed of elongated cells, characteristically gathered around vessels and oriented mostly radially. Moreover the tumor cells formed conspicuous palisade structure, adjacent to pia. Texture of the tumor partially resembled that of ependymoma. Cells were immunopositive for GFAP and EMA . Ependymal traits were confirmed by electron microscopy (numerous cilia) . These morphological features and protein expression pattern is pathognomonic for AG. This case is an example of epileptogenic, but benign neoplastic lesion of the brain. Differentiation toward astroglia and ependyma-originated cells observed in AG, may suggest common progenitor cell that gives rise to this type of neoplastic growth. (Prepared under tutorship of prof. D. Adamek, Chair of Pathology and Neuropathology Dept. CM-UJ).

### ***The progression of Huntington's Disease symptoms during 4.5 years follow-up – a case study***

**Michał Błaż**

Department of Neurology, Jagiellonian University Medical College, Krakow, Poland

Huntington's disease (HD) is a progressive neurodegenerative disorder which is caused by HTT gene mutation. In this case report we present gradual decline of an HD patient's motor, cognitive and behavioural symptoms which have been consistently assessed throughout the course of the disease. The patient is a 56-year old female who presented with involuntary movements, apathy and depression which appeared in 2007. The genetic test revealed 40 CAG repeats and confirmed the diagnosis of HD. During six consecutive visits of a 4.5 years follow-up the patient's symptoms were evaluated with use of the Unified Huntington's Disease Rating Scale (UHDRS). The baseline UHDRS score was: 18 in motor, 123 in cognitive, 15 in behavioural section and 19 in Functional Assessment (FA) section. The annual percent change of the scores during follow-up was: 18% for motor, 10% for cognitive, 3% for behavioural section and 3% for FA. Involuntary movements are usually the most noticeable symptom of HD. The case report shows that despite significant decline of motor symptoms, the deterioration of the patient's disability in daily functioning was mild. This suggests that motor disturbances are not the major factor that influences functioning in HD.

## ***A 64-year-old male with sudden loss of orientation and changes in behavior***

**Kamil Polok**

Jagiellonian University Medical College, Krakow, Poland

A 64-year-old male was admitted to a neurological unit due to sudden deterioration of orientation and alarming changes in behavior. Neurological examination exhibited qualitative consciousness disturbances - the patient was conscious, obeyed doctor's commands but verbal contact was very limited. Moreover, right-sided hemiplegia was discovered. Magnetic resonance imaging revealed multiple disseminated hyperintensive areas. The most evident lesions were located in temporal, frontal and parietal lobes of the left hemisphere, frontal lobe and temporoparietal junction of the right hemisphere and in mesencephalon and pons. Laboratory tests revealed elevated WBC in the blood and elevated protein and glucose concentration in CSF. On the basis of symptoms, MRI and laboratory tests results presumptive diagnosis of encephalitis was put forward and therapy with glucocorticoids (Prednisone, Methylprednisolon), antibiotic (Ceftriaxone) and Acyclovir was introduced. It proved to be ineffective and the patient's condition deteriorated and the second MRI showed progression of lesions so suspicion of Acute Disseminated Encephalomyelitis (ADEM) was put forward. The patient underwent plasmapheresis but good effects were observed for only few hours. Later patient started to exhibit quantitative consciousness disturbances and fell into sopor. The diagnosis remains unclear and primary brain tumor or lymphoma are suspected but they can be confirmed only by a brain biopsy.

### ***Case Report: Neurosurgical Treatment of Drug-Resistant Epilepsy***

**Anna Drózdź**, Justyna Rybus, Stanisław Kwiatkowski

Students' Research Group at the Department of Pediatric Neurosurgery of Jagiellonian University Medical College, Krakow, Poland

Epilepsy is characterized by seizure episodes with temporary loss of consciousness, sensation or mental function. Pharmacological treatment often remains effective. Neurosurgical therapy might be beneficial to those who respond poorly to drugs. Analysis of medical records from the Pediatric Neurosurgery of Jagiellonian University Medical College. Evaluation of the effectiveness of neurosurgical treatment in patient with drug-resistant epilepsy. A seven-year-old male patient has been treated at the Department of Pediatric Neurosurgery since 2004. He was diagnosed with drug-resistant epilepsy due to hemimegalencephaly and cortical dysplasia. The patient presented with partial epileptic seizures and left-sided hemiparesis. The defect of the right hemisphere was operated three times. The first stage of treatment involved parietal lobectomy and titanium clamp closure of the distal middle cerebral artery. Successive stages were performed within several months. In 2005 patient underwent ventriculoperitoneal shunt implantation due to hydrocephalus. Two years later an excision of certain parts of cortex was performed to treat recurrent epileptic seizures following viral infection. He was discharged home in good overall condition. This method of neurosurgical treatment, saving certain active regions of the brain, was beneficial to the patient and allowed further psychomotor development of the child.

### ***A patient with subacute onset of memory impairment, gait disturbances and urinary retention***

**Anna Maria Łopatkiewicz**

Jagiellonian University Neurology Student Club, Department of Neurology,  
Jagiellonian University Medical College, Krakow, Poland

A twenty-nine-year-old woman was admitted to the Department of Neurology Jagiellonian University Medical College with subacute onset of gait and balance difficulties, dizziness, memory impairment and urinary retention. The symptoms appeared three years prior to admission and their severity did not change significantly since then. There was no evidence of infection before the onset of symptoms. The patient suffers from epilepsy, the diagnosis was made eight years ago and the patients is treated with

valproic acid and levetiracetam. On neurological examination there was horizontal gaze nystagmus, loss of joint and vibration sense, diminished deep tendon reflexes and cerebellar ataxia in four limbs, mild proximal muscle weakness affected lower limbs. The patient had positive Romberg test. MRI examination revealed bilateral symmetric hiperintensity in the upper parts of the thalami on T2 images with no pathological contrast enhancement. Complete blood cell count, biochemical profile and urinalysis were within normal limits. MRI findings, subacute onset and stable course of the disease indicated deep venous thrombosis, therefore the patient was diagnosed with idiopathic venous bithalamic stroke. Systemic diseases, prothrombic conditions and hematologic disorders must be considered. The differential diagnosis of bithalamic lesions includes also primary neoplasm, infection, metabolic and toxic disorders.

### ***Idiopathic bilateral hypertrophic olivary degeneration (HOD) – case report***

**Urszula Skrobas**, Jacek Jaworski, Anna Sojka, Konrad Rejdak

Department of Neurology, Medical University of Lublin, Poland

A 57 years old woman was admitted to the Department of Neurology at SPSK 4 in Lublin, because of speech disorders, swallowing problems and involuntary movements of the mouth lasting for about 2 years before admitting. Neurological examination revealed: dysarthria, pharyngeal reflexes preserved, visible continuous contractions of the soft palate, and myoclonic jerks of a orbicularis oris muscle, no other deviation from the normal status was observed. T2-weighted MRI images showed hyperintense signal and hypertrophy of inferior olivary nucleus on both sides of medulla, with no other lesions- with particular emphasis on the structures included in the triangle of Guillain-Mollaret. Patient did not perceive any auditory click. Attempted to treat Pyridostigmine - without improvement. Based on the results of clinical and laboratory tests, it was assumed that the dysarthria and dysphagia were secondary to continuous myoclonus of the palate that was a symptom of spontaneous bilateral hypertrophic atrophy of the inferior olivary nucleus. After the treatment with Valproic acid patient's neurological condition improved and swallowing problems subsided. This clinical case represents a rare disorder, which has not been reported in literature of spontaneous bilateral HOD.

---

## **15.00 – 16.00: PLENARY LECTURE**

---

### ***The dynamic brain: Time as coding space in cortical processing***

**Wolf Singer**

- 1) Max-Planck Institute for Brain Research, Frankfurt am Main, Germany
- 2) Frankfurt Institute for Advanced Studies (FIAS), Frankfurt am Main, Germany
- 3) Ernst Strüngmann Institute (ESI) for Neuroscience in Cooperation with Max Planck Society, Frankfurt am Main, Germany

Higher cognitive functions require the coordination of large assemblies of spatially distributed neurons in ever changing constellations. It is proposed that this coordination is achieved through dynamic coordination of temporally structured activity. Since there is no supra-ordinate command centre in the brain, the respective patterns of coherent activity need to self-organize within the fixed architecture of anatomical connections. Evidence will be provided that dynamic coordination supports response selection by attention, subsystem integration, flexible routing of signals across cortical networks and access to the work-space of consciousness. The precision of temporal coordination is in the millisecond range suggesting the possibility that information is encoded not only in the co-variation of discharge rates but also in the phase relations of discharges relative to population oscillations. This phase coding could account for the high speed with which cortical circuits can encode and process information. Recent studies in schizophrenic patients indicate that this disorder is associated with abnormal synchronisation

of oscillatory activity in the high frequency range (beta and gamma). This suggests that some of the cognitive deficits characteristic for this disease result from deficient binding and subsystem integration.

---

## **16.10 – 17.40: NEUROPATHOLOGY**

chaired by: **Katarzyna Starowicz-Bubak** (Department of Pharmacology of Pain, Institute of Pharmacology, Polish Academy of Sciences, Krakow, Poland)

---

### ***Role Of Endocannabinoid And Endovanilloid Tone In Antinociception***

**Katarzyna Starowicz-Bubak**

Department of Pharmacology of Pain, Institute of Pharmacology, Polish Academy of Sciences, Krakow, Poland

The heat- and capsaicin-activated transient receptor potential vanilloid-1 (TRPV1) receptor is involved in peripheral and central nociceptive processing and is a therapeutic target for pain. TRPV1 is also one of the most widely recognized alternative molecular targets for the endocannabinoids anandamide and *N*-arachidonoyldopamine. Over the last decade, the interaction between cannabinoid receptors (CB<sub>1</sub>) and TRPV1 receptors has been shown to occur both in peripheral tissues and brain, during both physiological and pathological conditions. We provided evidence that glutamatergic neurons of the ventrolateral periaqueductal gray (VL-PAG) respond to TRPV1 stimulation by releasing glutamate into the rostral ventromedial medulla (RVM), thereby activating other TRPV1-expressing glutamatergic neurons (presumably OFF cells) in this area to produce analgesia. We have shown that TRPV1 in the VL-PAG tonically contributes to brain stem descending antinociception by stimulating glutamate release into the RVM and OFF neuron activity. An update of the relationship CB<sub>1</sub> and TRPV1 channels and their possible implications for neuropathic pain will also be provided. The data focused on endogenous spinal mechanisms of pain control by anandamide, and the current and emerging pharmacotherapeutic approaches that benefit from the pharmacological modulation of spinal endocannabinoid and/or endovanilloid systems under chronic pain conditions will be discussed. Bases for the possible future development of new therapeutic approaches that, by specifically targeting TRPV1 receptors, might be used for the treatment of pain will be suggested.

### **Involvement of phosphorylation state in the regulation of TRPV1 receptor activity in neuropathic pain**

**Natalia Małek**, Michał Korostyński, Barbara Przewłocka, Katarzyna Starowicz

Institute of Pharmacology PAS, Krakow, Poland

Neuropathic pain represents a large unmet clinical need. Attention is focused on alteration of gene expression in dorsal root ganglia and spinal cord, e.g. TRPV1, receptor involved in neuropathy development. The process of phosphorylation and dephosphorylation is crucial for its function, decreasing or increasing channel activity respectively. In this study we focused on expression of TRPV1 and enzymes responsible for its activity on mRNA level in animal neuropathic pain model. Chronic constriction injury (CCI) 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 samples dissection. Gene expression quantitative PCR were performed using Assay-On-Demand Taqman probes. CCI of the sciatic nerve resulted in changes of key enzymes responsible for phosphorylation and dephosphorylation of TRPV1. Alteration in PKC and CamKII expression was observed, highest seven days after CCI. At the same time there was strong downregulation of gene encoding calmodulin in all time points. Although there was no substantial upregulation of TRPV1 gene, expression of enzymes responsible for its activation was modified, which in turn may be responsible for TRPV1 increased sensitivity to painful stimuli and consequently the development of neuropathic pain. (Support: LIDER/29/60/L-2/10/NCBiR/2011).

***Quantitative magnetic resonance and immunohistochemical analysis of animals with experimentally-induced cerebral dysplasia***

**Michał Kiełbiński** (1), Kinga Gzielo-Jurek (1), Zuzanna Setkowicz-Janeczko (1),  
Władysław Węglarz (2), Krzysztof Janeczko (1)

(1) Department of Neuroanatomy, Institute of Zoology, Jagiellonian University, Poland  
(2) Laboratory of In Vivo Imaging, Institute of Nuclear Physics, Polish Academy of Sciences,  
Krakow, Poland

Prenatal gamma-irradiation is an animal model of cerebral dysplasia, a developmental disorder associated with epilepsy. However, a quantitative comparison of changes in anatomical structure and neuronal or glial composition of brains irradiated at different stages of postnatal development is not available. Here, we used T2-weighted MRI images taken from adult, male Wistar rats exposed to 1 Gy radiation on prenatal days 13, 15, 17 or 19 (E13, E15, E17, E19, respectively), as well as normal controls. Using a modified Cavalieri method, we estimated total brain volume. Later, we assessed GFAP and NeuN immunoreactivity in hippocampal formations of the previously MRI scanned brains, using an automated local thresholding method identical for all images. Brain volume in all irradiated groups was significantly reduced, following a gradual relationship from the least (E19) to most affected (E13). When compared to controls, GFAP immunoreactivity in the hippocampus was significantly lower in E13, E17 and E19, but not in E15. Conversely, NeuN reactivity was increased in all experimental groups. We suggest a possible differential effect of radiation on neurogenic and gliogenic precursor pools lasting until adulthood. We hope our ongoing research will bring molecular and functional context to these findings.

***Efficient isolation of rare stem and precursor cell populations responding to the central nervous system traumatic injury by use of fluorescence activated cell sorting***

**Katarzyna Konarzewska** (1), Bartosz Wylot (1), Marta Brewińska-Olchowik (2),  
Katarzyna Piwocka (2), Małgorzata Zawadzka (1)

(1) Laboratory of Transcription Regulation, Nencki Institute of Experimental Biology, Warsaw, Poland  
(2) Laboratory of Cytometry, Nencki Institute of Experimental Biology, Warsaw, Poland

The central nervous system is populated by a number of stem and progenitor cell populations which, when responding to the tissue injury, might have potential to support regenerative processes in damaged tissue. The aim of present study was to develop a strategy for highly effective and pure sorting of these unique populations. We used fluorescence activated cell sorting, which appears to be the ideal tool for efficient isolation of such populations. We have chosen mouse model of stab wound injury of cerebral cortex, of which 3 or 6 days after injury we were obtaining material for further analysis. Intact and injured brain cortex was dissociated and the cell suspension was cleared of myelin followed by the lineage-positive cells depletion. Rare populations of Sca1+lin-CD45- (so called very small embryonic-like stem cells) as well as Sca1+lin-CD45+ hematopoietic stem cells and oligodendrocyte precursor cells were sorted with FACS Aria I according to the specific cell markers. Using immunohistochemical staining and gene expression analysis we confirmed an identity of isolated populations. Proposed strategy of effective isolation of rare stem and precursor cell populations may be a useful tool for further functional studying their biology and differentiation potential in vitro and in vivo.

---

## 16.10 – 17.40: AUDITORY PROCESSING

chaired by: **Raffaele Cacciaglia** (Department of Psychiatry and Clinical Psychobiology, University of Barcelona & Department of Psychology, University Jaume I, Castellón de la Plana, Spain)

---

### ***Auditory deviance detection in the human brainstem: direct evidence from functional magnetic resonance imaging***

**Raffaele Cacciaglia**, Lavinia Slabu, Ana Sanjuán, Sabine Grimm, Noelia Ventura-Campos, César Ávila, Carles Escera

Department of Psychiatry and Clinical Psychobiology, University of Barcelona & Department of Psychology, University Jaume I, Castellón de la Plana, Spain

Pre-attentive detection of novel sounds has been related to the mismatch negativity (MMN), a component of the human event-related potentials. Recent studies have quantified auditory mismatch responses at earlier latencies than those of MMN, suggesting that acoustical novelty is already processed in regions upstream to the auditory cortex. Accordingly, animal studies have shown that neurons of the inferior colliculus (IC) and medial geniculate body (MGB) display MMN-like responses to rare sounds. However, an involvement of the IC and MGB in human auditory deviance detection remains to be tested. We used functional magnetic resonance imaging during an oddball paradigm designed to probe brainstem responses. Twelve participants took part in the experiment, which comprised the following conditions: standard sounds (STD), standard embedded with deviants (DEV), plus a condition controlling for neural refractoriness (CON). In the DEV& STD condition, significant activations of the superior temporal gyrus, left IC, and bilateral MGB, were found. Importantly, the IC and the MGB were also significantly activated in the DEV& CON condition. Our results are the first indicating that pre-attentive encoding of acoustical regularity takes place in the human IC and MGB, and support the idea that auditory novelty detection spans from low- up to high-level in the hierarchy.

### ***Are auditory-steady state responses gender-sensitive?***

**Inga Griskova-Bulanova**, Osvaldas Ruksenas

Department of Neurobiology-Biophysics, Vilnius University, Lithuania

The aim of the study was to investigate gender differences and effect of menstrual cycle phase on phase-locking index (PLI) of auditory steady-state response to periodic 40Hz stimulation. Additionally, short-term habituation pattern and repeatability of the response were addressed. Auditory steady-state response (ASSR) was recorded twice two weeks apart in 14males, and twice in 16 females (follicular phase during the first recording in 9 subjects, and luteal phase in 7 subjects). Recordings were made using 9 electrodes (F3, Fz, F4, C3, Cz, C4, P3, Pz, P4). 60 stimuli of 500ms white noise 1.5ms bursts were presented. In both male and female group ASSR at the time period of 200-300 ms was most precise. Short-term habituation, assessed through comparison of first 20 responses to the middle 20 and the last 20 responses, was not seen in either group. There was a trend in the male group for larger PLIs during the second recording. In female group, significant interaction between recording session and phase of the menstrual cycle emerged, revealing a group with larger PLIs in both phases. These values were also larger when comparing to male group.

## ***Diagnosis of consciousness in DOC patients using auditory steady-state responses (ASSRs)***

**Urszula Górska (1), Marek Binder (2)**

(1) Jagiellonian University, Poland

(2) Psychophysiology Laboratory, Jagiellonian University, Poland

According to Giulio Tononi's theory of consciousness as the integrated information being conscious require the cortical circuits to be both highly integrated and differentiated. That is why a crucial aspect of consciousness is a presence of effective connectivity among different regions in thalamocortical system. Patients with disorders of consciousness (DOC) after severe brain injury may not be able to communicate, move or show evidence of any purposeful behaviour while they retain ability to have conscious experiences. Besides the recent development of approaches which try to detect higher-order processing in this subjects, it is still a challenge to develop methods which do not depend on patient ability to follow instructions or display higher-order sensory processes. In this study we tested usefulness of auditory steady-state responses (ASSR) as a diagnostic tool for detecting consciousness not requiring volitional activity on 19 patients with severe brain injury. We presented them series of 1 kHz sine-wave auditory stimuli modulated by the set of amplitude modulation (AM) frequencies (4Hz, 8Hz, 20Hz, 40Hz, 80Hz) while measuring their brain activity with 32-channel EEG system. In order to test how the ASSR propagates through different cortical regions we analysed the topography of the frequency peaks for the used AM frequencies. Our preliminary results suggest that the ability to be conscious in patients is primarily correlated with an invariant pattern of scalp distributions of ASSRs across different AM stimulation frequencies, which can be interpreted as a marker of at least partially preserved effective connectivity.

---

## **18.00 – 19.00: CLOSING LECTURE**

---

### ***CNS Remyelination – from biology to therapy***

**Robin Franklin**

Wellcome Trust-MRC Cambridge Stem Cell Institute, University of Cambridge, UK

Remyelination, the process by which new myelin sheaths are restored to demyelinated axons, represents one of the most compelling examples of adult multipotent stem cells contributing to regeneration of the injured CNS. This process can occur with remarkable efficiency in multiple sclerosis (MS), and in experimental models, revealing an impressive ability of the adult CNS to repair itself. However, the inconsistency of remyelination in MS, and the loss of axonal integrity that results from its failure, makes enhancement of remyelination an important therapeutic objective. There is now compelling evidence that ageing is the major contributor to the declining efficiency of remyelination and that this is largely due to a failure of stem cell differentiation. This talk will review recent studies we have undertaken aimed at obtaining a detailed understanding of the mechanisms of regulating differentiation during remyelination and hence identifying novel therapeutic targets.

**18.30 – 20.00: POSTER SESSION**

---

1

***Evoked potentials in medical diagnostic***

**Agnieszka Nowik**

Department of Biophysics, The Poznan University of Medical Sciences, Poland

In 1890 at the department of Physiology at the Jagiellonian University, a young scientist Adolf Beck has defended his thesis entitled 'Die Bestimmung der Localisation des Gehirn- und Rückenmarksfunctionen Vermittelst der Electricischen Erscheinungen'. The aim of this work was the use of electrophysiology for localization of functions in the brain. This research has enabled the development of many examination and diagnostic techniques used not only in medicine. Based on the results of electrophysiological studies we are able to detect developmental disturbances in children, to determine the kind of brain lesions following accidents, or to early detect the first symptoms of disturbances of cognitive processes in the cases of serious autoimmunological diseases. The knowledge obtained from this research enables us to apply appropriate teaching methods for affected children, rehabilitation techniques for victims of accidents, or to start early treatment for Alzheimer's disease or multiple sclerosis. Future perspectives in the development and application of electroencephalographic methods, combined with functional magnetic resonance imaging (fMRI), and transcranial magnetic stimulation (TMS), will be discussed.

2

***Hemispheric asymmetries for emotional verbal stimuli in Polish-English bilinguals***

**Rafał Jończyk**

Faculty of English, Adam Mickiewicz University, Poznań, Poland

To date, a plethora of studies have reported potential hemispheric asymmetries for emotional language among monolingual populations. Little is known, however, whether these findings would be replicated among bilingual participants. The goal of this study was to investigate hemispheric specialization for emotional words in highly proficient Polish-English bilinguals. The participants in the study were 64 right-handed females. The experimental stimuli comprised positive, negative, neutral, and pseudo-words. To examine laterality of emotion, the stimuli were presented unilaterally for 180ms using the Divided-Visual Field paradigm. During the experiment the participants were asked to distinguish between real English words and pseudo-words in a lexical decision task. Following the on-line task, a free-word recall task and a subsequent word recognition task were administered to investigate hemispheric asymmetries of memory for emotional verbal stimuli. The perceptual data collected in the study pointed to the inhibition of the effect of hemispheric specialization for emotional words. The analysis of memory data, by contrast, provided partial support for the right cerebral sensitivity to negative verbal stimuli. Furthermore, the study provided solid support for the negativity-bias and the left cerebral advantage in language processing reported in previous research.

### ***Functional and structural abnormalities in Broca's area in ADHD***

**Michał Pikusa**

Faculty of English, Adam Mickiewicz University in Poznan, Poland

There is considerable evidence that attention-deficit/hyperactivity disorder (ADHD) is associated with linguistic difficulties. However, the pathophysiology underlying these difficulties is yet to be determined. That is why in this study I set out to investigate functional and structural abnormalities in Broca's area, which is associated with speech production and processing, in people with ADHD by means of resting-state fMRI and structural MRI analyses. Data for the study was taken from ADHD-200 project and included 269 ADHD patients (110 with combined inattentive/hyperactive subtype and 159 with inattentive subtype) and 479 typically-developing control (TDC) subjects. The analyses of fractional amplitude of low-frequency fluctuations (fALFF) and voxel-based morphometry in Broca's area were performed on the data and results were compared statistically across the groups of subjects. fALFF was found to be significantly lower in ADHD patients as compared to TDC, while gray matter density (GM) was found to be higher. There was also a significant negative correlation between fALFF and GM in ADHD inattentive group. The results suggest that there are in fact structural and functional abnormalities in Broca's area in people suffering from ADHD. These findings might help explore the underlying causes of specific language difficulties in ADHD.

### ***Differences between high and low dialogue activity in silent speech revealed by event-related potentials (ERPs)***

**Andrzej Cudo, Paweł Stróżak, Piotr Oleś, Piotr Francuz**

Catholic University of Lublin, Experimental Psychology Unit, Poland

The aim of the study was to determine whether there are significant differences in the brain activity patterns between subject with high and low dialogical activity (treated as a trait) performing silent speech task. Twenty-four right-handed healthy men ( $M = 21.75$ ,  $SD = 1.89$ ) took part in the experiment. They were selected from a group of 232 people on the basis of their results in the Internal Dialogical Activity Scale (IDAS). Half of the subjects had a low level of dialogical activity and the second half had a high level of this trait. The procedure was based on a study conducted by Fujimaki et al. Statistically significant differences were observed in the N2, P3 and SW (*slow wave*) domains between silent speech and control conditions. There were also statistically significant differences between subjects with low and high level of dialogical activity in the LSW (*late slow wave*) domain. Late slow waves reflect performance of complex mental operations, such as conceptual processing. It is assumed that subjects with high level of dialogical activity involve more strongly in performing this type of operations than subjects with low level of dialogical activity.

### ***ERPs of novel metaphors, literal and anomalous statements: influence of task type***

**Karolina Rataj (1), Anna Przekoracka-Krawczyk (1), Marta Izydorczyk (1), Konrad Tomczyk (1),  
Rob van der Lubbe (2,3)**

(1) Adam Mickiewicz University, Poznań, Poland

(2) University of Twente, the Netherlands

(3) University of Finance and Management, Warsaw, Poland

Novel metaphor comprehension seems to require additional cognitive effort compared to literal language understanding, which has been demonstrated in several ERP studies. However, the precise influence of the task used remains unclear. Two experiments using ERPs were carried out to investigate this issue

with the same set of novel metaphoric, literal and anomalous sentences in Polish. While in Experiment 1 participants were asked to read the sentences, in Experiment 2 they were asked to read the sentences and perform a semantic decision. In both Experiments, no differences were observed between the novel metaphoric and anomalous conditions, which corroborates the hypothesis that novel metaphors are, at least initially, perceived as anomalous. In Experiment 1, significantly larger amplitudes for novel metaphoric sentences and anomalous sentences as compared to literal sentences were observed over the Cz and CP2 electrode in the Early (321-340ms) and late (401-420ms) window. In Experiment 2, larger amplitudes for anomalous as compared to literal sentences were observed in the late window over the CP2 electrode. However, no differences were observed between the literal and metaphoric conditions, which may suggest that novel metaphor processing is modulated by task type.

## 6

### ***Negative expectations facilitate mechanical hyperalgesia after high frequency conditioning stimulation of human skin***

**Emanuel N. van den Broeke** (1), Nicole Geene (1), Clementina M. van Rijn (1), Oliver H.G. Wilder-Smith (2), Joukje Oosterman (1)

- (1) Donders Institute for Brain, Cognition, and Behaviour, Radboud University Nijmegen, the Netherlands  
(2) Department of Anesthesiology, Pain & Palliative Medicine, Radboud University Nijmegen Medical Centre, the Netherlands

High frequency conditioning stimulation (HFS) of human skin not only induces an increased pain sensitivity in the conditioning area but also an increased pain sensitivity to mechanical punctate stimuli in the non-conditioned surrounding skin area. The aim of the present study was to investigate whether this heterotopically increased mechanical pain sensitivity can be facilitated through the induction of negative expectations. In two independent conditions; a placebo (N = 15) and control condition (N = 15) we applied mechanical pain stimuli before, directly after, ten and twenty minutes after HFS in the skin area surrounding the conditioning area and measured the reported pain intensity (visual analogue scale, VAS). All subjects (of both conditions) received a written instruction about the HFS protocol but only the instruction in the placebo condition was extended by the following text (in Dutch): "After the HFS stimulation, your skin will become more sensitive to the pinprick stimulation". Our results clearly show that induced expectations of increased mechanical pain sensitivity after HFS facilitates the reported pain intensity after HFS more than when no information is given. This study shows for the first time that brain mechanisms, via the induction of negative expectations, can facilitate heterotopic mechanical hyperalgesia after HFS of human skin.

## 7

### ***Alpha-Band Activity, Chronic Pain, and Attentional Networks***

**Jeff Martin**, Marjan de Vries, Emanuel N. van den Broeke, Oliver H.G. Wilder-Smith, Marijtje LA Jongasma, Clementina M. van Rijn

- Donders Institute for Brain, Cognition and Behavior, Behavioral Science Institute, Radboud University Nijmegen, the Netherlands  
Department of Anesthesiology, Pain & Palliative Care, Radboud University Nijmegen Medical Centre, the Netherlands

Patients with chronic pain show a pronounced shift in their dominant peak alpha frequency (8-10Hz) and/or power amplitude compared to controls. This shift is detectable during both eyes-closed and eyes open recordings. This latter condition is of particular interest as altered alpha activity may indicate deviations in the attentional network's resting-state in chronic pain patients. This altered default mode of available attentional resources might affect task performances, as well as resting state arousal - where chronic pain might be considered to be especially salient or pronounced. In the current project, the findings of the alpha band change are described with reference to attentional networks and the often

reported clinical phenomenon of 'inward attention' in patients with chronic pain. Finally, future research directions are outlined in light of these findings.

## 8

### ***The disappearance of the ERP N100 effect observed after HFS when attention is directed to the stimulus***

**Casper van Heck** (1), Emanuel N. van den Broeke (1), Clementina M. van Rijn (1), Oliver H.G. Wilder-Smith (2)

(1) Donders Institute for Brain, Cognition and Behavior, Radboud University Nijmegen, the Netherlands

(2) Department of Anesthesiology, Pain & Palliative Medicine, Pain & Nociception Neuroscience Research Group, Radboud University Nijmegen Medical Centre, the Netherlands

High Frequency electrical Stimulation (HFS) of primary nociceptive afferents in human skin results in an increase of pain perception to mechanical stimuli in the heterotopic skin. The aim of the present study was to measure the perceived intensity (visual analogue scale, VAS) and event-related potentials (ERPs) in response to electrical non-painful stimuli applied in the heterotopic skin area before and forty minutes after HFS. During stimulation subjects (N = 21) were instructed to count the stimuli and therefore keep attention to the received stimuli. We observed no statistically significant differences after HFS on the perceived intensity (VAS) as well the event-related potentials of the stimulated arm. In conclusion, under the task of attending somatosensory stimuli there is no difference in N100 ERP amplitude after HFS, which suggest that the previous reported ERP N100 difference observed after HFS (Van Den Broeke et al., 2010, 2011) might reflect a cortical correlate of spatial attention.

## 9

### ***Working memory capacity and individual differences in response to memory load***

**Marta Zakrzewska**, Aneta Brzezicka

Interdisciplinary Center For Applied Cognitive Studies (ICACS), University of Social Sciences and Humanities, Warsaw, Poland

Oscillatory activity in the theta band (4 – 8 Hz) is connected to the process of encoding, maintaining and retrieving information from memory. Theta power is enhanced especially when memory load increases. The aim of this thesis was to investigate the relationship between working memory capacity and frontal theta response to memory load. Data was collected from 81 participants who performed Sternberg task (with EEG registration) in which they had to remember 2 to 5 digits. Additionally, they performed Operation span task (OSPAN) and were divided into two working memory capacity groups with regard to their score. Results showed that there is a linear increase in frontal theta power with load, however only in the high working memory capacity group and only in the 4 – 6 Hz sub-band. Furthermore, a positive correlation was found between working memory capacity (OSPAN score) and average theta power increase from lower to higher loads.

## 10

### ***Is the precuneus part of the default network?***

**Szymon Biduła**

Institute of Psychology, Adam Mickiewicz University, Poznań, Poland

Default network (DN) is a set of brain regions that commonly deactivate during performance of a cognitive demanding task. Despite intensive research concerning this cerebral system its anatomy is still a matter of debate. Particularly, it was suggested that precuneus is not a component of the DN. Functional magnetic resonance was used to estimate neural responses in one participant. Data was

acquired during twelve runs on a 3 Tesla scanner. In each run subject performed a one-back repetition detection task. Stimuli were gray-scale images of objects. Subsequently, DN was determined by means of the independent component analysis (single-session and multiple-session temporal concatenation). Components of interest were identified using anatomical landmarks and registered to the atlas space. Next, precuneus was defined as in the Harvard-Oxford template implemented in FSL. After this, we visually tested whether precuneus was a part of the DN. In each measurement of the DN from a single run precuneus was a component of this network. Also, in the mean image of the DN from the multiple-session temporal concatenation precuneus was in the border of DN. Precuneus is a part of the DN. Further studies should evaluate its exact role in this cerebral system.

## 11

### ***Disorders of pitch production; Assessment with the Sung Performance Battery (SPB)***

**Magdalena Berkowska** (1), Jakub Sowiński (1), Simone Dalla Bella (1,2)

(1) Department of Psychology, University of Finance and Management, Warsaw, Poland

(2) EuroMov, Movement to Health (M2H) Laboratory, University of Montpellier-1, Montpellier, France

Singing is as natural as speaking for the majority. Yet, a few individuals in the general population (approximately 10–15%), referred to as “tone deaf” exhibit notorious difficulties in carrying a tune. The deficits of sung performance can be very specific, selectively affecting particular musical abilities (e.g., production of absolute or relative pitch), leading to different poor singing phenotypes. Each of these deficits is likely to reflect the malfunctioning of dedicated mechanisms within the human song system (i.e., within the “vocal sensorimotor loop”). Deficits can involve, for example, perceptual and motor planning, memory retrieval, or auditory-motor mapping. To uncover different phenotypes of poor singing, we created a new tool for assessing singing proficiency in the general population (the Sung Performance Battery, SPB). Data analysis is realized with acoustical methods providing objective measures of pitch accuracy and precision (i.e., in terms of absolute and relative pitch) as well as of time accuracy. To illustrate the SPB, we report the results obtained with a group of 50 occasional singers. The results indicate that the battery is useful for characterizing proficient singing and for detecting cases of inaccurate singing.

## 12

### ***Rhythm deafness in general population***

**Maciej Nowaczyk** (1), Jakub Sowiński (1), Magdalena Berkowska (1), Simone Dalla Bella (1,2)

(1) Department of Psychology, University of Finance and Management, Warsaw, Poland

(2) EuroMov, Movement to Health (M2H) Laboratory, University of Montpellier-1, Montpellier, France

A great deal of research has been devoted to rhythm perception and production in ordinary musicians. Much less is known about connections between rhythm perception and production in the general population. Recent data suggest that some individuals (so-called “rhythm deaf”) may exhibit impaired rhythm perception and inaccurate sensorimotor synchronization (SMS), while showing spared pitch processing. In this study we examined more in depth rhythm perception and SMS in non-musicians. 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 perception tasks. The analyses confirmed that 7 participants were poor synchronizers. In particular, 2 of them exhibited normal rhythm perception. This finding points to a possible mismatch between perception and action in the rhythm domain, similar to what previously observed in the pitch domain.

***Handedness, sex and executive attention in the Stroop Effect*****Agata Gutarewicz** (1), Agnieszka Gorzelana (1), Justyna Różycka (2), Małgorzata Gut (1,3)

(1) University of Finance and Management, Warsaw, Poland

(2) Jagiellonian University, Poland

(3) Nicolaus Copernicus University, Toruń, Poland

It is well known that some cognitive functions are lateralized in the brain, also executive attention. Moreover, the hemispheres asymmetry patterns differentiate males and females as well as left- and right-handers. This is why we examined the effect of handedness and sex on the reaction time (RT) and percentage of correct responses in the Stroop Task paradigm. Fifty participants (males, females, right- and left-handed) participated in the experiment. Each trial consisted of the word - a name of the color ("red", "green", "blue" or "yellow") and participants were asked to determine their font color. The half of the stimuli was congruent (the font color and the word referred to the same color, e.g. „blue” word written in blue) and the half was incongruent (e.g. “red” word written in green). The results revealed main effect of congruency (but only in RT) and congruency x handedness interaction. The greatest differences between RT to congruent vs. incongruent stimuli were obtained in the sub-groups with a slight hands asymmetry. Moreover, there is no effect of sex on behavioral indices of executive attention. It may suggest that the brain and hand lateralization do not affect executive functions processes.

***Cognitive control modified on-the-fly in the Eriksen task*****Justyna Różycka** (1,2), Blandyna Żurawska vel Grajewska (2), Martyna Jakubiak (2), Rob van der Lubbe (2,3)

(1) Psychophysiology Lab, Institute of Psychology, Jagiellonian University, Poland

(2) Department of Cognitive Psychology, University of Finance And Management, Warsaw, Poland

(3) Department of Cognitive Psychology and Ergonomics, University of Twente, the Netherlands

In perceptual-motor tasks, the influence of flankers can be modified. Their influence can increase when they are more often congruent with the target and decrease when they are more often incongruent. The black horizontal string of shapes was presented on a white background. The string contained: the two flanker arrows in the middle, one target arrow on the left or right, and the square on the opposite side of the flankers. In one half of trials the target was more often congruent (arrow pointing in the same directions as flankers) when it was presented on the left, in the second it was more often congruent when it appeared on the right. Our results showed that the reaction time for incongruent trials was shorter when the target was presented on the side with predominance of incongruent targets than for incongruent trials with target presentation on the side with predominance of congruent targets. Reactions were faster for congruent than for incongruent trials in both cases of predominance. Related results were observed in the modulation of N2PC amplitude. The influence of flankers can be modified by changing the proportion of congruent targets in the selected location.

***How many roads are there to act upon visual stimuli?*****Izabela Szumska** (1,2), Rob van der Lubbe (1,3), Michael Herzog (2)

(1) University of Finance and Management in Warsaw, Poland

(2) Laboratory of Psychophysics, Brain Mind Institute, Ecole Polytechnique Federale de Lausanne, Switzerland

(3) Cognitive Psychology and Ergonomics, University of Twente, the Netherlands

It has regularly been proposed that there are different visual routes to action. The dorsal visual processing route is thought to be involved when objects require manual actions whereas the ventral route is crucial for judgments about object identity. It has also been proposed that all information goes through a global workspace before a conscious response concerning an object can be elicited. In the current experiment, a diamond was presented to either the left or the right from fixation accompanied by a distracting square on the other side. Participants had to report the side of the diamond either by making a button press, a saccade, or by giving a verbal response. Meta-contrast masking was employed at various SOAs to manipulate the visibility of the target and distractor. Not surprisingly, response perceptual sensitivity ( $d'$ ) increased as a function of SOA, but importantly, there were no differences between the response modalities. The latter results suggest that the different responses rely on the same information, which favors theories in which information first enters a global workspace, before an action with one of the response modalities is elicited.

16

### ***Awareness of Stimulus Presence vs. Stimulus Shape***

**Marzena Wasilewska (1), Izabela Szumska (1,2), Rob Van der Lubbe (1,3)**

(1) University of Finance and Management in Warsaw, Poland

(2) Laboratory of Psychophysics, Brain Mind Institute, Ecole Polytechnique Federale de Lausanne, Switzerland

(3) Cognitive Psychology and Ergonomics, University of Twente, the Netherlands

Currently popular views on consciousness assume that there is a kind of workspace in which information enters after which it becomes globally available. The latter condition is accompanied with the phenomenal awareness of that specific stimulus. As an example, if we present a stimulus and subsequently mask it, then we either might be aware of that specific stimulus (i.e., it entered global workspace), or not. Psychophysical experiments, however, suggest that there are different thresholds for different types of information, which contradicts this idea of global availability. In our experiment, this issue was further explored. A square or diamond consisting of a grey contour was presented on a black background in the centre of the screen. The stimuli were meta-contrast masked with different stimulus onset asynchronies (SOAs). On 33 % of the trials, no stimulus was presented. In one condition, participants had to report on stimulus presence and in another condition on stimulus shape. Results revealed that perceptual sensitivity ( $d'$ ) increased as a function of SOA. This increase, however, was much steeper when participants had to report on stimulus presence than when they had to report on stimulus shape. These findings seem to suggest that awareness is not unitary.

17

### ***The implicit learning and the SNARC effect for numbers and letters***

**Małgorzata Gut (1,2), Karolina Szygoska (1)**

(1) University of Finance and Management, Warsaw, Poland

(2) Nicolaus Copernicus University, Toruń, Poland

The example of 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 examined the behavioral indices of implicit learning in the task of reaction to numbers and letters, without any response mapping between stimuli magnitude and side of reaction (left/right). Each trial started with a centrally presented stimulus, which was one of six digits (1,2,3,7,8 or 9) in the half of participants or letters (A,D,G,R,U or Z) in the second half. Each participant could respond with right or left key and no particular instruction, however immediately after every motor response a feedback "CORRECT" or "WRONG" was displayed. The response was defined as "correct" in case of the left hand reaction to 1,2,3,A,D,G and right hand reaction to 7,8,9,R,U,Z. The goal was to gain as many "CORRECT" feedback answers as possible. The obtained results showed that

39

reaction time and percentage of correct responses increased quickly in time, what is a clear sign of implicit learning (of a rule related to the SNARC effect). However, this effect was more pronounced for numbers than for letters.

18

***The effect of number magnitude on volume of activation in the brain – an fMRI study on the spatial-numerical association***

**Magda Dzierżawska** (1), Małgorzata Gut (1,2), Marek Binder (3), Piotr Jaśkowski (1), Robert Winiarski (4), Robert Blaut (4), Wojciech Szeszkowski (4), Andrzej Cieszanowski (4)

(1) Department of Cognitive Psychology, University of Finance and Management, Warsaw, Poland

(2) Faculty of Humanities, Nicolaus Copernicus University, Toruń, Poland

(3) Psychophysiology Laboratory, Institute of Psychology, Jagiellonian University, Poland

(4) 2nd Department of Clinical Radiology MRI Laboratory, Medical University of Warsaw, Poland

Brain representations of numbers are spatially represented on the mental number line. We investigated the activation patterns related to the number magnitude and its spatial position during fMRI scanning. Each trial started with a fixation point replaced by a cue stimulus - one of four digits (1,2,8 or 9) or non-digit symbols (#, %, < or §). The target stimulus consisted of a pair of such digits and/or symbols. Participants responded by indicating the position (left/right) of the cue digit/symbol within the target, which could be either congruent (e.g. 8 on the right) or incongruent (e.g. 9 on the left). The behavioural results showed faster reactions to low than high number magnitude and fMRI results showed the asymmetry patterns dependent of the digit magnitude, irrespectively of stimuli congruency. In trials with low digit magnitude the right hemisphere as well as left cerebellum preponderance was observed, while in trials with high digit magnitude the opposite pattern was present. However, the analysis of the volume of activation calculated in each condition and hemisphere, showed the main effect for magnitude of digit, but no significance for congruency and hemisphere. These results suggest that number magnitude processing affects the volume of activation but not its lateralization.

19

***Brain Mechanisms underlying the Startle Reflex and its fear-potentiation in Healthy Adults***

**Katarzyna Paluch** (1), Alfons Hamm (2), Julia Wendt (2), Katja Linder (2)

(1) Faculty of Psychology, University of Warsaw, Poland

(2) Institute für Psychologie, Ernst Moritz Arndt Universität Greifswald, Germany

Startle reflex is a fast twitch of body flexor muscles exhibited in response to a sudden and intense stimulus which provides a basic model of defensive reaction. Its magnitude alters under different conditions and is augmented by fear. Its underlying brain mechanism is well described in animals and comprises of: ventral cochlear nucleus, nucleus reticularis pontis caudalis and spinal cord motoneurons. Fear-potentiated startle requires recruitment of additional structures such as: amygdala, anterior cingulate cortex (ACC) and insula. In our study startle probe (50ms of 85dB white noise) was presented during fear conditioning experiment in three variants: 1) during aversive visual cues (STRCS+), 2) safe visual cues (STRCS-) and 3) interstimulus time interval (ITI STR). F test conducted with the small volume and FWE correction revealed significant activation within: pons ( $F=11.13$ ;  $pFWE_{corr}=0.024$ ), thalamus (right: $F=13.96$ ;  $pFWE_{corr}=0.002$ ; left: $F=14.22$ ;  $pFWE_{corr}=0.002$ ), primary auditory cortex (right: $F=10.61$ ;  $pFWE_{corr}=0.005$ ; left: $F=9.61$ ;  $pFWE_{corr}=0.009$ ), anterior insula (right: $F=8.17$ ;  $pFWE_{corr}=0.001$ ; left: $F=6.03$ ;  $pFWE_{corr}=0.030$ ) and right ACC ( $F=6.32$ ;  $pFWE_{corr}=0.013$ ). Subsequent ANOVA analysis showed escalated response for fear-potentiated condition, reflected in significant condition effect for: pons ( $\eta^2=0.48$ ), thalamus ( $\eta^2=0.15$ ), primary auditory cortex ( $\eta^2=0.27$ ), anterior insula ( $\eta^2=0.33$ ) and right ACC ( $\eta^2=0.23$ ). Thus, our results are partly in line with fear-potentiated startle models investigated on animals.

40

***Manipulation of the N170 ERP component via social context*****Jakub Michalak (1), Michał Bilewicz (1), Olga Kamińska (2)**

(1) University of Warsaw, Poland

(2) University of Social Sciences and Humanities, Warsaw, Poland

The study was designed to check if the N170 ERP component (human face perception) can be manipulated via semantic stimuli. For perceptual flexibility human faces were morphed with chimpanzee faces. The semantic manipulation was a cover story informing about edibility of the morphed animal. The story was supposed to create a dissonance caused by the meat-paradox. Studies suggest that this dissonance makes people exclude edible animals from the human realm. The main hypothesis states that such moral disengagement can affect the N170 component amplitude making it less negative (less characteristic for human faces) for people that heard the manipulation story. Eighteen non-vegetarian people participated, half received the manipulation story - the experimental group, the other half formed the control group. EEG activity was recorded for all participants while they were watching morphed faces. One-way ANOVA showed marginally less negative N170 component values in the experimental group,  $F(1,15) = 3.94$ ,  $p = .066$ ,  $\eta^2 = .21$ , indicating an effect of semantic information on face perception. An additional regression analysis used perceived capacity to suffer as a predictor variable and revealed a significant interaction term of group x perceived animal suffering,  $t = -2.8$ ,  $p = .015$ ,  $b = -2.72$ . Hence, people who deny animal suffering perceive edible animals as having fewer human characteristics than non-edible ones. The results provide some support for stating that semantic context can influence face perception.

***Between emotions - processing fluency and modulation of N170 ERP potential during ambiguous facial stimuli viewing*****Olga Kamińska (1), Michał Olszanowski (2), Aneta Brzezicka (1), Mateusz Gola (2), Piotr Winkielman (2, 3)**

(1) Interdisciplinary Center for Applied Cognitive Studies, University of Social Sciences and Humanities, Warsaw, Poland

(2) University of Social Sciences and Humanities, Warsaw, Poland

(3) University of California, San Diego, USA

In social relations, face is the most important stimuli. The ease of its processing elicits more positive affect and increases perceived attractiveness in opposition to the faces which are difficult to process. We investigated this issue adjusting the difficulty of processing level. In the easy condition participants were assessing the gender of presented faces and in difficult they had to categorize emotional expression. In our study presented pictures exhibited clear emotional states of anger or happiness as well as morphed expressions gradually changing from one to another. Behavioral results indicates that categorization of difficult stimuli (morphed expressions) is related to decrease of processing fluency revealed in longer reaction time comparing to the easy one. These results are in line with our previous findings. In this study for the first time we show that attenuation of processing fluency is accompanied by the increase of the face-specific N170 ERP amplitude. Larger N170 amplitude may be interpreted as greater neural activity during ambiguous content processing. This finding suggests that that processing fluency is affected at the very early stages of stimulus perception.

***Childhood abuse impacts visuospatial working memory for emotional information***

**Sofie Cromheeke, Sven C. Mueller**

Department of Experimental Clinical and Health Psychology, Ghent University, Belgium

Childhood abuse is an important risk factor for depression, anxiety disorders and substance abuse disorder later in life. One possible mechanism underlying this association could be its adverse effect on critical cognitive functions such as working memory, especially when processing emotional information. In this study, we compared the performance of adult females with (N= 20, mean age = 19.9 years) and without (N=19, mean age = 20.1 years) a history of childhood abuse on a visuospatial working memory task with emotional stimuli, the SEMTOS task (spatial emotional match to sample task). We hypothesized that emotional valence would negatively impact working memory in the trauma group, due to heightened sensitivity to affective interference. As expected, women reporting a history of childhood/adolescent sexual and/or physical abuse were less accurate relative to non-traumatized comparisons at remembering the location of happy faces compared to neutral or angry faces when working memory demands were high. This finding is consistent with the hypothesis that childhood abuse can have a persistent influence on cognitive control processing in adulthood, and thus increases the risk for psychopathology by potentially dampening responses to positive stimuli.

***Is emotional content salient? Eye movements while viewing emotional scenes***

**Joanna Pilarczyk (1), Szymon Wichary (2), Michał Kuniecki (1)**

(1) Psychophysiology Laboratory, Jagiellonian University, Poland

(2) Interdisciplinary Center for Applied Cognitive Studies, University of Social Sciences and Humanities, Warsaw, Poland

Emotional objects preferentially engage visual attention and so do physically salient regions. We explored relative strength of physical and semantic saliency maps to predict attention shifts. Total of 60 images (positive, negative and neutral) was selected from International Affective Pictures System. Participants, using a web tool, encircled regions determining emotional meaning of each picture. After averaging their selections and applying a 10% area threshold, we obtained „semantic” map of emotional regions for each image. Similarly, visual saliency maps based on simple physical features were generated for each picture using Koch and Itti's model and also thresholded to 10% of total picture area. Subsequently, we conducted an eye-tracking study using free-viewing paradigm. The fraction of first four fixations falling within the regions indicated by visual saliency and semantic maps were calculated. Visual saliency model accounted for an average of 8% of fixations, with significant effect of valence (9.5% for neutral pictures and 7.7% for emotional ones). Semantic maps on average predicted one third of fixations, with valence of the picture also significantly impacting on this result: 30% for neutral pictures and 37% for emotional pictures. Thus, semantic features strongly dominate over simple physical attractors in attention deployment while viewing natural scenes. This tendency is modulated by valence, with attention being guided slightly more by physical characteristic of the stimulus in case of the neutral pictures than in case of emotional ones. (This work has been supported by grant N N106 288939 from Polish Ministry of Science and Higher Education).

***The type of the picture stories sequencing and its depending on the presented content***

**Natalia Jermakow, Katarzyna Kupczak, Remigiusz Szczepanowski**

University of Social Sciences and Humanities, Wrocław Faculty, Poland

According to The Empathizing–Systemizing Theory researchers assume that men need more time than

women to process pictures with intentional situations than with mechanical stories and also people who score greater on the empathy scale can find the beginning of visual stories with intentional situations faster than in mechanical ones. Participants comprised with 28 healthy volunteers, 18 females and 10 males. Subject were asked to fulfilled The Cambridge Behaviour Scale (Baron-Cohen & Wheelwright, 2004). Subject were instructed to look at pictures (mechanical, behavioral, and intentional) and find a picture of the beginning of each story sooner than 9 sec and press the space bar after finishing the task. There were 12 stories of three types of situations (Baron-Cohen & Frith, 1986). SMI eye tracker was employed to examine type of sequencing while processing the pictures. It was found that participants need more time to find the beginning of the stories when presented with intentional situations as compared to the mechanical condition ( $t(27)=8,075$ ,  $p<0,001$ ). The eye-tracking measures showed also that there was no connection between sexual differences and time duration of first fixation on intentional pictures. This suggests that participants present a specific pattern of information processing when intentional situations involved.

## 25

### ***Near and Far Space dissociation reflected in cortical activity related to Vergence Eye Movements***

**Anna Przekoracka-Krawczyk** (1), Katarzyna Przekoracka (2), Monika Czaińska (1), Fabrizio Zeri (2), Rob van der Lubbe (3)

(1) Laboratory of Vision Science and Optometry, Faculty of Physics, Adam Mickiewicz University of Poznań, Poland

(2) CdL in Ottica e Optometria-Dipartimento di Fisica „E. Amaldi”, Università Degli Studi Roma, Italy

(3) Department Cognitive Psychology and Ergonomics, University of Twente, the Netherlands

Vergences are believed to be the most important cue for localization of the visual targets in three-dimensional space. Despite the high importance of the vergence system in visual space perception, functional anatomy of the human cortical network related to this process is still unexplored area. The aim of the study was to explore cortical activity as a effect of binocular disparity processing and vergence eye movements preparation. 16 young subjects participated in the experiment. All had normal or corrected to normal visual acuity. Six LEDs were positioned at eye level on two isovergence circles at two distances: near (20 cm) and far (1m). The eccentricity of the lateral LEDs was 60 for both distances. Fixation LEDs and target LEDs duration were 2 sek. The subject was instructed to fixate the target LED as quickly as accurately as possible. Pure saccades and combined vergences were performed. The EEG was recorded from 64 electrodes. Early lateralized potentials (ELPs) were analyzed related to the target LED's onset. Convergence evoked the strongest cortical activity especially in the occipito-parietal channels. Divergence showed strong activity in the area of occipito-temporal cortex. Stimuli called for eye movements in the extrapersonal space evoked activation in the ventral visual stream but stimuli called for eye movements in the peripersonal were related to the dorsal cortical stream processing. The results showed clear differences between far and near space segregation in human visual cortex.

## 26

### ***Cortical activity related to binocular vision***

**Monika Czaińska** (1), Anna Przekoracka-Krawczyk (1), Rob van der Lubbe (2)

(1) Laboratory of Vision Science and Optometry, Faculty of Physics, Adam Mickiewicz University of Poznań, Poland

(2) Department Cognitive Psychology and Ergonomics, University of Twente, the Netherlands

In normal humans the cortical visual evoked potential(s) (VEPs) evoked by binocular stimulation is generally larger in amplitude than that evoked by monocular stimulation. Usually, the superiority of binocular vision is attributed to the activity of the binocular cells in visual cortex. The aim of the study was to examine binocular summation effects in higher cortical levels. Twelve young subjects with corrected refractive errors, and no interocular suppression were examined. Cortical activity was measured with 64 channels (Quick Amp). Two different sizes (15' and 60') reversed pattern

checkerboard was presented with 1 Hz frequency. Three different visual conditions (dominant eye, non dominant eye, binocular) were tested. Binocular summations were observed for both stimuli size in area of visual cortex as well as parietal and frontal areas. Binocular summation was related with theta oscillations in visual cortex and alpha & beta oscillations in visual and parietal cortex. Strong cortical activity related to binocular vision can not be related only to binocular visual cells activity. The effects of binocular summation can be observed in parietal and frontal cortex. This method seems to be proper way for measuring of binocular visual functions in normal subjects as well as in strabismic individuals.

27

### ***Influence of sleep on context-dependent memory***

**Katarzyna Jurewicz (1), Björn Rasch (2)**

(1) Faculty of Psychology, University of Warsaw, Poland

(2) Division of Biopsychology, University of Zurich, Switzerland

Sleep after learning is often beneficial for memory. When the context of the study episode is reinstated, declarative memory performance is typically superior to that found when the retrieval context is different. This study examined how post-learning sleep, relative to wakefulness, impacts upon context-dependent memory effects. Forty-nine participants saw 240 nouns exposed in the first session, superimposed on unrelated short videos, constituting the context. Memory for all previously studied words was tested in the second session, using a recognition task with confidence ratings. It consisted of 120 word-video pairs for each context condition (matching, non-matching and new). A mixed design was used with between-subject factor of group, defined by the type of the 12 h interval between sessions (wake or sleep) and within-subject factor of context condition. Unequal variance signal detection model was employed to obtain empirical ROC curves. Mixed model ANOVA, performed for overall sensitivity measure  $dA$  and area under the curve, revealed superior memory when learning and retrieval context were matching. Between-group comparison was insignificant, however, with a trend toward better memory after wake period. These findings do not support hypotheses about differential memory consolidation during sleep with regard to contextual content.

28

### ***Human EEG Under Monotonous Auditory Stimulation***

**Daniel Georgescu, Marius Georgescu, Dragos Alexandru, Maria Iancau**

Department of Functional Disciplines, University of Medicine and Pharmacy of Craiova, Romania

Monotony constitutes the effect of continuous stimulations that are repetitive or predictive, representing a central nervous system functional state, described by diminished cerebral activity. The study group was made up of 11 volunteers (average age 23 years). The EEG was recorded while stimulated by 3 different auditory stimuli (S1 - recording of a car over a rough road, S2 - recording of a rainforest, S3 - Mozart's K448 Sonata), for periods of 20 minutes of stimulation and a 5 minute period of silence prior to and following stimulation. Highest variance domain resulted under S3 stimulation, frequency bands Alfa1, Beta2 Theta, S2 for bands Delta, Beta1, Alfa2, with S1 only slightly elevated for the total frequency spectrum. S1 presents statistically significant differences between mean values for the high frequency bands when making the stimulation/post-stimulation comparison. S2 yields statistically significant differences between mean values similar to S3, with the exception of Beta1. S3 presents the fewest statistically significant values – solely for the Delta and Theta indexes. The present work will enlarge knowledge of the effects of monotonous auditory stimulation on brain activity and help accumulate fresh data on superior cognitive processes.

44

***Oscillatory alpha band activity and time estimation***

**Aleksandra Kołodziej**, M. Magnuski, Z. Moszczyńska, M. Wodyk, M. Gola

University of Social Sciences and Humanities, Warsaw, Poland

The main purpose of the study was examination of relation between oscillatory alpha band activity (10-12 Hz) and time estimation. Subjects had to reproduce time periods lasting from 2 up to 3.2 seconds. We have investigating the accuracy of those reproductions in two intergroup conditions - low attentional engagement (high alpha-band power) and high attentional engagement (low alpha band power). In addition we introduced intergroup alpha power manipulation by evoking the steady-state visual evoked potential (SSVEP) during the trial (increased alpha power) or asynchronies blinking (no alpha change). Behavioral results indicates that the accuracy of time reproduction is significantly higher for conditions related to high alpha band power. Participants taking part in the passive condition present more accurate time reproduction and irrespectively to the group all participants presented better time reproduction during the SSVEP trials in comparison to asynchronous blinking. Alpha band activity was verified by EEG data analysis. The main conclusion of the study is positive correlation between alpha band power and accuracy of time reproduction. This results suggest that alpha band oscillatory activity may play a significant role in the timing processes.

***Disturbed attentional control in Parkinson's disease: an fMRI investigation***

**Aleksandra Gruszka**, Adam Hampshire, Roger A. Barker, Adrian M. Owen

Dysexecutive syndrome, including deficits in attentional control, is common in PD and occurs even in the early stages of the disease. Although presumed to be related to a dysfunction in dopaminergic frontostriatal networks, its exact neurochemical and anatomical basis remains unclear. In this study we investigated the behavioural and brain correlates of attentional set-shifting deficits in PD using event-related fMRI in 18 non-demented medicated patients with early PD and 16 age-matched controls. The study revealed that PD is characterised by a general loss of efficient problem-solving strategy while searching for solutions during the visual discrimination with a concomitant decrease in neural activity in the caudate nuclei (CN) and the anterior cingulate cortex (ACC). Putting the current observations in the context of our previous findings (Hampshire et al. 2008), our results suggest a that there is a dissociation in the neuronal correlates of PD and normal ageing in attentional control with ageing being primary related to a hypofunction of the ventrolateral prefrontal cortex rather than CN and ACC.

***Narratives: neurocognitive functioning assessment tool in stroke patients***

**Anna Rita Ambroziak**, Emilia Łojek

Warsaw International Studies in Psychology, Faculty of Psychology, University of Warsaw, Poland

Despite modern neuroimaging techniques providing valuable information on brain structure and functions, it is the interview, however, that equips clinicians with the knowledge of patients' subjective experience of illness. This study, being in line with research in narrative medicine, attempts to reveal narratives' use in neuropsychological diagnosis of stroke patients. A total of 12 participants, 5 left- (LHD) and 7 right-hemisphere-damaged (RHD) stroke patients undertook an experimental method of an interview and standardized neuropsychological tests of memory, thinking, attention, activity rate, expressive, executive and emotional functions. Analysis of patients' self-reports and neurocognitive functioning showed that RHD and LHD groups did not report most of their deficits, however, they mentioned problems not revealed in testing (especially within expressive functions). Moreover, narratives demonstrated impact of deficits on patients' daily functioning, suggesting the focus of individually

accustomed neurorehabilitation. The study affirms the importance of discourse analysis in clinical setting, as it brings a deeper and more relevant understanding of patient's state and level of mental functioning. Thus, narratives seem to be a useful and beneficial source of data adding to neuropsychological diagnosis and rehabilitation planning.

## 32

### ***Does education have a beneficial effect on behavioral abnormalities in Huntington's disease?***

**Anna Maria Łopatkiewicz (1), M. Błaż (1), K. Banaszkiwicz (2), K. Polok (1)**

(1) Jagiellonian University Medical College, Poland

(2) Krakow's Academy of Neurology, Poland

Huntington's disease (HD) is a genetically transmitted neurodegenerative disorder which manifests with motor, cognitive and behavioral disturbances. It has been reported that behavioral symptoms are less severe in better educated patients. We aimed to investigate the relationship between education and severity of particular behavioral symptoms in HD patients. Forty HD patients were examined with use of Irritability Questionnaire (IRQ) for irritability, Leyton Obsession Inventory for obsessive-compulsive symptoms (OCS), Beck Depression Inventory for depression, Lille Apathy Rating Scale for apathy, Modified Overt Aggression Scale for aggression and motor part of the Unified Huntington's Disease Rating Scale for motor HD symptoms respectively. The group was then divided into two subgroups according to the length of education with 12 years as a cutoff level. Patients with longer education presented less irritability than those with shorter education (IRQ 36.0 vs.48.6,  $p=0.03$ ). There was no difference between the groups in terms of depression, aggressive behavior, OCS and apathy. Irritability, but not other behavioral symptoms was influenced by the length of education. The possible explanation is that the neuronal circuit which is responsible for behavioral control improves during school education.

## 33

### ***Factors associated with cognitive functioning in older adults***

**Jacek Suwalski (1,2), Joanna Pniewska (3), Sylwia Łukasik (1,4), Lubomira Rola (1,5), Wiktor Pałys (6), Dorota Łojko (6), Aleksandra Suwalska (6)**

(1) Students' Scientific Association "Neuroscience", Poznan University of Medical Sciences, Poland

(2) Adam Mickiewicz University, Institute of Psychology, Poznan, Poland

(3) Poznan University of Medical Sciences, Department of Neurological and Psychiatric Nursing, Poland

(4) Adam Mickiewicz University, Institute of Anthropology, Poznan, Poland

(5) Adam Mickiewicz University, Faculty of Biology, Poznan, Poland

(6) Poznan University of Medical Sciences, Department of Adult Psychiatry, Poland

The increasing life expectancy in the Polish population raises the question of how the elderly can maintain their cognitive functioning. The aim of the study was to delineate factors associated with cognitive functions in the group of non-demented community-dwelling individuals. Fifty six older adults (7M, 49F, mean age  $65.3 \pm 4.6$ , range 58-79 years) entered the study. Selected tests from the Cambridge Automated Neuropsychological Test Battery: visuospatial planning test - Stockings of Cambridge (SOC), Spatial Working Memory (SWM), Spatial Span (SSP) and Paired Associate Learning (PAL) measuring memory and learning were employed. Gender-related differences were detected – significantly longer SOC Mean initial thinking time in men. Older participants (aged 65 or more) scored significantly worse in PAL and had significantly longer mean subsequent thinking time than younger ones. Highly physically active participants had significantly better planning ability and significantly longer Spatial Span. Normal-weight participants had also better planning abilities than overweight and obese subjects. The trend towards better results in overweight individuals than remaining participants in SWM was observed. The results suggest that obesity and low physical activity might contribute to the cognitive deficits in the older population. Further studies are needed to confirm the relationship.

***Pain perception and the relation with EEG-changes in an endometriosis rat model*****Maria Panagiotou** (1,2), Saskia Mulder (2), Ard Peeters (2), Clementina M. van Rijn (1)

- (1) Donders Institute for Brain, Cognition and Behaviour, Radboud University Nijmegen, the Netherlands  
 (2) Chardon Pharma, Druten, the Netherlands

This study investigated the perception of pain in an animal model for endometriosis. Two main goals have been set in this research; First, the establishment of the model as a chronic pain model: behavioral testing (Skinnerbox experiments) was conducted. Second, the pain perception was correlated to EEG parameters by attending the resting states, the oscillations & the connectivity between thalamus and cortex. The behavioral results demonstrated that the endometriosis rats consumed significantly less pellets compared to control rats, most likely because of the abdominal pain. No significant differences can be seen by correlating the pellets' consumption to the estrus cycle. EEG data analysis is ongoing and results will be presented.

***Decreased synchronization in rats chronically treated with a cannabinoid antagonist*****Martin F.J. Perescis** (1,2), Annika Lüttjohann (1), Lyudmila Vinogradova (3), Gilles van Luijtelaar (1), Clementina M. van Rijn (1)

- (1) Donders Institute for Brain, Cognition and Behaviour, Radboud University Nijmegen, the Netherlands  
 (2) HAS Den Bosch University of Applied Sciences, 's Hertogenbosch, the Netherlands  
 (3) Institute of Higher Nervous Activity and Neurophysiology, Russian Academy of Sciences, Moscow, Russia

Cannabinoid CB1 antagonists have been widely investigated for possible treatment of obesity, metabolic syndrome and drug addiction. Previously we observed that long term blockade of the endogenous cannabinoid system can induce epileptic seizures. In the present study EEG was recorded from healthy Wistar rats chronically treated with either 3 (male) or 2 (female) mg/kg.day of a CB1 antagonist during six months. Analysis of the synchronization likelihood of randomly selected segments of the background EEG demonstrated that, although only 26% of animals in the treatment group had seizures, coherence between activity of the cortex, the thalamus and the hippocampus in the theta band was significantly lower than controls. This suggests that the risks of blocking the on-demand protection the endocannabinoid system provides against the consequences of a variety of injuries goes beyond the scope of seizures.

***The anti- nociceptive and orexigenic activities of the aqueous extract of pistacia lentiscus leaves*****Mohamed Yeslem Ould Mohameden** (1), M. Mountassir (1), K. Hanane (1), M. Ould Tijani (1), Hind Ferehane (1), A. Chait (1), A. Benharref (2)

- (1) Laboratory of Neurobiology, Pharmacology and Behaviour, Faculty of Sciences Semlalia, Marrakesh, Morocco (2) Laboratory of Chemical of Naturals, Substances and Heterocycles, Faculty of Sciences Semlalia, Marrakesh, Morocco

*Pistacia lentiscus* is an evergreen shrub of the family Anacardiaceae, can reach 3 m in height, grows wild in arid areas and is characteristic of Mediterranean countries. The aerial part has traditionally been used as a stimulant, for its diuretic properties, and to treat hypertension, coughs, sore throats, eczema, stomach aches, kidney stones and jaundice. The aim of this work, is to study the anti-nociceptive and orexigenic activities of the leaves of Moroccan *P. lentiscus*. Male Swiss mouse, weight between 24g and 30 g, and male Sprague–dawley rats weighting between 180-230g are used in this study. All tested animals have receiving the aqueous extract of *Pistacia lentiscus* leaves. The plant was carried from Rfal,

locality of AZILAL Moroccan town. Results have shown that no toxicity was observed at the used doses. No analgic effect was obtained in the hot plat test. In the writhing test, the extract of this plant has shown a significant analgic effect. In food intake test, the extract decreases quantity of consumed aliments in tested rats. The aqueous extract of *P. Lentiscus*, has demonstrated a significant analgic and anorexigenic activities in mouse and rat.

37

***Impact of triclosan in caspase-3 activation and LDH release in mouse neocortical cells***

**Konrad A. Szychowski**, A.M. Szybińska, A.K. Wójtowicz

Laboratory of Genomics and Biotechnology, Animal Sciences Faculty, University of Agriculture,  
Kraków, Poland

Triclosan is an antimicrobial component added to personal care and sanitizing products, such as soaps, toothpaste, and hair products, as well as in household items, such as plastic cutting boards, sports equipment, textiles and furniture. Triclosan has been detected in human breast milk, blood samples and as triclosan metabolites in the urine. The aim of the present study was investigated the effect of triclosan on viability and apoptosis in cultured neocortical mouse neurons. 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. For experiment cells were exposed to triclosan in increasing nM, and  $\mu$ M concentration. Cell cultures were exposed to chemicals for 6 and 24 hours and after this time measured of LDH and caspase-3 activity. Additionally number of apoptotic bodies was determined by Hoechst33342 staining. Our preliminary data demonstrated that the high concentration of triclosan stimulated both the LDH activity as well as the caspase-3 activity in the cells culture. The proapoptotic action of triclosan was confirmed by the increase in the number of apoptotic bodies. In summary, the study demonstrated that exposure to triclosan can cause neuronal cell death.

38

***Preliminary study applying tracing techniques and silver staining methods unravels Bombina corpuscle (BC) innervation and blood supply***

**Ewa E. Bres**

Institute of Zoology, Jagiellonian University, Poland

Naked warts (NWs) mark the presence of a male specific skin organ named Bombina corpuscle (BC). The BCs are globular in shape, 60-70  $\mu$ m in diameter and consist of multiple expanded axon endings separated by flattened lamellar cells ( Hofman and Szymura, in prep.). The BCs are located on digits, hands, forearms, clavicular regions of *Bombina bombina*, *Bombina variegata* and *Bombina orientalis* and, with the exception of *Bombina bombina*, on jaw margins (Hofman and Szymura, in prep.). TEM and histological preparations have provided some insight into the BCs structure leading to the conclusion that the BCs are most likely mechanoreceptors responsible for vibration perception (Hofman and Szymura, in prep.). To further understand the innervation pattern of the BCs, silver nitrate and Sudan Black stainings on formaldehyde fixed *Bombina orientalis* tissue and Dil tracing experiments on paraformaldehyde fixed *Bombina variegata* tissue were performed. In this poster we present the preliminary results of the above techniques, together with an overview of the location of the BCs in *Bombina orientalis*. Further modification of the Sudan Black and silver staining methods together with immunohistochemical and neurophysiological approaches is needed to reconstruct the details of the corpuscle's 3D structure and elucidate its function and evolution.

48

***Orexin A-induced theta oscillations in hippocampal formation slices***

**Paulina Kazmierska**, Ilona Ubraniak, Paulina Klos-Wojtczak, Bartosz Caban, Renata Bocian, Tomasz Kowalczyk, Henryk Golebiewski, Marek Wieczorek, Jan Konopacki

Department of Neurobiology, University of Lodz, Poland

The theta rhythm is a sinusoidal, high-voltage activity (from 0.2 to 2 mV) with a frequency band ranging from 3 to 12 Hz. Many years of research conducted with the use of the model of hippocampal slice preparations allowed to determine the specific role of the cholinergic and GABAergic systems in providing the adequate level of neuronal excitation necessary for hippocampal theta to appear. Orexins appears to be particularly interesting in terms of rhythmicity development, since axons of orexinergic neurons create a wide network reaching many brain structures, including the hippocampal formation. Orexin A, but not orexin B, induces a state-dependent long-term potentiation of synaptic transmission (LTPox) in hippocampal slices of adult mice. The aim of present study was to investigate the effect of Orexin A on microEEG activity recorded from hippocampal preparations. Field potentials and extracellular recordings were made from the CA3c hippocampal field during the bath perfusion of Orexin A in a range of concentrations in the following  $\mu\text{M}$  ratio: 1: 3: 10: 30 and 100. Experiments were performed on 105 HPC slices obtained from 20 Wistar rats in accordance to Local Ethical Commission. Besides epileptiform discharges, oscillatory activity in theta band was observed only in the slices perfused with 0,1  $\mu\text{M}$  Orexin A. This demonstrates that synchronization of neuronal networks needs the appropriate and precise level of excitation. In addition, we conclude that theta oscillations can be modulated not only cholinergically or GABAergically but also by orexinergic mechanisms. (This work was supported by the National Science Centre, grant No. 2011/01/N/NZ4/01722).

**Effect of imipramine and caffeine on dopamine, glutamate and adenosine extracellular level in frontal cortex of rats treated with low doses of reserpine**

**Katarzyna Kamińska**

Institute of Pharmacology of the Polish Academy of Sciences, Krakow, Poland

In our study we tried to understand the early changes in DA synapses and glial cell responses which may provide insights on PD pathology. We investigated the changes in extracellular concentration of DA, GLU and ADN in the frontal cortex of rats treated with repeated small doses of reserpine (REZ), which irreversibly blocked VMAT2 in cortical monoamine neurons. The release of DA, GLU and ADN was measured using microdialysis in freely moving rats. Animals received REZ (0,25 mg/kg) for 7 or 14 days and were subjected for surgery after cessation of treatment. Separate groups of animals were injected with imipramine (5 mg/kg) or caffeine (10 mg/kg) together with REZ. Obtained results indicate that under conditions of damaged vesicular transport there is significant overflow of ADN as well as increase in DA release in the rat frontal cortex. Vesicular storage of DA may cause increase in cytosolic concentration of DA and ATP. Marked increase in extracellular ADN release by REZ May lead to activation of adenosine A2A receptors located in cortical DA and GLU terminals or glial cells causing damage through induction of oxidative stress by glutamate or dopamine.

***Antidepressant-like activity in mice of 1-{4-[4-(2-methoxyphenyl)piperazin-1-yl]butyl}-3',4'-dihydro-2'H-spiro[imidazolidine-4,1'-naphthalene]-2,5-dione hydrochloride (Acz-37), a multireceptor ligand representing a new series of arylpiperazine analogues***

**Anna Wasik**, Anna Partyka, Dagmara Wróbel, Magdalena Jastrzębska-Więsek, Anna Czopek, Agnieszka Zagórska, Marcin Kołaczkowski, Maciej Pawłowski, Anna Wesołowska

On the basis of our preliminary findings, Acz-37 was selected as an interesting multireceptor (5-HT<sub>1A</sub>, 5-HT<sub>2A</sub>, 5-HT<sub>7</sub>, D<sub>2</sub>) ligand producing an antipsychotic-like effect in mice. In the course of study, its potential antidepressant and anxiolytic activity was evaluated in the forced swim (FST) and the four-plate tests, respectively, and compared with that of aripiprazole used as a reference antipsychotic drug. In order to exclude the possibility of competing behaviors such as general locomotor activity, its doses effective in FST and the four-plate tests were examined in the spontaneous locomotor activity model in mice. Our results showed that ACz-37 (2.5 and 5 mg/kg) evokes antidepressant-like properties, shortening the immobility time of mice 37% and 45%, respectively, while aripiprazole (0.01-0.1 mg/kg) was inactive in that test. Effective antidepressant doses of the investigated agent did not stimulate the spontaneous locomotor activity in mice during the time identical to the observation period in FST. The results obtained in the four plate test in mice showed that neither ACz-37 (0.312-5 mg/kg) nor aripiprazole (0.06-0.5 mg/kg) produced anxiolytic-like effects in mice. This data suggest that a new synthesized compound Acz-37 produced specific antipsychotic/antidepressant-like activity and may find application in the treatment of schizophrenia and/or affective disorders.

## 42

### ***GABAA receptors involved in tonic and phasic inhibitory transmission show different sensitivity to $\alpha$ -thujone***

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

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

In the addicted drinkers of absinthe, pathological effects such as seizures or hallucinations were observed and  $\alpha$ -thujone, a component of wormwood oil, was suspected for these effects. However, subsequent studies showed that  $\alpha$ -thujone, at concentrations used in absinthe, was unlikely to induce these disorders. Nevertheless, at higher doses,  $\alpha$ -thujone could induce epilepsy, suggesting an interaction with GABAA receptors. GABAA receptors are, however, very heterogeneous and different receptors are responsible for tonic and phasic inhibition. In the present study we investigated effects of  $\alpha$ -thujone on:  $\alpha$ 1 $\beta$ 2 $\gamma$ 2L (responsible for phasic currents),  $\alpha$ 1 $\beta$ 2,  $\alpha$ 1 $\beta$ 2 $\delta$ ,  $\alpha$ 4 $\beta$ 2 $\delta$  (mainly tonic) GABAA receptors. We show that  $\alpha$ -thujone affects all considered receptors, but the strongest effect was observed for  $\alpha$ 1 $\beta$ 2 $\delta$ , indicating that tonic inhibition is more sensitive to this compound than phasic one. This result was supported by experiments on cultured neurons, where a submicromolar GABA concentration was used to mimic tonic currents. Currents evoked by low [GABA] were inhibited by  $\alpha$ -thujone to a larger extent than responses to higher [GABA] or synaptic currents. Altogether, our data indicate that different GABAA receptors, involved in tonic or phasic inhibition, show different sensitivity to  $\alpha$ -thujone.

## 43

### ***Head-to head comparison between mGlu1 and mGlu5 receptor enhancement in the treatment of absence epilepsy***

**Valerio D'Amore** (1,2), L. Lionetto (3), C.M. van Rijn (2), F. Nicoletti (1,3), R.T. Ngomba (1), G. van Luijtelaar (2)

(1) I.N.M. Neuromed, Pozzilli, Italy

(2) Donders Centre for Cognition, Donders Institute for Brain, Cognition and Behaviour, Radboud University Nijmegen, the Netherlands

(3) Department of Physiology and Pharmacology, University of Rome "Sapienza", Italy

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 3rd until day 8rd, while the brain concentration of mGlu5 agonist remains unchanged over the days. These data suggests that a possible pharmacokinetic tolerance occurs for RO0711401, while no tolerance is present for VU0360172. These findings confirmed that mGlu5 agonist could be developed for the treatment of absence epilepsy.

#### 44

### ***Noradrenergic, serotonergic and dopaminergic activity in the rat hippocampal slices during orexin-induced theta rhythm***

**Ilona Ubraniak, Paulina Kaźmierska, Marek Wieczorek, Jan Konopacki**

Orexins are two neuropeptides appearing to be particularly interesting in terms of hippocampal EEG development since axons of orexinergic neurons reach to many brain structures, including the hippocampal formation (HPC). Recent studies conducted in our laboratory demonstrated that orexin A induce epileptiform discharges in HPC slices and in certain concentrations may also evoke theta oscillations. The lack of data concerning the influence of orexins on the changes in the activity of other neurotransmission systems encouraged our research. Thus the aim of the study was to investigate the changes in the activity of monoaminergic neurotransmitter systems in isolated hippocampal slices, which were used in EEG recordings. Experiments were performed on 40 HPC slices obtained from 5 Wistar rats in accordance to Local Ethical Commission. Slices were subjected to neurochemical analysis immediately after the section, for 45 min incubation in the Artificial Cerebrospinal Fluid (ACSF), and after incubation in ACSF with Orexin A (0,01 and 0,03) for additional 45 min. Analysis of the concentration of monoamines and their metabolites was determined using high-performance liquid chromatography with electrochemical detection. Specifically, we determined the concentration of norepinephrine, dopamine, serotonin, 3-methoxy-4-hydroxyphenylglycol, 3,4-dihydroxyphenylacetic acid, homovanillic acid and 5-hydroxyindoleacetic acid and calculate utilization indexes, ratio of metabolite to its parent amine, of particular neurotransmitter systems. Preliminary results show a statically significant increase in the serotonergic, noradrenergic and dopaminergic system activity in hippocampal slices perfused with Orexin.

#### 45

### ***Neuronal tuning to instantaneous stimulation interval in the barrel cortex***

**Anna Pitas, Ana L. Albarracin, Manuel Molano, Miguel Maravall**

Instituto de Neurociencias de Alicante, CSIC-UMH, Spain

Neurons in the barrel cortex (BC) are sensitive to whisker identity, but also to dynamical (temporally varying) stimulus features, and this additional feature selectivity is essential to their function. For example, whisker-mediated tactile discrimination is thought to depend on the temporal pattern of whisker motion fluctuations evoked upon contacting an object, and BC neurons encode the physical parameters (e.g. velocity) of fluctuations in the sequence. It is unknown whether BC neurons have the capacity to integrate such sequences of whisker fluctuations over time, and thus to encode specific temporal stimulation patterns, or whether sensitivity to patterns emerges at higher levels of processing. Here we addressed whether BC neurons are tuned exclusively to single intervals (implying sensitivity to instantaneous frequency) or to sets of several intervals (implying integration over time). We performed

juxtacellular recordings in anesthetized mice. Stimulation was applied with a piezoelectric wafer and consisted of different sequences of stimuli applied at periodic and non-periodic intervals. We found that neurons carry information about the latest single intervals, rather than about interval sequences. Our results place limits on the amount of temporal integration that can be carried out by neurons in the primary somatosensory barrel cortex.

46

***Prenatal stress-induced attenuation of long-term potentiation in the rat hippocampus and frontal cortex***

**Joanna Sowa** (1), B. Bobula (1), J. Ślusarczyk (2), K. Głombik (2), A. Basta-Kaim (2), G. Hess (1,3)

(1) Department of Physiology, Institute of Pharmacology, Polish Academy of Sciences, Krakow, Poland

(2) Department of Experimental Neuroendocrinology, Institute of Pharmacology, Polish Academy of Sciences, Krakow, Poland

(3) Institute of Zoology, Jagiellonian University, Poland

Prenatal maternal stress can affect the development of the embryo and can cause adverse changes in its central nervous system, which become evident in adulthood. Effects of prenatal stress have been investigated in several brain regions, however, it is not well known how it influences excitatory synaptic transmission and long-term plasticity. The aim of this study was to compare the effects of maternal exposure to chronic stress during pregnancy on glutamatergic transmission and long-term potentiation (LTP) in the hippocampus and frontal cortex of adolescent offspring. Pregnant female rats were subjected to chronic mild stress. Its effects were studied *ex vivo* in 8 weeks old male offspring. Extracellular field potentials (FPs) were recorded from frontal cortical and hippocampal slices and LTP induction was attempted using standard protocols. The amplitude of FPs in the frontal cortex of stressed animals was increased but no change in hippocampal FPs was evident. Both in frontal cortical and hippocampal slices originating from prenatally-stressed rats the magnitude of LTP was reduced. These results suggest that prenatal stress enhances glutamatergic transmission in the frontal cortex but not in the hippocampus and attenuates long-term synaptic plasticity in both structures.

47

***The involvement of TNF-family in diabetic neuropathy in mice***

**Magdalena Zychowska** (1), Ewelina Rojewska (1), Grzegorz Kreiner (2), Irena Nalepa (2), Barbara Przewlocka (1), Joanna Mika (1)

(1) Department of Pain Pharmacology, Institute of Pharmacology, Polish Academy of Sciences, Krakow, Poland

(2) Department of Brain Biochemistry, Institute of Pharmacology, Polish Academy of Sciences, Krakow, Poland

Diabetes-neuropathy is an important clinical issue. The goal of study was to examine the spinal changes of TNF-family proteins in diabetic neuropathic pain model in Swiss mice. We examined, after intraperitoneal (i.p.) injection of streptozotocin (STZ; 200mg/kg), the blood glucose concentration, body weight, allodynia, hyperalgesia and potential role of microglia and TNF-family proteins. The minocycline (30mg/kg, chronically i.p. administered, 7 days), a potent inhibitor of microglial activation was used. The experiments were carried out according to IASP rules. The STZ-injection induced a significant hyperalgesia and allodynia along with increased plasma glucose and decreased body weight. Quantitative Real-TimePCR and western blot/immunohistochemistry revealed upregulation of C1q mRNA and CD11b/IBA-1 protein. Protein Antibody Array showed upregulation of TNF-family proteins: IFN $\gamma$ , sTNFR1, sTNFR2 and no changes of TNF $\alpha$ . We demonstrated that minocycline significantly attenuated the allodynia, hyperalgesia and blood glucose in parallel to decrease of microglia activation and increase of the level of sTNFR2 protein as measured on day 7 after STZ-treatment. These findings indicate that development of neuropathy in diabetic mice could be modulated by changes in

52

microglia activity and suggest that sTNFRII can play an important role in attenuating neuropathic pain during diabetes mellitus. Acknowledgements: Supported by the NCN-grants 2011/03/B/NZ4/00043 and 2012/05/N/NZ4/02416.

48

***Effect of hyperhomocysteinemia on the production of reactive oxygen species and the enzyme activities after induced ischemia-reperfusion injury and ischemic tolerance***

**Martin Petráš**, Mária Kovalská, Zuzana Tatarková, Silvia Mahmood, Ján Lehotský, Anna Drgová  
Comenius University in Bratislava, Jessenius Faculty of Medicine in Martin, Department of Medical Biochemistry, Martin, Slovakia

Hyperhomocysteinemia (HHcy) is associated with the occurrence of various conditions including the ischemic brain stroke. Homocysteine (Hcy) continuously gets oxidized which leads to the formation of reactive oxygen species (ROS) and his metabolites cause the protein homocysteinylation. As the ischemic stroke is the third leading cause of disability and death worldwide there is very important to develop stroke prevention strategies. The aim of this study was to monitoring HHcy impact on ROS, as well as changes in activities of antioxidant enzymes in combination with induced ischemic tolerance, brain ischemia and varying periods of reperfusion. The male Wistar rats were divided into the control group, group premedicated with Hcy (2 weeks), group with induced ischemic tolerance and group with induced ischemia and different times of reperfusion. Homogenized cortex and mitochondria were used for biochemical and histological analysis. Ischemic tolerance decreased the lipid peroxidation after ischemia. The HHcy increased the lipid peroxidation and protein oxidation. Ischemic tolerance significantly decreased the superoxidismutase (MnSOD) activity as well as ROS formation and MnSOD protein production in comparison to ischemia-reperfusion (IR) groups. The immunoreactivity of MnSOD was in correlation with the protein production.

49

***Effects of protein aggregation induced by bortezomib in neural cells***

**Ivana Pilchova**, K. Klikova, A. Stefanikova, K. Klacanova, P. Racay  
Institute of Medical Biochemistry, Jessenius Faculty of Medicine, Comenius University,  
Martin, Slovak Republic

Massive aggregation of polyubiquitinated insoluble proteins is a common feature of various neurodegenerative diseases including ischemia and reperfusion. Mechanism of ischemic delayed neuronal death is still unclear but aggregation of misfolded proteins is considered as a possible cause. To induce protein aggregation we incubated human glioblastoma cell line T98G with different concentrations of proteasomal inhibitor bortezomib (Velcade, PS-341). Concentration dependent cell death was determined by MTT assay and results were compared with relative amount of proteins detected by Western blot analysis of cell extracts incubated with bortezomib for 4 and 24 hours. Significant increase of the level of polyubiquitinated proteins was observed after 4 and also 24 hours but only 24 hours of incubation is associated with decrease in cell survival. Bortezomib induces cytoplasmatic stress response resulting in increased levels of heat shock proteins Hsp70 and Hsp90. However overexpression of these cytoprotective chaperones is not accompanied with cell survival. Changes in relative levels of Bcl-2 family proteins (prosurvival Mcl-1 and proapoptotic Noxa) regulated through proteasome were determined after 24 hours and correlate with induction of cell death. Our results suggest that protein aggregation induced by bortezomib is not the primary cause of T98G cell death (Supported by APVV-0245-11).

53

***Inducible inactivation of NMDA receptors on neurons expressing dopamine D1 receptors: behavioral and molecular consequences***

**Joanna Zajdel** (1), Magdalena Sikora (2), Magdalena Smutek (2), Jakub Kubik (2),  
Jan Rodriguez Parkitna (2)

(1) Faculty of Biochemistry, Biophysics and Biotechnology of the Jagiellonian University, Krakow, Poland

(2) Department of Molecular Neuropharmacology, Institute of Pharmacology of the Polish Academy of Sciences, Krakow, Poland

Motivation drives behavior towards maximizing rewards and minimizing punishment. This is possible through mechanisms that evaluate outcomes of actions, selectively energize optimal behaviors, and compare outcomes to expectations. To investigate neuronal basis of these processes, controlled by an interaction between dopamine and glutamate signaling, we created a transgenic mouse line with a deletion of glutamate NMDA receptors restricted to neurons expressing dopamine D1 receptors. The ablation of a floxed variant of the NR1 gene (*Grin1*) was induced by tamoxifen treatment (0.1 mg/g twice daily for 5 days). Unlike mice with constitutive NR1 ablation, NR1D1CreERT2 mice exhibited no developmental deficits. Although mutant animals showed normal ability to learn instrumental responding for rewards, they had attenuated drug-conditioned place preference. Furthermore, their cocaine-induced locomotor activity was significantly elevated. A tendency towards increased rearings number when exposed to novel environment was also visible. Despite these clear behavioral alterations, no changes in transcript levels of NMDA and AMPA receptor subunits in the striatum were observed. These preliminary results indicate a specific role of NMDA receptors on dopaminergic neurons in control of motivated behaviors. (Supported by the Grant N405 143238 from the Polish Ministry of Science and Higher Education and the statutory funds of the Institute of Pharmacology of the Polish Academy of Sciences).

***Late-onset of neuropathic pain symptoms after pharmacological modulation of endocannabinoid system***

**Natalia Kolosowska**, Wioletta Makuch, Barbara Przewlocka, Katarzyna Starowicz

Institute of Pharmacology of the Polish Academy of Sciences, Krakow, Poland

Anandamide produces its pharmacological effects mostly by activating CB1 and also TRPV1 receptors. Targeting endocannabinoids can be an alternative approach to achieve analgesia in the case of neuropathic pain. We tested the hypothesis that up-regulated anandamide levels, achieved by inhibition of FAAH, might decrease pain and/or delay the development of neuropathic pain symptoms. Wistar rats were implanted with an intrathecal catheter and subsequently subjected to CCI procedure. We tested the effects of pharmacological inhibition of FAAH (URB597 100µg/10µl i.t.) on the development of hyperalgesia 1-14 days after CCI. Western Blot analysis of NAPE-PLD and FAAH were performed. A single dose of URB597 administered preemptively before CCI did not prevent and/or attenuate the development of neuropathic pain. Chronic administration of URB597 started before nerve injury and continued for 3 days after CCI significantly prevented the development of neuropathic pain. Pharmacological inhibition of FAAH was shown to delay neuropathic pain development in CCI rats. This may, via accumulation of AEA, lead to the activation of CB1 receptors as well as activation/desensitisation of TRPV1. These data provide an evidence on the complexity of cross-talk between CB1 and TRPV1 in the control of ascending pain pathways and in the development of CCI-induced hyperalgesia.

***Cooperative involvement of serotonergic signaling and extracellular matrix in synaptic plasticity***

**Monika Bijata** (1), I. Figiel (1), E. Ponimaskin (2), L. Kaczmarek (1), J. Włodarczyk (1)

(1) Nencki Institute of Experimental Biology, Polish Academy of Sciences, Warsaw, Poland

(2) Center for Physiology, Hannover Medical School, Germany

The brain plasticity is a re-organization of the neuronal and synaptic networks that allows for changes in response to incoming environmental stimuli. Pathological forms of neuronal plasticity underlie the multiple neuropsychiatric disorders like depression. Clinical observations on the efficacy of antidepressants targeting serotonergic system strongly suggest that serotonin and its receptors play a pivotal role in modulation of pathological plasticity. It is known that MMP-9 is one of the most important biomarker in depression and polymorphism in this protein affect bipolar disorder. However, underlying molecular mechanisms, and in particular possible interplay between serotonergic system and ECM, remain poorly understood. We have recently shown that MMP-9, having an established role in synaptic plasticity, influences dendritic morphology in a similar way to that obtained after the 5-HT<sub>7</sub> receptor stimulation, e.g. induces formation of long, thin dendritic spines. It is also known that stimulation of 5-HT<sub>7</sub> receptor leads to activation of small Rho GTPase - Cdc42 in fibroblast cell line and in neurons. In this work we investigate whether MMP-9 substrate represents a novel downstream effector of 5-HT<sub>7</sub> receptor. Our results indicate that stimulation of the 5-HT<sub>7</sub> receptor increases MMP-9 activity toward its synaptic substrates and results in activation of small Rho GTPases.

***Chronic caffeine treatment modifies responses of red wood ants (*Formica polyctena* Först.) to allospecific ants (*Formica fusca* L.) during dyadic aggression tests***

**Paweł J. Mazurkiewicz** (1,2,3), Beata Symonowicz (1), Anna Mirecka (1,5), Róża K. Węglińska (1,4), Anna Szczuka (1), Ewa J. Godzińska (1)

(1) Laboratory of Ethology, Department of Neurophysiology, Nencki Institute of Experimental Biology PAS, Warsaw, Poland

(2) College of Inter-Faculty Individual Studies in Mathematics and Natural Sciences, The University of Warsaw, Poland

(3) Department of Animal Physiology, Faculty of Biology, The University of Warsaw, Poland

(4) Faculty of Biology, The University of Warsaw, Poland

(5) Institute of Ecology and Bioethics, Cardinal Stefan Wyszyński University, Warsaw, Poland

Caffeine, a methyloxanthine commonly used as a neurostimulant in humans, is also known to influence behavioural and physiological processes in other vertebrates and in invertebrates including social Hymenoptera. The effects of caffeine treatment were, however, never investigated in ants. We investigated the effects of chronic oral caffeine treatment (3 weeks, two caffeine doses: 25 ppm and 100 ppm) on responses of workers of the red wood ant (*Formica polyctena* Först.) to allospecific ants (*Formica fusca* L.) during dyadic aggression tests. The doses used in our experiment were known to influence significantly food preferences in honeybees. During the test two ants were confined in a set of two test tubes and their behaviour was videorecorded. Caffeine treatment had no significant effect on occurrence and duration of various patterns of aggressive behaviour displayed by workers of *F. polyctena*. However, the rate of occurrence of withdrawals after an antennal contact with another ant was higher in both experimental groups than in the control one, although that effect was significant only in the case of the higher caffeine dose. This implies that caffeine affects responses of *F. polyctena* to other ants, although the exact mechanism of that effect remains to be unraveled.

***Effects of morphine on contextual fear conditioning in mice – implications for PTSD*****Przemysław Cieślak (1,2), Klaudia Szklarczyk (1), Ryszard Przewłocki (1,2)**

(1) Department of Molecular Neuropharmacology, Institute of Pharmacology Polish Academy of Sciences, Krakow, Poland

(2) Institute of Applied Psychology, Jagiellonian University, Poland

Post-traumatic stress disorder (PTSD) is a chronic and debilitating anxiety disorder that can develop after exposure to a traumatic event. It is characterized by exaggerated fear and impaired extinction of traumatic memories. Clinical studies suggest that there is a correlation between morphine treatment and a decrease in severity of PTSD symptoms. However, these correlational studies do not give direct evidence of morphine's efficacy. We used an animal model of fear conditioning and employed C57BL/6J mice to investigate whether morphine would disrupt consolidation of fear memories associated with footshocks. The efficacy of post-training and post-retrieval systemic injections of morphine in doses 5, 10, and 20mg/kg was tested. Systemic administration of morphine immediately after training does not prevent consolidation of fear memories. However, post-retrieval injections of morphine disrupt fear conditioned memory retention in a dose-dependent manner, suggesting that morphine would targets memory reconsolidation. Moreover, morphine treated animals were resistant to reinstatement of conditioned fear, measured two weeks later. Our results provide support for the effectiveness of morphine in inhibition of traumatic memory retrieval, which is consistent with clinical studies. Therefore, opiates may be a potential treatment for mental disorders resulting from traumatic memories.

***Desipramine does not affect feedback sensitivity of rats in the probabilistic reversal learning task*****Ewa Szczech, Rafał Ryguła**

Institute of Pharmacology Polish Academy of Sciences, Krakow, Poland

Depressed patients show cognitive deficits that may depend on an abnormal reaction to positive and negative feedback. The precise neurochemical mechanisms responsible for such cognitive abnormalities have not yet been clearly characterized. The present study was designed to investigate the effects of acute administration of 3 different doses of Desipramine (noradrenaline reuptake inhibitor) in rats performing a probabilistic reversal learning task that measures response to feedback. The animals which were tested in the operant Skinner boxes had to learn from feedback (reward and punishment) which of the two levers was associated with the greater probability of reward. For successful completion of the task subjects had to learn to ignore infrequent, spurious or misleading negative (and positive) feedback, arising from the 70:30 probabilistic nature of the discrimination. We show that in contrary to 5-HT, boosting NA neurotransmission does not affect feedback sensitivity in rats. [This work was supported by the Foundation for Polish Science "Homing Plus" Programme co-financed by the European Regional Development Fund (Innovative Economy Operational Programme 2007-2013)].

***Physical activity increases reactive gliosis in the hippocampus after traumatic brain injury in rats*****Emilia Kosonowska, Kinga Gzielo-Jurek, Michał Kiełbiński, Krzysztof Janeczko, Zuzanna Setkovicz**

Institute of Zoology, Jagiellonian University, Poland

Traumatic brain injury (TBI) disturbs homeostasis of neural tissue and hence causes activation of glial cells which undergo hypertrophy, upregulate GFAP expression and activate cell proliferation (reactive gliosis). It is also known that physical activity has neuroprotective effects by endogenously increasing expression of proteins important in neuronal plasticity and repair. Moreover, it increases proliferation of astrocytes in healthy rats. The purpose of this study was to analyse how physical activity affects gliosis. To examine this, we used 30-day-old male Wistar rats which underwent the procedure of traumatic brain injury (TBI). After 5 days of recovery, animals exercised 20 minutes per day on a treadmill for 4 weeks. Brain sections were then processed for GFAP immunohistochemistry to evaluate the area of reactive gliosis in particular brain regions. TBI but also running exercises alone evoked bilateral increases of GFAP-immunoreactivity in the superficial part of the cerebral cortex and in the hippocampal formation. Additionally, in the contralateral dental gyrus, the TBI-induced GFAP-immunoreactivity was significantly higher in running rats than in their non-running counterparts. The results suggest that physical exercises after TBI might have a negative effect on the injury outcome. This should be taken into consideration during physical rehabilitation after TBI.

57

### ***Space-Temporal Distribution of Gangliosides in the Human Brain by Mass Spectrometry***

**Alina F. Serb** (1), Željka Vukelić (2), Corina Flangea (3), Ana-Maria Zagrean (4), Eugen Sisu (1),  
Alina D. Zamfir (3)

(1) "Victor Babes" University of Medicine and Pharmacy, Timisoara, Romania

(2) University of Zagreb Medical School, Zagreb, Croatia

(3) "Aurel Vlaicu" University of Arad, Romania

(4) "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

Gangliosides (GGs), sialylated glycosphingolipids are plasma-membrane components of all vertebrate cells with particular abundance in the nervous system. GGs participate in numerous signaling events and are involved in major biological processes: brain development, maturation, aging, neurodegeneration and malignant transformation. Determination of GGs composition in defined brain regions represents a fundamental requirement for correlating the specificity of the identified structures with the specialized function of each area of the central nervous system in health and disease. Native ganglioside mixtures were extracted from two brain regions: occipital lobe (82 years male) and frontal lobe (20 years male) according to literature data. The screening of GG distribution in both samples was accomplished in a high-throughput regime using a fully automated chip-based nanoelectrospray (nanoESI) mass spectrometry (MS) methodology. Comparative screening mass spectra provided direct evidence of differential gangliosides expression in the frontal and occipital lobe. Both samples were dominated by mono-, di- and trisialylated GGs, but with varying prevalence of different glycoforms exhibiting a high degree of heterogeneity in the ceramide motifs. This work first enabled the complete characterization of ganglioside profiles of human frontal and occipital lobes at different evolution stages, contributing new data to overall brain ganglioside mapping.

58

### ***Accumbal spontaneous high frequency oscillations are altered in the developmental rat model of schizophrenia***

**Sailaja A. Goda**, Stefan Kasicki, Mark J. Hunt

Nencki Institute of Experimental Biology, Department of Neurophysiology, Warsaw, Poland

We have shown previously that NMDAR antagonists (used to model schizophrenia) increase the power and frequency of high frequency oscillations (HFO, 130-180Hz) in the nucleus accumbens (NAc) of freely moving rats. Here, we examined whether HFO recorded in local field potentials (LFPs) of the NAc were altered in the MAM-E17 developmental rat model of schizophrenia. We found that the power and

57

frequency of spontaneous HFO were significantly higher in MAM compared to sham rats. In both groups, MK801 (0.05, 0.15, 0.3 mg/kg) dose-dependently increased the power of HFO, with no significant difference between the groups. In contrast, MK801 dose-dependently increased the frequency of HFO in the sham group alone. We conclude that abnormal spontaneous HFO are a characteristic of the MAM model and the MAM rats are not hypersensitive to the MK801-induced enhancement of HFO power in the NAc. These data provide further evidence supporting the notion that altered HFO may be a fundamental change associated with models of the schizophrenia.

59

***Effects of chronic stress and citalopram treatment on feedback sensitivity of rats in the probabilistic reversal learning task***

**Marta Lemieszewska, Rafał Ryguła**

Institute of Pharmacology Polish Academy of Sciences, Krakow, Poland

Aberrant cognition has long been associated with a range of mood and anxiety disorders. In major depression, for example, erroneous logic can perpetuate low mood by overemphasizing minor errors and ignoring major achievements. Depressed patients tend to ruminate over perceived negative feedback and have difficulties deriving enjoyment from positive stimuli. One of the best ways of measuring abnormalities in feedback processing is performance on a probabilistic reversal learning task, where subjects must determine which of the two stimuli is associated with the greatest probability of reward and to ignore infrequent, but misleading feedback. Here we present the results of an experiment where the abnormalities in feedback processing were investigated in an animal model of depression. In a series of experiments we implemented the probabilistic reversal learning task in rats and then subjected the animals to the chronic restraint stress and concomitant antidepressant treatment (citalopram 10mg/kg b.i.d. for 2 weeks). We report that chronically stressed animals were impaired on the probabilistic reversal learning and that this impairment was not reversible by chronic citalopram treatment. [This work was supported by the Foundation for Polish Science “Homing Plus” Programme co-financed by the European Regional Development Fund (Innovative Economy Operational Programme 2007-2013)].

60

***Chronic electrical stimulation of the bed nucleus of the stria terminalis increases cytotoxic activity of NK cells in the peripheral blood of rats with different models of behavior***

**Izabela Michalska, Karolina Plucińska, Alena Mankevich, Kacper Ptaszek, Magdalena Podlacha, Wojciech Glac, Beata Grembecka, Magdalena Listowska, Dorota Myślińska**

The bed nucleus of stria terminalis (BST) is a limbic forebrain structure, a part of the “extended amygdala”, formation responsible for emotional aspects of behavior, involved in neuroendocrine and autonomic reactions. Based on our previous study we assumed that the BST also influenced the primary, antitumor and antiviral immune response. In the present study, we examined if immunoenhancing effect of the BST stimulation depends on behavioral differences in rats. Male Wistar rats were submitted to novelty test and implanted with stimulating electrodes at the BST area, then divided into four groups: LR (low locomotor response in new environment) stimulated (n=14), HR (high locomotor response) stimulated (n=14), operated but non-stimulated LR sham controls (n=14), operated but non-stimulated HR sham controls (n=14). After chronic 14-day electrical stimulation we evaluated both blood and spleen natural killer cell cytotoxicity (NKCC) (51Cr-release assay). Stimulation of the BST caused a significant augmentations of NKCC in the peripheral blood, more significant in HRs. No such effect was found in the spleen. A week after termination of the stimulation procedure all the measured parameters returned to the baseline. The obtained results suggest that immunoenhancing effect on blood NK cell function is dependent on the behavioral outcome of the BST stimulation as well as on individual behavioral characteristics. (This work was supported by a research grant NN303819040 from the Ministry of Scientific Research and Information Technology).

58

***Pharmacological assessment of impact of  $\alpha 1F64$  mutation on conformational transitions of GABAA receptor***

**Magdalena Kisiel, Marta Magdalena Czyżewska, Marcin Szczot, Jerzy W. Mozrzymas**

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

GABAA receptors play a crucial role in inhibition in adult mammalian brain. Receptor activation comprises ligand binding and channel gating but their structural and functional coupling is not fully understood. We tested influence of  $\alpha 1F64$  (GABA binding site) mutations on receptor function using patch-clamp technique with ultrafast perfusion on recombinant GABAARs. Pentobarbital (activating the receptor through different pathway than GABA) elicited currents with similar amplitudes when applied to mutated ( $\alpha 1F64C$ ) and non-mutated receptors but when GABA was used, currents mediated by mutants were dramatically smaller. Analysis of currents showed that mutated and non-mutated receptors had undistinguishable single-channel conductance. Thus, when activated by GABA, mutants show substantially lower open probability. We found that mutations ( $\alpha 1F64C/L/A$ ) resulted in a strong reduction of desensitization and to see whether this is caused by binding impairment, we used high affinity agonist -muscimol. In non-mutated receptors, muscimol did not change desensitization compared to GABA. However, in  $\alpha 1F64L\beta 1\gamma 2L$ , in muscimol-elicited currents we observed acceleration of desensitization whereas  $\alpha 1F64C\beta 1\gamma 2L$  remained non-desensitizing both for GABA and muscimol. In addition, we found that for both mutants muscimol enhanced the efficacy (favored channel's opening). Our quantitative analysis indicate that  $\alpha 1F64$  mutation decreases the receptor's efficacy which is functionally coupled with desensitization.

***Role of Relaxin-3/RXFP3 Signalling in Neural Control of Feeding – in vitro patch clamp study***

**Alan Kania (1), Agnieszka Grabowiecka (1), Andrew Gundlach (2), Anna Blasiak (1)**

(1) Department of Neurophysiology and Chronobiology, Institute of Zoology, Jagiellonian University, Poland

(2) The Florey Institute of Neuroscience and Mental Health, The University of Melbourne, Victoria, Australia

The relaxin-3 is recently discovered peptide which belongs to insulin superfamily. The highly-conserved relaxin/insulin-like family peptide receptor 3 (RXFP3) signalling system is associated with arousal, stress responses and affective behaviour, and central relaxin-3 injections stimulate feeding via RXFP3 in the paraventricular nucleus (PVN). We hypothesize that relaxin-3 exerts its orexigenic effect through inhibition of oxytocin synthesising PVN neurons activity. To investigate the possible influence of selective RXFP3 agonist on the activity of magnocellular PVN neurons whole cell patch clamp recordings were performed on the brain slices from 2 – 3 weeks old male Wistar rats. We have shown that selective RXFP3 agonist applied by bath perfusion, repetitively and reversely inhibits activity of magnocellular PVN neurons. Characterization of the recorded neurons was performed on the basis of their electrophysiological properties and subsequent identification of their neurochemical content. Our preliminary data shows predicted, inhibitory influence of RXFP3 selective agonist on PVN magnocellular neurons. Responsiveness of relaxin-3 neurons to stress factors and their involvement in feeding behaviour allow to treat this peptide as a bridge between chronic stress and obesity. Future patch clamp experiments with relaxin-3 antagonist, tract-tracing and behavioural studies will further allow to characterize the emerging role of relaxin-3 in mentioned phenomena.

***Group III metabotropic glutamate receptor activators are protective against MPP+-neurotoxicity in human neuroblastoma SH-SY5Y cells***

**Anna Gręda, Danuta Jantas**

Department of Experimental Neuroendocrinology, Institute of Pharmacology, Polish Academy of Science, Krakow, Poland

The role of group III metabotropic glutamate receptors (mGluR<sub>III</sub>) in models of neuronal cell injury not directly connected with excitotoxicity is not fully recognized. The aim of the study was the investigation of neuroprotective effects of mGluR<sub>III</sub> agonist, ACPT-I and mGluR<sub>8</sub> positive allosteric modulator, AZ12216052 against 1-methyl-4-phenylpyridinium ion (MPP<sup>+</sup>)-evoked cell death in human neuroblastoma SH-SY5Y cells. AZ12216052 (0.1 and 1 μM) when given alone increased the cell viability and cell proliferation rate of undifferentiated (UN-), as well retinoic acid (RA)-differentiated SH-SY5Y cells whereas ACPT-I (0.01-100 μM) did not reveal such effects. Both, ACPT-I (10 μM) and AZ (0.001-1 μM) demonstrated neuroprotection against MPP<sup>+</sup>-toxicity only in UN-SH-SY5Y. Moreover, the neuroprotective effects of these mGluR<sub>III</sub> activators were not connected with attenuation of apoptotic markers like MPP<sup>+</sup>-induced caspase-3 activation and DNA fragmentation. Further studies revealed that ACPT-I decreased the MPP<sup>+</sup>-dependent necrotic changes in UN-SH-SY5Y as confirmed by PI staining. The neuroprotection mediated only by ACPT-I was blocked by specific mGluR<sub>III</sub> antagonist, UBP1112. Interestingly, the inhibitor of necroptosis, necrostatin-1 diminished protective effects of tested mGluR<sub>III</sub> ligands. The obtained data indicate that selective activation of mGluR<sub>III</sub> is neuroprotective against the MPP<sup>+</sup>-evoked cell damage and this effect is associated with attenuation of necrosis.

***Influence of orexin A on h-current in the intergeniculate leaflet neurons***

**Katarzyna Palus, Ł. Chrobok, D. Pękala, M.H. Lewandowski**

Department of Neurophysiology and Chronobiology, Jagiellonian University, Poland

The thalamic intergeniculate leaflet (IGL) is involved in the regulation of circadian rhythms generated by suprachiasmatic nuclei. IGL neurons exhibit low threshold spike (LTS) bursts, dependent on activation of hyperpolarization-activated cation current (I<sub>h</sub>), which is a major regulator of neuronal excitability. Previous findings have shown that IGL neurons are sensitive to arousal peptide – orexin A (OXA). In the present study we have used tight seal current clamp recordings to investigate if OXA modulate LTS bursts by direct influence on depolarizing voltage “sag”, characteristic for neurons expressing I<sub>h</sub>. Experiments were performed on brain slices from 2-3 weeks old male Wistar rats. All drugs were applied by bath perfusion. At the end of recording neurons were filled with biocytin and further visualized with immunohistochemical stainings. Results showed that OXA (200 nM) reduced the voltage sag and decreased the amplitude of LTS. The duration of LTS did not change. The majority of the neurons were neuropeptide Y-negative. Our data suggests that OXA may be an important factor influencing neuronal excitability in the IGL and that modulation of I<sub>h</sub> contribute to this influence. Further experiments will be performed to investigate currents underlying LTS in details and their probable modulation by OXA.

***MR spectroscopy in brain tumors: preliminary results***

**Romana Richterová (1,2), M. Bittšanský (1), V. Ilovská (1), B. Kolarovszki (2), J. De Riggo (2), J. Šutovský (2), M. Benčo (2), P. Račay (1), H. Poláček (3), D. Dobrota (1)**

(1) Department of Medical Biochemistry, Jessenius Faculty of Medicine in Martin, Comenius University, Slovakia (2) Neurosurgery Department, University Hospital, Martin, Slovakia

Brain tumors create a heterogeneous group with high life-quality disturbance and serious prognosis. Conventional magnetic resonance imaging (MRI) is standardly provided and gives crucial informations for clinical decision making. MR spectroscopy (MRS) gives additional information about biochemical situation within brain tissue. Patients (n= 18) who underwent MRI with suspicion of brain tumor were indicated to brain tumor surgery. All patients underwent preoperatively 1H MRS in 1,5 Tesla clinical scanner. Surgery was performed in all cases with histological evaluation of tumor type. After this evaluation we divided patients with brain tumors into 3 groups: meningioma (n=5), glioblastoma multiforme - GBM (n=8) and metastasis (n=5). We focused on comparing ratios of metabolites N-acetylaspartate (NAA), creatine (Cr), choline (Cho), alanine (Ala) : NAA/Cho, Lac/Cr, Ala/Cr in voxels located in centre, peripheral part and outside of the tumor. We observed significant ( $p \geq 0,05$ ) differences between value of NAA/Cho between peripheral voxel and outside of the tumor and between centre and outside of the tumor, what makes this ratio relevant marker of tumor presence. Significant differences were also observed between value of Lac/Cr in all studied voxels. Ratio Ala/Cr showed significant differences especially in meningiomas, with no statistical significance in GBM and metastases. Our results show potential of MRS as additional method giving informations about metabolic situation within tumor. NAA/Cho shows presence of tumor and helps to distinguish between tumor and tumor-like lesion. Lac/Cr with increasing value shows presence of anaerobic glycolysis which is preferred in tumor. Increasing Ala/Cr refers to presence of meningioma. All of these data serve as complementary informations to established diagnostic protocol. However, there is a need for more data before definitive conclusion could be made.

66

***Caloric restriction and ketogenic diet effects on pilocarpine-induced seizure in rats with mechanical brain injury***

**Joanna Osoba, Z. Setkowicz, K. Gzielo-Jurek, M. Kiełbiński**

Department of Neuroanatomy, Institute of Zoology, Jagiellonian University, Poland

Traumatic brain injury (TBI) remains one of the most common causes of acquired epilepsy nowadays. The ketogenic diet (KD) is a specialized high-fat diet which mimics the anticonvulsive effects of fasting. Dietary restriction seems a promising alternative to classic ketogenic diet. It has been shown that chronic administration of calorically restricted (CR) may provide protection in the event of TBI and could possibly act as a neuroprotective factor. The aim of this research was to study the changes in susceptibility to pilocarpine-induced epileptic seizures in rats with mechanical brain injury performed at postnatal day 30 (P30). In order to check how the KD and CR alone influence the epileptic seizure susceptibility, rats were fed KD or CR until P60. At P60, seizures were induced by pilocarpine injection. During the following 6-h period, the animals were continuously observed and motor seizures intensity were rated on a 6-point scale. We have found that KD significantly increases the maximum intensity and duration of pilocarpine-induced seizures, compared to CR and normal diets. Surprisingly, KD and CR seem to have opposite effects. Our findings suggest that in pilocarpine-induced epilepsy KD does not suppress seizures. By contrast, CR lowers the susceptibility to seizures resulting from brain injury.

67

***The use of conditioned place preference paradigm (CPP) with unbiased procedure in rats as the preclinical predictive analysis of vulnerability to cocaine addiction***

**Ewa Niedzielska (1), Małgorzata Filip (1,2)**

(1) Jagiellonian University Collegium Medicum, Faculty of Pharmacy, Toxicology Department,

Krakow, Poland  
(2) Polish Academy of Science, Department of Pharmacology, Laboratory of Drug Addiction  
Pharmacology, Krakow, Poland

Despite progress in research, addiction to psychostimulants is still an unresolved medical and social problem. It is worth noting, that addiction with drug craving and relapses, develops only in 20% humans who began to abuse these substances. Similar phenotypic variability in response to drugs of abuse was observed in experimental animals (del Castillo et al, 2009). The aim of our study was to establish a fine animal model by means of which it will be possible to determine the variable vulnerability to psychostimulant addiction. For this purpose, male Wistar rats (260-340g) underwent a 10-day conditioned place preference (CPP) with cocaine (15 mg/kg, ip) as an animal model for studies of reinforcing and drug-seeking behaviors. We used self-created CPP box with conditions that allow to conduct unbiased procedure in over 80% of used rats. The results of CPP test indicated that over 65% of rats showed signs of addiction (spent more time in cocaine paired chamber) while less than 35% demonstrated insusceptibility to addiction. In conclusion, our CPP model provide conditions to determine the differential vulnerability to cocaine addiction in rats. In addition, using an unbiased procedure seems to create better advantage than its biased version.

68

### ***Effect of Ferula hermonis roots extract on Neurotransmitters levels on Laboratory mice***

**Mohammad S. AL-Harbi**

Biology Department, Faculty of Science, Taif University, Saudi Arabia

*Ferula hermonis* is an endemic plant grows at the joint borders of Lebanon and Syria. Its roots are ingested as a liquid solution. It has been used against frigidity and impotence, to increase sexual energy. This study aims to investigate the effect of the aqueous extract of the *Ferula hermonis* root on some neurophysiological aspects through measuring the effects of different doses on neurotransmitters levels in seven brain areas in laboratory mice. There are three different doses with concentrations of 1.5, 3, 6 mg/Kg for 3, 6 weeks, and also the same doses combined with Vitamin C, third group had replaced the doses with Vitamin C, and the fourth group had stopped ingestion (withdrawal) for 3, 6 weeks. Also there are acute ingestion by different doses for 30 minutes, 24, 48, 72 hours. The results showed that acute ingestion made significant increasing in some neurotransmitters levels after 30 minutes, 24, 48 hours, and no significant level after 27 hours. And showed that there are very high significant differences in neurotransmitters levels after ingestion with different doses for 3 and 6 weeks, the doses combined with vitamin C, and replacement of doses by vitamin C resulted in reduce the significant difference, and showed high significant difference after different doses withdrawal. That may be due to direct effect of *Ferula hermonis* roots extract on Calcium ions release that effect on Nitric Oxide (NO) production which excite neurotransmitters to release.

69

### ***PPAR $\gamma$ and Nurr1 effects on Mitochondrial Membrane Potential in PC12 cells***

**Mohamad Jodeiri** (1), Kamran Ghaedi (1,2), Abbas Kiani (2), Mohammad Hossein Nasre Esfahani (2)

(1) Department of Biology, School of Sciences, University of Isfahan, Iran

(2) Department of Molecular Biotechnology at Cell Science Research Center, Royan Institute for Biotechnology, ACECR, Isfahan, Iran

Parkinson's disease (PD) as a second prevalence neurologic disorder has largely unknown pathology. The cardinal symptoms of tremor, dystonia and postural instability result from degeneration of dopaminergic neurons in the substantia nigra pars compacta (SNpc). Mitochondrial complex I is inhibited

62

in PD by MPTP and this phenomena mitochondrial membrane potential (MMP). Mitochondrial dysfunction generates oxidative stress and reactive oxygen species formation which escalate neurodegeneration in substantia nigra. Nurr1 and PPAR $\gamma$  as nuclear receptors have critical roles in many pathways control detecting in PD, in addition Nurr1 is important factor in stem cells differentiation into dopaminergic neurons. In this study we used PC12 as an in vitro model of Parkinson's disease. These cells were treated with various concentration of MPP $^{+}$  which induces apoptosis in PC12 cells. GW1929 (PPAR $\gamma$  agonist) and 6-mercaptopurine (Nurr1 agonist) act as neuroprotective agents in in this experiment and we analyzed MMP by flow cytometry in the absence and presence of MPP $^{+}$ . We found that PPAR $\gamma$  and Nurr1 agonists could improve MMP in the presence of MPP $^{+}$  and they protected PC12 cells by this pathway. We can suggest that these agonists have enough potential to improve PD by their effects on mitochondria.

70

***The effect of intracerebroventricular injection of 5,7-dihydroxytryptamine on the activity of cytochrome P450 isoforms***

**Marta Rysz**, Ewa Bromek, Anna Haduch, Władysława Anna Daniel

Institute of Pharmacology, Polish Academy of Sciences, Krakow, Poland

It is known that the growth hormone, thyroid hormones, glucocorticosteroids and indirectly sex hormones play the most important role in physiological control of cytochrome P450 (CYP) activity. As all these hormones remain under strict control of hypothalamic-pituitary-secretory organ axes we hypothesize that by modulating hypothalamic serotonergic innervation we could influence cytochrome P450 activity in the liver. The experiment was carried out on male Wistar rats. 5,7-Dihydroxytryptamine (5,7-DHT), a serotonergic neurotoxin was injected intracerebroventricularly. Ten days after the injections, the levels of neurotransmitters and their metabolites in brain structures, the activity of cytochrome P450 isoforms in the liver, and serum hormone concentrations were measured (HPLC, ELISA). Intracerebroventricular 5,7-DHT decreased serotonin level in the hypothalamus and other brain structures examined. In the liver, the increased activity of CYP1A, CYP3A and CYP2C11 was observed. The activity of CYP2A and 2B remained unchanged. Simultaneously, a rise in the serum concentration of the growth hormone was noted. The obtained results indicate the involvement of the brain serotonergic system in the neuroendocrine regulation of liver cytochrome P450 activity. These findings may be of physiological and pharmacological significance, especially in pathological states or psychopharmacotherapy when serotonergic neurotransmission is affected (e.g. depression, anxiety, anorexia).

71

***Effects of selected neuroleptics on rat hypothalamic neuropeptide expression and adult neurogenesis***

**Ewa Rojczyk-Gołębiowska**, Artur Pałasz, Ryszard Wiaderkiewicz

Department of Histology and Embryology, Medical University of Silesia, Katowice, Poland

Hypothalamus is considered as a target for antipsychotics. As this brain area contains neuronal circuits regulating food intake, neuroleptics can potentially change regulatory peptides expression, which may result in energy imbalance. This hypothesis would support the fact, that among numerous side effects of antipsychotics, one of the leading problems is significant weight gain. Novel sites of constitutive neurogenesis have been discovered recently e.g. hypothalamus, so neuroleptics may modulate local neuronal proliferation also in this region, which constitutes the second hypothesis of this study. Experiments were held on rats to assess effects of olanzapine, chlorpromazine and haloperidol. Hypothalami were isolated to perform RT-PCR, and brains were sliced for immunohistochemical (IHC) assay. ICH was used to determine colocalization of cell proliferation and growth markers informing about neuroleptic influence on adult neurogenesis. Both techniques were used to evaluate expression of orexigenic/anorexigenic neuropeptides and their receptors on protein and mRNA level. It was proven

63

that antipsychotic drugs have tendency to downregulate anorexigenic factors expression and to upregulate orexigenic factors expression. The strongest effect was observed after haloperidol administration. The results could help to better understand the causes of neuroleptic side effects. They can also provide suggestions about interplay between hypothalamic neurogenesis and eating disorders.

72

### ***Application of teucrium polium in ovariectomy induced neurodegeneration***

**Karen Simonyan**

Orbeli Institute of Physiology, Republic of Armenia

Over the past years, different compounds have been isolated from Germander (*Teucrium polium*) of which the main groups are terpenoids and flavonoids. Anticholinesterase effects of *Teucrium polium* in the nervous system are less studied. On the other hand numerous clinical and experimental studies of postmenopausal women and ovariectomized (OVX) animals testify about neurodegenerative alterations in various structures of the brain, associated with mental function (in particular, hippocamp and basal nucleus of Meynert). With the purpose of getting ecologically clean product, programmed chemical compound and productivit *Teucrium polium* has been included into growing culture. Expediency of growing the plant in hydroponic condition is established. According to electrophysiological data in neurons of basal nucleus of Meynert under high frequency stimulation of hippocamp causes excitation and inhibition responses by equal quantity. After 6, 8 weeks of bilateral OVX in placebo control group about deficiency of neurotransmitters and damage of synaptic transmission testify sharp increase in number of areactive neuronal units. I/m injection of *Teucrium polium* (20 mg/kg within 3 weeks) starting from 3th week after OVX prevents neurodegenerative alterations exhibited in placebo-control on the 6, 8th weeks (according to criteria of expression of excitatory and inhibitory responses, correlation of reactive and areactive units). Thees data suggest the anticholinesterase activity of *Teucrium polium* and abilities its bioactive compounds to modulate some neurotransmitter systems. Thus, hydroponic *Teucrium polium* is advisable to recommend for approval in clinical practice to postmenopausal women for prevention of mental disturbances.

73

### ***Association of induced neuronal death and ischemic tolerance under experimental conditions***

**Mária Kovalská (1), Martina Furjelová (2), Katarína Jurková (2), Marian Adamkov (1),  
Ján Lehotský (2)**

(1) Department of Histology and Embryology, Comenius University, Jessenius Fac. Med. Martin, Slovakia

(2) Department of Medical Biochemistry, Comenius University, Jessenius Fac. Med. Martin, Slovakia

Global brain ischemia causes delayed cell death in hippocampal CA1 pyramidal neurons after reperfusion. Hyperhomocysteinemia (hHcy) is a risk factor for neurological disorders promoting neuronal cell death. High level of Hcy in patients after stroke could lead to incidence of secondary vascular injuries [3]. Ischemic tolerance evoked by preconditioning (IPC) represents phenomenon of adaptation of CNS to subsequent ischemia. The p38 MAPK pathway is associated with neurodegeneration and/or death of cells. The aim of this research was to study changes in p38 MAPK pathway after IPC and hHcy on IR-associated alterations. Global brain ischemia was induced by 4-vessels occlusion. Rats were preconditioned by 5 min of sub-lethal ischemia and 2 days later, 15 min of ischemia with reperfusion period of 1h, 3h, 24h and 72h was induced. hHcy was induced twice a day by subcutaneous injection of Hcy (0.45  $\mu\text{mol/g}$ ). The highest level of p38 protein as well as number of p38+ cells was detected in hHcy group at the reperfusion time after IRI. Considerable lower effect was observed during reperfusion time after IPC. The present study indicates for the neurodisturbant effect of p38 MAPK in tissues response to IRI and IPC in association with hHcy.

64

***The effect of methanol and its metabolites on cultured neural cells***

**Mária Kovalská** (1), Henrieta Škovierová (2), Silvia Mahmood (2), Jozef Hatok (2), Radovan Murín (2)

Methanol is commonly used solvent, occasionally present in low quality beverages. The intoxication with methanol is associated with development of neurological symptoms. To evaluate, if methanol or its metabolites – formaldehyde and formate – may affect the survival of the neural cells, we used the glioblastoma (C6 and T98G) and neuroblastoma (NS-20 and SH-SY5Y) cell lines as study model. The culture media were supplemented with methanol or formaldehyde or sodium formate up to concentration 25 mM. After 72 h incubation, the viability of the cells was tested by determining the total enzymatic activity of lactate dehydrogenase in cell lysates and visualization of cell nuclei. The both methods revealed that methanol in the level up to 25 mM had no toxic effect on the survival of all tested types of cell lines. Supplementation of culture media with sodium formate up to the level of 2.5 mM had no effect on all tested types of cell lines. In contrast, formaldehyde even at the concentration 2.5  $\mu$ M induced cell death in all tested cells. Our results show that among the metabolites of methanol, formaldehyde is the most toxic compound. (This work was supported by project “Center of Excellence for Research in Personalized Therapy (Cevypet)”, code: 26-220120053, and VEGA grants 1/0475/12 and 1/0242/13).

***Evaluation of the osteoarthritis of spine using spectrophotometry analysis. Preliminary report based on example of surgically treated spinal disk disease***

**Martyna Śniegocka** (1), Maciej Śniegocki (2), Wojciech Smuczyński (3, 4), Kamila Woźniak (3,4)

(1) Faculty of Biochemistry, Biophysics and Biotechnology, Jagiellonian University, Poland

(2) Department of Neurotraumatology, Ludwig Rydygier Collegium Medicum in Bydgoszcz, Poland

(3) Ludwik Rydygier Collegium Medicum in Bydgoszcz, Poland

(4) Nicolaus Copernicus University, Toruń, Poland

Collagen is a protein that builds extracellular matrix and ensure integrity of organs and structures. The properties of collagen contributes to the fact that the arteries are resistant to high blood pressure without losing their elasticity and extensibility. This is also the reason why intervertebral discs provide the spine's support, protective and motor functions. The knowledge about importance of maintaining an appropriate amount of collagen and the accurate proportion between the different types of this protein, lead to the statement that research in field of controlling the amount of collagen are needed. It is possible that this knowledge could be used in the diagnosis and prevention of diseases of the spine. One of the main cause of back pain is damage of the intervertebral disc and the annulus fibrosus. The consequence of this is pressure on the spinal canal's structures. Because the anatomical structures contain significant amounts of collagen, the aim of this research was to correlate the severity of spine's osteoarthritis with the spectrophotometry images of discs removed during the surgery. Blood serum was tested as well. Obtaining such a correlation would give the opportunity to more efficient monitoring of the degenerative disease or the effects of therapy. For the moment, everything indicate, that the results are promising.

***Do prions and  $\beta$ -amyloid cooperate in cognitive impairment?***

**Adrian Chrobak**

Jagiellonian University Medical College, Poland

Though Alzheimer Disease (AD) and Creutzfeldt – Jakob Disease (CJD) are characterized by distinct neuropathological changes, they share common pathological features. They are both conformational diseases related to accumulation of altered proteins that results in a loss of global cognitive functions. There is scarce data concerning interactions between prion proteins and  $\beta$ -amyloid, both in their physiological and conformationally changed form with regard to cognitive functions and dementia. Cellular prion Protein (PrPc) is a glycolipid-anchored cell membrane sialoglycoprotein localized in the presynaptic membranes related to i.a. long-term memory, modulation of the neurotoxicity and possibly shows the receptor like affinity to  $A\beta$ . On this interaction indirectly indicate some cognitive performance measurements. We report some conspicuous autopsy findings of immunohistochemically detected coexpression of prion protein within senile plaques (immunopositivity both for prions and  $\beta$ -amyloid). This finding may shed a light on the interactions of these proteins, adding some important premise to the discussion on these correlations. Further studies are necessary to elucidate whether this coexpression play a significant role in cognitive impairment. This study was made in cooperation with Maria Hejnold, chair of Pathomorphology Department and Professor Dariusz Adamek, chair of Neuropathology Department of Jagiellonian University Medical College.

77

### ***IL7RA and VDR gene polymorphisms in relation to progression rate of multiple sclerosis***

**D. Čierny (1), J. Michalik (2), D. Dobrota (1), J. Lehotský (1)**

(1) Department of Medical Biochemistry, Jessenius Faculty of Medicine, Comenius University, Slovakia  
(2) Department of Neurology, University Hospital in Martin, Slovakia

Multiple sclerosis (MS) is demyelinating autoimmune inflammatory disease of central nervous system. In susceptibility to MS, role of single nucleotide polymorphisms (SNPs) in vitamin D receptor (VDR) gene (rs7975232-Apal, rs10735810-FokI, rs731236-Taql) and interleukin-7 receptor  $\alpha$  (IL7RA) gene (rs6897932) has been confirmed in many studies. In our study, we wanted to determine whether allele variants of these SNPs can influence disease progression rate. According to the values of EDSS score and duration of MS, we chose patients with very rapid (n=18) and very slow disease progression (n=21). DNA samples were extracted from peripheral blood leucocytes, genotyped by PCR and restriction analysis technique. Allele frequencies were compared to 55 healthy individuals. In rapidly progressing group, we observed significantly higher frequencies of allele f of FokI SNP (OR=2.48, .95CI=1.14–5.35, p=0.016, compared to control group) as well as allele a of Apal SNP (OR=2.5, .95CI=0.99–6.26, p=0.04, compared to slow progressing group) in VDR gene. We found no association of SNP Taql of VDR and SNP rs6897932 of IL7RA with character of MS progression. Our results provide evidence that allele a of Apal and allele f of FokI VDR gene polymorphism are significantly associated with more rapid progression of MS.

78

### ***A new approach in the study of endothelial cells functionality in vitro***

**Luisa Georgiana Băcă (1,3), Cholsoon Jang (1,2), Zoltan Arany (1,2)**

(1) Cardiovascular Research Institute, Beth Israel Deaconesses Medical Center, Boston, MA, USA  
(2) Harvard Medical School, Boston, MA, USA  
(3) "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

Numerous neurological pathologies as well as metabolic diseases are linked to defects in transport of various bioactive small molecules including neurotransmitters and metabolites from the vascular lumen to interstitial tissues such as the brain and heart. We aimed to establish primary isolated endothelial cells(EC) as an in vitro model to study transendothelial transport of cellular substrates. Until now, the rat brain endothelial cells (RBEC) have been prevalently used because they have inherently superior tight

junctions known as the blood brain barrier (BBB). Here we employed a puromycin-based RBEC purification protocol and obtained almost pure primary RBECs. After 7 days from plating, RBECs were passaged and tested for EC-specific markers. In qPCR analysis, Pdgf-beta, Angiopoietin-2, Flt1, and Idr1 levels were much higher in RBEC compared to rat cardiomyocytes. Expression of tight junction proteins such as Occludin-1 was also confirmed in RBEC by immunostaining. Compared to human umbilical vein endothelial cells, the isolated RBECs present many advantages including tight intercellular association and high Trans Endothelial Electric Resistance, allowing a better analysis of transendothelial transport of substrates such as fatty acids without pericellular leakage. Further data show that this protocol can be used to study the blood-brain barrier function as well as metabolite transport across the endothelium, specially with high impact in fatty acid transport studies.

79

***Electrical stimulation of the medial septal nucleus increases cytotoxic activity of NK cells in the peripheral blood of rats with different models of behavior***

**Alena Mankevich**, Karolina Plucińska, Magdalena Podlacha, Wojciech Glac, Beata Grembecka, Magdalena Listowska, Izabela Michalska, Kacper Ptaszek, Dorota Myślińska

Department of Animal and Human Physiology, University of Gdańsk, Poland

The medial septal nucleus (MS) is a forebrain limbic structure playing a modulatory role in behavioral and autonomic activities. A lot of studies approve the neural connections of MS with neural regulating centers and immunomodulatory areas. The electrolytic lesion of the MS can cause depression of the peripheral blood natural killer cell cytotoxicity (NKCC) and the number of leukocytes. Previously, in the respective sham operated group the mere insertion of electrodes into the MS evoked enhancement of NKCC. To check this effect in the present study, we evaluated both spleen and blood NKCC and large granular lymphocytes (LGL) number after chronic electrical stimulation of the MS of rats divided into groups according to locomotor reactivity: LR (low) and HR (high) locomotor response in new environment. The chronic stimulation caused augmentation of blood NKCC in comparison to the sham group which was more significant in HRs. No such effect was found in the spleen. The obtained results suggest that immunoenhancing effect on blood NK cell function is dependent on the behavioral outcome of the MS stimulation as well as on individual behavioral characteristics. (This work was supported by a research grant NN303819040 from the Ministry of Scientific Research and Information Technology).

80

***Morphometric changes in the anterior thalamus of the guinea pig during development***

**Witold Żakowski**, Maciej Równiak, Anna Robak

Department of Comparative Anatomy, Faculty of Biology and Biotechnology,  
University of Warmia and Mazury in Olsztyn, Poland

The aim of this study is to revealed morphometric alterations during development of the anterior thalamus (AT), which is a key component of significant circuit of the limbic system related to mnemonic processes. The study was performed on the embryonic (E40, E60) and postnatal (P0, P80) brains of the guinea pig. To evaluate morphometric parameters, i.e. volume of the AT, density and total number of neurons, two methods were used: Nissl staining and immunohistochemistry using NeuN as a pan-neuronal marker. The results demonstrate that since E40 to E60 two opposite processes take place in the AT, i.e. density of neurons decreases over three times, while the volume is three times larger. As a result, the total number of neurons in the AT decreases significantly. Since E60 to P80 the density of neurons is virtually invariable, whereas the volume continues to increase. In consequence, the total number of neurons in the AT increases, especially during postnatal period (P0-P80). In conclusion, the rapid morphometric changes between E40 and E60 may be expected due to apoptotic reorganization of

67

neuronal populations. Postnatal increase of the total number of neurons in the AT may be related to new environmental stimuli and learning processes.

81

***Activation of nucleus incertus neurons by orexin A suggests functional cooperation of two peptide systems***

**Marcin Siwiec** (1), A.L. Gundlach (2), A. Blasiak (1)

(1) Department of Neurophysiology and Chronobiology, Institute of Zoology,  
Jagiellonian University, Poland

(2) The Florey Institute of Neuroscience and Mental Health, The University of Melbourne,  
Victoria 3010, Australia

The nucleus incertus (NI) is a group of GABAergic neurons located at the floor of the fourth ventricle. It is the main source of relaxin-3, a newly discovered neuropeptide. Accumulating evidence suggests NI involvement in appetite control, modulation of arousal and stress responses, as well as regulation of hippocampal theta rhythm. Possible functions and neuroanatomical targets of the relaxin-3 system seem to overlap with those of orexins—well known neuropeptides expressed in the lateral and perifornical hypothalamus. Therefore, analysis of interactions between these two systems could shed light on their reciprocal dependence. In order to examine NI neurons' intrinsic properties as well as their responsiveness to orexins, we performed whole-cell patch clamp recordings from NI in rat brain slices. Furthermore, to investigate postsynaptic receptor mechanisms and calcium dependence of orexin A actions, recordings were made in the presence of tetrodotoxin and calcium channel blockers: nickel chloride and nifedipine. We found that orexin A depolarized NI neurons and that this effect was reduced when calcium channel blockers were present. These findings suggest interactions between LH/orexin and NI/relaxin-3 networks and that orexin activation of the NI might reinforce arousal, exploratory and/or other activities, in the context of stress responses and motivated behaviors.

82

***Results Of Spinal Cord Stimulation In Myelopathic Disorders Are Disappointing – Mechanism Based Hypothesis Illustrated By 3 Cases***

**Luuk Schreuder**, E. Kurt, J. Vranken, R. van Dongen

Radboud University Medical Center, Nijmegen, the Netherlands

Many forms of neuropathic pain can be treated with spinal cord stimulation (SCS). However, SCS has shown disappointing results in spinal cord pathology in the past. To date, the reason for this remains unclear; in this article, we aim to find an explanation for the disappointing results of SCS in patients with pain related to spinal cord pathology. In the present study, we describe three illustrative cases with chronic pain after different kinds of spinal cord injury and evaluate the lack of success of SCS with respect to their pathology. The three patients had no benefit following SCS, despite excellent coverage of the painful area by paresthesia in two of these patients. Based on what is known about the mechanism of pain suppression by SCS, we hypothesize about the possible explanation for the poor results in neuropathic pain following myelopathy. We consider the dorsal columns, the dorsal horns and the spinothalamic tracts as essential for spinal cord stimulation and hypothesize that testing of these tracts before applying this treatment may help in assessing its' potential success.

68

***Achromatopsia caused by damage to colour centre in the cerebral cortex after right hemisphere stroke***

**Julia Wyszomirska**

Health Center Mikołów Neurological Rehabilitation Ward, Poland

Cerebral achromatopsia is a rare type of colour-blindness. The syndrome is caused by cortical damage to a specific part of brain - the inferior surface of the temporal-occipital regions, in particular single region fusiform gyri called area V4. Patients are unable to see the world in colours. They often describe their views as switching to black and white on a colour TV. They see the world in dirty shades of grey and is ugly, sad, pale. This medical case report presents achromatopsia as the most severe symptom after right hemisphere stroke. The process of neuropsychological rehabilitation and the dynamic of symptoms regression seem to be even more interesting due to patient professional relationship with a colourful world. Until the stroke a distinguish of colours, their shades, saturation and noticing discrete differences in several characteristics was for the patient an easy task. As professional of construction industry he was familiar with many colour palettes, talked about colours in very sophisticated way. This was the reason for unique course of therapy consisted of colour perception training, an intellectual analysis of colour features and re-learning based on preserved images of colours.

***A patient with Parkinson's syndrome and probable dementia with Lewy bodies***

**Dorota Ciosmak, Agata Zelent-Witowska**

60 year-old man with Parkinson's syndrome diagnosed in 2010 was admitted to the hospital because of the cognitive-behavioral symptoms, visual illusions, time-orientation disorders, hallucinations, that have been occurring for 3 months and happened mostly at night. The medical history of the patient reveals muscle rest tremor of upper limbs (mainly right hand), bradykinesia, (little hand-writing and little steps), muscle stiffness. The patient has other characteristic symptoms like impulsiveness, active aggression, apraxia, problems with fluency while speaking, hypomimia, fear. The patient's wife admits that he has short-memory problems, has overdosed Parkinson's medications, suffers from stable coronary artery disease and has had right coronary artery angioplasty. The most probable diagnose is Parkinson's syndrome with dementia with Lewy bodies.