Fifth Conference of Lithuanian Neuroscience Association

PROGRAM AND ABSTRACTS

Organizer

Lithuanian Neuroscience Association

Sponsors

6 – 7 December, 2013
National Open Access Scholarly Communication and Information Center (MKIC), Saulėtekio avenue 5, Vilnius
## PROGRAM

6 December 2013

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PROPERTIES AND FUNCTIONS OF GLIAL CELLS

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Glial cells that make up a large part of the nervous system have properties quite different from those of nerve cells. They have higher resting potentials, are electrically coupled and do not give action potentials. Many of the essential functions they perform have been known for years. These include the formation of myelin, guidance for growth of pathways during development and regeneration, uptake of transmitters, and formation of the blood brain barrier. New findings suggest that they perform a key role in controlling the local blood flow in response to neuronal activity.
GENDER DIFFERENCES IN PHARMACOLOGICAL TREATMENT OF ALCOHOL USE DISORDERS (AUDS)

R. Agabio\textsuperscript{1,2}, A. Preti\textsuperscript{3,4}, G. L. Gessa\textsuperscript{1,5}, F. Franconi\textsuperscript{6}

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Excessive alcohol consumption is a major health problem associated with enormous social and individual costs. Worldwide, it constitutes the 8th and 3rd cause of preventable mortality and morbidity, respectively. In the US, lifetime prevalence of alcohol use disorders (AUDs) has been estimated to correspond to 30% of general population.

Several gender differences have been evidenced in prevalence of AUDs (AUDs are two times more prevalent in men than in women), in the pharmacokinetics of alcohol (after drinking equivalent amounts of alcohol, women achieve higher blood alcohol levels than men of similar body weight), in vulnerability to alcohol-related morbidity and mortality (women present a major vulnerability to alcohol-related morbidity, and have specific alcohol related problems such as breast cancers, and foetal alcohol syndrome), and in the entry into treatment for AUDs (women seek and receive treatment for AUDs less frequently than men).

However, as occurs in many other fields, women are underrepresented or absent in clinical trials conducted to evaluate the effectiveness and safety of medications to treat AUDs, and findings obtained mainly in men are translated to women. As a result, women receive medications that are less in line with the principles of evidence-based medicine compared to men.

Considering that in the July of 2013, WHO included gender as one of the priorities for medicine throughout Europe and the rest of the world. Evidence relating to the effectiveness and safety of medications to treat AUDs in women were reviewed with the aim of identifying the most appropriate agents for women affected by these disorders, taking into account the fact that in women effectiveness and safety of medications may vary during the different phases and physiological periods of life (pregnancy, breastfeeding or taking oral contraceptives).

This information may contribute towards improving the quality of treatment of women affected by AUDs and increasing the number of women requiring access to treatment. Nevertheless, it emphasizes the need for further clinical (and preclinical) research with a gender-focused approach.
EFFECT OF SEX AND PHASE OF MENSTRUAL CYCLE ON SUBJECTIVE, BEHAVIORAL AND PHYSIOLOGICAL MEASURES OF MENTAL WORKLOAD

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The long-lasting workload is related to mental fatigue which often is the reason for impaired performance, workplace errors etc. Some evidence suggests that fluctuation of progesterone during menstrual cycle can influence women ability to keep speed and attention during long-lasting and effort-requiring mental activity.

Mental rotation (MRT) is a sex-specific task often requiring more mental resources from women than from men. The present study was carried out to investigate effect of sex and phase of menstrual cycle (follicular/low progesterone vs luteal/high progesterone) on subjective, behavioral and physiological measures of mental workload.

31 women (15 in follicular and 16 in luteal phase of MC) and 18 men performed prolonged MRT (1600 trails, ~1.5 h duration). Visual analogue scales were used for subjective evaluation of fatigue and motivation. Performance on MRT was measured as accuracy and response time. Heart rate variability (from ECG) and ongoing EEG activity were used to evaluate physiological changes. Salivary levels of 17β-estradiol and progesterone were assessed by ELISA in women groups.

The results of our study show that: i) increase of subjectively evaluated mental fatigue and decrease of motivation are weaker in men group (Δ 19.8 %) as compared to women in follicular (Δ 26.7 %, p=0.1) and luteal (Δ 39.0%, p=0.03) phases; ii) accuracy on MRT was higher in men group as compared to both groups of women during all the task (all p<0.001); men were faster as compared to both groups of women, but women in luteal phase were slower than women in follicular phase (significant differences on the start and at the end of the task (p<0.05)); iii) the time variables of the heart rate variability (STD and RMSSD) tended to be lower in women during luteal phase as compared to women in follicular phase and men. Preliminary results of EEG power analysis suggest that over the course of the task power in delta (1-4 Hz), theta (4-8 Hz) and alpha (8-12 Hz) bands was lower in men as compared to women, with the highest values in women obtained during the luteal phase of their menstrual cycle.
SEX DIFFERENCES IN THE RESPONSE TO AFFECTIVE STIMULI

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Since the number of patients with mental disorders in which the alteration of any emotional aspect is a common characteristic has grown lately, the interest in the neuroscience of emotions has also increased. To treat these mental illnesses, it is necessary to identify the way emotion is processed in the human brain. However, the majority of investigations have often neglected to take a factor of gender into account. Men and women are often mixed or studied separately, leaving aside the fact that they seem to process emotions and react to them differently.

The current study aimed at investigating the influence of gender on the evaluation of affective pictures and on electrophysiological responses. Event-related potentials were recorded while twenty-four participants (10 men, 14 women, Mage=23±2.7) viewed 90 pictures from International Affective Picture System. The Self-Assessment Manikin (SAM) was used to rate the affective dimensions of valence and arousal. EEG was recorded from 64 electrodes, but only Pz electrode was chosen for specific analyses.

The results showed that mean amplitudes of the early component N1 in a time window of 80 to 200 ms after stimulus onset and the late positive potential (LPP) in a window lasting from 440 to 660 ms after stimulus onset differ between genders. Examination of broad categories (i.e., pleasant, neutral, unpleasant) revealed that: (1) women rate pleasant visual stimuli relatively higher than men; (2) emotional images elicit the larger N1 mean amplitude in men than in women; (3) the mean LPP amplitude is larger in men than in women when viewing both emotional and neutral images.
SEX DIFFERENCES IN EYE MOVEMENTS

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Over the past decades scientific studies have revealed a number of sex differences in the human brain. Difference of cognitive abilities in men and women also attracts attention of the researchers. All this leads to the assumption that eye movements should reflect difference between genders. The scientists’ challenge is to investigate what sex differences here are undeniable, what is their origin – biological, social or environmental, how they emerge and vanish in the life span, etc. Yet there is not more or less thorough summing-up on this matter.

Eye movements with regard to gender have been explored in several aspects. Firstly, it is interesting what difference is in pure eye movements’ pattern. The other aspect is closely related to sexual, social and cultural different behavior. Particular interest is devoted to investigation of difference in observation of sexual cues. Much research has been done for different face perception, visual scene observation and other visual perception tasks. Exploration of sex differences in various cognitive tasks also involves eye movements recording, thus reflecting both individual and sex differences. On the other hand, inconsistent declarations on sex differences in eye movements still exist. All mentioned aspects and questions require some arrangement and clearing out.
PROPRIOCEPTION AND SOMATOSENSORY PROCESSING IN SCHIZOPHRENIA

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After a brief recapitulation of brain physiology related to somatosensory stimulus processing, referring to the newest imaging and EEG data, focus is on bodily perception and the dual nature of the somatosensory sense, by which it contrasts to the external visual and auditory senses. Proprioception is deeply entangled with movement execution. Considering this, stimulus design for this type of research is technically challenging, and different examples are presented. Behavioural data on experimental distortion of somatosensory perception and examples of parietal lobe damage show that we can modulate higher somatosensory processing.

In psychiatry several types of symptoms point towards pathology of somatosensory processing. Sensory over-responsivity and tactile hyper-sensitivity is seen across a range of childhood mental disorders, while pain insensitivity and catatonia is seen in schizophrenia. Somatosensory processing has been researched in schizophrenia with nearly consistent findings of lower activity in left somatosensory cortices. Recent findings of aberrance in proprioceptive information processing in schizophrenia support the information processing theories of aberrance in collateral discharge (Frith) and lack of effect of regularity (Hemsley). This type of somatosensory processing aberrance is also meaningful, when schizophrenia is understood as a disorder of self-awareness at a pre-conceptual level. The first data to support this relationship between self-disorders and proprioceptive evoked oscillations are presented.

Further studies in this field are necessary to increase our understanding of the complexities of bodily stimulation and pathological experience.
NEUROTOXIC EFFECTS OF IMMUNE COMPLEXES OF ANTIBODIES WITH OLIGOMERIC ANTIGENS

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S. Jankeviciute¹, P. Cizas¹, R. Morkuniene¹

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Recent evidence suggests that neuroinflammation, a complex biological response of the brain to injury, is involved in pathogenesis of various neurodegenerative diseases, including Alzheimer’s disease and virus-related pathologies. Neuroinflammation is characterized by recruitment and activation of brain immune cells – microglia, however, the mechanisms of activation as well as mechanisms of microglia-mediated neuronal loss is not entirely understood. In our study, we investigated whether immune complexes formed by antibodies against beta amyloid peptides or various viral proteins (hamster polyomavirus major capsid protein, human metapneumovirus nucleocapsid protein and measles virus nucleocapsid protein), are capable to induce microglial activation and neuronal death.

We present data showing that immune complexes formed by antibodies with their specific multimeric antigens stimulate microglial proliferation, production of pro-inflammatory cytokines and induce neuronal death and loss in mixed neuronal-glial cerebellar granule cell (CGC) cultures. These effects were found to be related to activation of microglial Fc-receptors as truncated antibodies, lacking Fc-domains, were unable to induce microglial activation and neuronal death. In contrast, immune complexes formed by monomeric antibodies-antigens did not cause any inflammatory response or neuronal death in CGC cultures.

Our findings suggest that oligomeric/multimeric structure of antigens in immune complexes is crucial in causing neuronal death in vitro by the mechanism involving Fc-receptor-mediated activation of microglia. Such mechanism can be also involved in neuroinflammatory responses caused by viral infections especially when brain – blood barrier is disrupted leading to penetration of antibodies into brains.
THE PROTECTIVE EFFECT OF NO AGAINST ISCHEMIA INDUCED INJURY TO BRAIN MITOCHONDRIA

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In this study we sought to determine, whether preconditioning of the brain with nitric oxide (NO) donor can protect against ischemia-induced damages to mitochondria.

NO donor (NOC-18) was infused to vena cava and after that followed 90 min. ischemia. Isolated total brain mitochondrial fraction used for mitochondrial respiration rate and calcium retention capacity (CRC) measurements. For evaluation of necrosis was measured released of lactate dehydrogenase (LDH) in medium during ischemia. To test whether protective effect is via activated protein kinase G (PKG) and protein kinase C (PKC) were used inhibitors KT 5823 and Ro 32-0432.

Mitochondria sensitivity to Ca after 90 min. ischemia increased by 44 %, comparing with control mitochondria, pre-treatment with NOC-18 increased mitochondria CRC practically till the control level. Protective effect of NOC-18 on brain mitochondria CRC which is indicator of permeability transition pore (PTP) opening was abolished by PKG and PKC inhibitors. Ischemia reduced mitochondrial respiration rate, the negative effect of ischemia to brain mitochondria was due to inhibition of complex I activity but not to loss of cytochrome c. NOC-18 had no beneficial effect to mitochondrial respiration rate. Pre-treatment brain with NOC-18 ischemia induced release LDH was abolished by 33% comparing to ischemia. PKG and PKC inhibitors applied together with NOC-18 abolished NOC-18 protective, this indicating that PKG and PKC mediate the protective action of NO donor against necrosis.

These findings suggest that NO increases mitochondria CRC and protects brain mitochondria from ischemia induced mitochondrial PTP and necrotic cell death in PKG and PKC depending manner.
THE USE OF P300 POTENTIAL AS A TREATMENT EFFICACY MARKER IN TRANSCRANIAL MAGNETIC STIMULATION THERAPY

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Transcranial magnetic stimulation (TMS) is an electrophysiological method of treating drug resistant psychiatric disorders. Today it is mainly used for the depressive disorder therapy. Although generally effective and surpassing the placebo effect, TMS sometimes fails to induce a sufficient clinical effect for some patients. For the better understanding of therapeutic TMS mechanism and better evaluation of TMS course efficacy, various electrophysiological markers, correlating with the clinical outcome, have been searched for.

In our study we measured the cognitive evoked potential P300 before and after TMS therapy and it's relationship with the clinical test scores. 82 patients with recurrent depressive disorder or schizoaffective depressive disorder participated in the study. They received high or low frequency TMS over the left or right prefrontal dorsolateral cortex using standard or neuronavigated coil placement.

Generally TMS tended to decrease P300 latency (-3.74 ms, p=0.021) and amplitude (-0.81 mV, p= 0.018). We found statistically significant (p<0.01) correlations between MADRS test score and P300 latency decrease (r=0.351) as well as HAM-D score and P300 latency decrease (r=0.302). Although being more clinically effective, neuronavigated TMS resulted in smaller changes to the P300 potential. This suggests that although some P300 potential characteristics are related to the positive clinical outcome, they cannot be used solely as a universal quantitative marker for TMS efficacy.
COMPUTATIONAL MODELING OF ASTROCYTE-NEURON INTERACTIONS IN THE BRAIN

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Modeling the structure and function of neuronal cells, and the networks they form, is becoming increasingly important in understanding how the brain works. Despite the growing awareness of the importance of astrocytes in the brain, the exact molecular and cellular level mechanisms underlying astrocyte-neuron communication, and the consequences of these interactions on local network level dynamics, still remain largely unclear. In this talk, I review the principal astrocyte functions and the interactions between neurons and astrocytes. I then address how the experimentally observed functions have been addressed in computational models for astrocyte-neuron interactions. The interactions are further illustrated by examples of some neurological and neurodegenerative diseases, where the miscommunication between glia and neurons is found to be important. Computational models facilitate the analysis of neural system responses to various stimuli and conditions that are otherwise difficult to obtain experimentally, in particular the responses at the subcellular level. Computational models can also help comparing the healthy and unhealthy functioning of cells and networks of cells in the brain.
Understanding how neural circuits work requires detailed knowledge of the connectivity patterns between different circuit elements, and ultimately the complete wiring diagram. To obtain such information, a number of strategies are currently being developed for the automated acquisition of three-dimensional image data of neural tissue at ultrastructural resolution. Serial sectioning combining a focused ion beam and a scanning electron microscope (FIBSEM; Knott et al., 2008), is a particularly promising strategy for achieving high spatial resolution in all three dimensions, which is essential to facilitate the automated tracing of dendrites, axons and glial processes in the neuropil as well as the identification of synapses. We have developed new approaches for extending the volume of tissue that can be imaged using FIBSEM, and are using this approach to study the connectivity motifs of interneurons and Purkinje cells in the molecular layer of the cerebellar cortex.
ADDITIONAL MÜLLER-LYER WINGS IN THE BRENTANO ILLUSION

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A number of experiments with the illusory figures of the Müller-Lyer type have demonstrated that misperception of length can be explained by wrong judgments of stimulus parts localization which occur due to neural processes of spatial integration in the visual system. The integration causes the weighted pooling of positional signals which are utilized by higher-level brain mechanisms to compute perceptual decisions; as a result, the visual objects are perceived to be located at their centroids.

Recently, we have developed a quantitative model which was successfully applied to account for the data obtained in experiments with illusory figures comprising different contextual flanks. It was demonstrated in experiments with the Brentano stimuli made of separate dots that the model accurately predicted illusion magnitude alterations caused by manipulations with extraneous non-target dots positioned in proximity of stimulus terminators. However, issue concerning the influence of manipulations with additional non-target elements for the Brentano figures composed of line segments still remains unclear.

In order to check the model and verify whether the manipulations with additional Müller-Lyer wings affect the judgments of length for the basic Brentano figure, the present psychophysical study was performed. In two series of experiments, either the length or internal angle of additional wings was varied.

It was demonstrated that the model calculations accurately predict illusion magnitude changes caused by manipulations with additional non-target stimulus elements. Such a result convincingly supports the suggestion on the perceptual positional shifts of stimulus terminators to be a cause of the illusion investigated.
There are a lot of still unresolved questions about visual system’s mechanisms dedicated to processing of 2-D image pairs. These 2-D image pairs are projections of the visual scene onto the retinas of the left and right eyes. It is not clear how binocular system assigns local features (disparity, direction, colour) to a local object through processing of two different projections. Current models of stereo vision try to explain coding of either disparity or visual direction making no associations with the colour coding.

We present a vector model of the feature coding system that characterizes position and colour of local object in visual space. Using the proposed model following features and explanations were derived: a) coding mechanisms of spatial coordinates (depth and direction) could be the same; b) model can quantitatively describe perceived depth and direction as a function of disparity and parallax, Panum’s fusional area, diplopia and the exponential decrease of depth sensitivity while object moves away from horopter; c) there are essential similarities between mechanisms that are involved in coding of colour and position.
Responses of neurons in visual cortex not only depend on sensory input but are also profoundly modulated by behavioral context. In primary visual cortex (V1) of the mouse, one such modulatory influence is locomotion, which has been shown to enhance spontaneous and stimulus-driven single-unit activity in supragranular layers (Niell & Stryker, 2010; Keller et al., 2012; Ayaz et al., 2013; Polack et al., 2013; Bennett et al., 2013).

We first asked whether this locomotion-related enhancement of neural responses could arise, at least partly, from changes in earlier stages of visual processing. We found that more eye movements occurred during locomotion relative to stationary periods, and that pupil size increased with locomotion speed. Consistent with these peripheral effects of locomotion, we observed response enhancement during locomotion at the level of the lateral geniculate nucleus.

Given the effects of locomotion on the input to V1, we next compared locomotion-based modulations across all layers of area V1. We found that around movement onset, the overall population activity increased in granular and supragranular layers. In infragranular layers, overall population activity was unaffected by locomotion. Together, this points to an important cortical contribution to locomotion-based response modulations.

Beyond this response enhancement, we then investigated how locomotion shapes the concerted activity of local V1 populations. We found that in supragranular and granular layers, locomotion decreased average noise correlations and broadened their distribution. We hypothesized that this locomotion-based broadening of the distribution of correlation coefficients in the V1 population arises from the modulation of V1 spiking by the LFP theta rhythm (~7-10 Hz), whose prevalence, power and frequency increased with locomotion. These oscillations modulated the spike timing of ~40% of the recorded V1 population, and they substantially impacted the structure of noise correlations: theta-modulated pairs showed a locomotion-related broadening of the distribution of noise correlations, while the distribution for non-theta-modulated pairs remained largely unaffected.

We conclude that locomotion has prominent effects on both single-unit and population activity along the early visual pathway. The observed increase of neuronal activity, decrease of noise correlations and enhancement of rhythmic synchronization are core features of active brain state in rodents and share similarities with effects of attention reported in the primate.

[Collaborative work with Sinem Erisken, Agne Vaiceliunaite, Heiko Schütt, Steffen Katzner, Anton Sirot]
THE INFLUENCE OF INCREASED MEMBRANE CONDUCTANCE ON THE EXCITABILITY OF SPINAL MOTONEURONS

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The pattern of action potential generation in spinal motoneurons depends on synaptic input and intrinsic response properties. Synaptic activity of premotor neural network not only directly excites and inhibits motoneurons, but it may also modulate intrinsic properties. During functional spinal neural network activity motoneurons receive massive balanced synaptic excitation and inhibition, and their membrane conductance increases significantly. This can substantially alter response properties of motoneurons.

It is straightforward to expect that increased conductance will increase the rheobase and decrease firing frequency of the neuron when it is stimulated with depolarizing current pulse. However, it is not trivial to predict how increased membrane conductance will influence the frequency-current relationship and the threshold for action potential generation.

In the present study we investigated this issue by using intracellular recordings from adult turtle motoneurons in spinal cord slices. Membrane conductance of spinal motoneurons was increased pharmacologically by extracellular application of GABA_A receptor agonist muscimol.

Our findings suggest that membrane conductance increased up to 50 % does not influence the threshold for action potential generation and causes a subtractive rather than a divisive effect on the frequency-current relationship of motoneurons.
ELECTROPHYSIOLOGICAL CORRELATES OF VERBAL STIMULI ANALYSIS DURING THEIR MONOCULAR PERCEPTION THROUGH DOMINANT AND NON-DOMINANT EYE IN EMOTIONAL STROOP-TEST

M. Rassomagina, V. Kravchenko, M. Makarchuk

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Emotional Stroop-test was used in an electroencephalographic study to assess pattern of brain activity using monocular perception of emotional verbal stimulus in situations when the semantic meaning of the word is nonrelevant in 30 right-handed and 30 left-handed volunteers (university students at the age of 18-21). 4 equal groups of participants: with right leading eye – 1) left open eye (right was covered with special bandage), - 2) right open eye; with left leading eye – 3) left open eye, - 4) right open eye, were asked to name the color of letters (red/green), when the word was presented in center while ignoring the semantic meaning of the words. All groups performed first task with mixed neutral and emotional words (TE) and second one with meaningless “words” (TP). We compared the spectral power (SP) of theta-, alpha-, beta- ranges during task performance and resting. Increased SP in beta-band in right handed persons was observed during TE, in left handed ones growth in SP of beta-band was accomplished with rise of SP of tetha-band in the case of dominant eye perception The disappearance of difference in latency of response between left and right hand when neutral information is perceived through leading eye was shown. It was found that there is no difference in brain wave dynamics during tasks with real words and meaningless words in the case of dominant eye monocular stimulation. Increased SP in theta-band in task which contains emotional connotation in case of non-dominant eye perception was revealed. Disappearance of difference in latency of response between left and right hand when emotional information is perceived through non-dominant eye was shown.

We concluded that irrelevant emotional information in this task can cause emotional tension in subject while exposing to non-dominant eye. Obtained data indicate the specificity of emotional information processing that depends on perception through leading and non-leading visual channel.
rTMS THERAPY EFFECT ON BRAIN RESPONSE TO FLICKERING LIGHT STIMULATION EVALUATED BY EEG

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A number of different repetitive transcranial magnetic stimulation (rTMS) protocols are recognized to have a positive effect on depression. The lack of rTMS side effects and simple procedure makes it better candidate for therapy than normally used electric convulsive therapy (ECT). Although treatment efficiency of rTMS today is smaller than ECT, exploration of neurophysiological changes caused by rTMS may lead to development of better rTMS therapy.

In our study 62 patients from Republican Vilnius Psychiatric Hospital were divided into two groups according to their treatment (1 or 10 Hz stimuli rTMS). We registered the electroencephalogram (EEG) responses to rhythmic (3, 6, 9, 12, 15 Hz) photic stimulation (RPS) before and after rTMS therapy. Power spectra was obtained with “Galileo NT” digital EEG system, statistics were calculated with “STATISTICA 8”.

We found that patients exhibited greater left than right alpha power in prefrontal cortex region during response to RPS. Study also showed that 1Hz rTMS tends to change alpha power asymmetry by increasing activity in left side prefrontal and temporal cortex while 10 Hz has no constant effect in these areas. Analysis of alpha power peak frequency variability failed to find difference between rTMS therapies, although trend of 1Hz rTMS therapy to increase the variability and the 10Hz rTMS to decrease it, was clearly visible. High and low frequency therapies were significantly different by their effects on beta1 and beta2 power change in response to the RPS (beta1, \(p = 0.002\) and beta2 \(p = 0.000; \alpha = .05\)). 1 Hz rTMS treatment was associated with increase of beta power, while 10 Hz rTMS - with decrease.

Our findings suggest that neurophysiological basis of 1 and 10 Hz rTMS effect is different. 1 Hz therapy may be acting on alpha power asymmetry while 10 Hz effect could be based on changes in beta activity.
Oxygen-glucose deprivation promotes the brain inflammation, glial activation and neurons death. Oxygen deprivation may contribute to the pathogenesis of Alzheimer’s disease. Data suggest that the neurons accumulate beta amyloid protein precursor (APP) after transient cerebral ischemia. It is known that beta amyloid (Aβ1–42) oligomers induce neuronal death, however unclear if oxygen deprivation, at the same time, induces a further damage. The aim of our study was to investigate whether factors such as inflammatory activation of glia and hypoxia can act synergistically with Aβ inducing neuronal cell death.

Our previous studies showed that small Aβ1–42 oligomers (dimers – pentamers) were directly toxic to neurons inducing rapid necrotic cell death over 24 h incubation at normoxic conditions. Large Aβ1–42 oligomers, fibrils and monomers did not directly affect viability of neurons in normoxic conditions. However, toxicity of large Aβ1–42 oligomers increased when CGC cultures were pre-treated with lipopolysaccharide to induce activation of glial cells. In this study we found that under hypoxic conditions large Aβ1–42 oligomers increased proliferation of microglia. In addition, neurotoxic effect of large Aβ1–42 oligomers as well as fibrils increased in hypoxic conditions. Our data suggest that small Aβ1–42 oligomers are directly toxic to neurons under normoxic conditions whereas larger aggregates can synergistically act together with inflammatory activated glia or hypoxia to induce neuronal death by the mechanism possibly involving activation of glia.

This result provide greater insight into the processes involved activation of microglia in oxygen deprivation conditions in pathogenesis of Alzheimer’s disease.
THE INFLUENCE OF CORTICAL FEEDBACK ON SIZE TUNING IN MOUSE LATERAL GENICULATE NUCLEUS

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One hallmark of neural responses in primary visual cortex (V1) is tuning for stimulus size. When the visual stimulus exceeds the boundaries of the classical receptive field (RF), responses decrease, an effect called surround suppression.

Surround suppression occurs not only in V1, but also in upstream structures, i.e. the retina and the dorso-lateral geniculate nucleus (dLGN) of the thalamus. In the dLGN, surround suppression might arise from feedforward, local inhibitory and feedback circuits, but their relative contribution is an open question. Here, we ask how surround suppression in mouse dLGN is modulated by cortical feedback circuits.

To measure size tuning in the dLGN, we presented gratings of different diameter at full contrast while recording extracellular activity with multicontact linear probes in awake head-fixed mice. To measure the influence of cortical activity on size tuning in the thalamus, we transiently silenced visual cortex by optogenetically stimulating parvalbumin–positive (PV+) inhibitory interneurons.

We find that numerous neurons in mouse dLGN exhibit surround suppression, and that we can alter this suppression by optogenetically silencing visual cortex. Activation of PV+ interneurons in V1 modulates size tuning in thalamus and majority of RFs center sizes expand, also loose they suppression strength. Moreover, we observed that V1 photostimulation suppresses responses to optimal visual stimuli in the dLGN whereas full size stimuli facilitate neural responses. We conclude that size tuning in dLGN is at least partly shaped by feedback mechanisms from visual cortex and this is similar to that of higher-order mammals (Webb et al, 2002; Jones et al., 2012).

THE ROLE OF MELATONIN IN THE INFLAMMATORY PROCESS

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Melatonin is a neurohormone that regulates many physiological circadian rhythms. It regulates and controls biological clock, stimulates the immune system and protects the central nervous system. Melatonin is secreted by the pineal gland in the brain. The production of melatonin occurs during the night in response to the darkness and is inhibited by the light. Neutrophils are the most abundant type of white blood cells in mammals. During the beginning (acute) phase of inflammation neutrophils are the first-responders of inflammatory cells to migrate towards the site of inflammation. Neutrophils migration is crucial for primary immune response.

The aim of our study was to investigate the effect of suppressed (caused by constant lighting) synthesis of melatonin on the migration of neutrophils into mouse peritoneal cavity. BALB/c mice were kept under normal light/dark conditions (LD) and under constant exposure to the light (LL). N-formyl-Met-Leu-Phe (fMCP) was injected into mouse peritoneum to induce migration of neutrophils. The mice were sacrificed 4 hours later and the numbers of neutrophils in peritoneal cavity were counted. The mice kept at LL had significantly more neutrophils in the peritoneal cavity than LD mice. This difference was observed during the dark time only. The amount of neutrophils in peritoneum of LD and LL mice did not differ during the light time. LD mice had more neutrophils in the peritoneum in the morning than in the night (when the concentration of melatonin is higher). The injection of MT2 antagonist 4P-PDOT three hours prior fMCP caused increased numbers of neutrophils in peritoneum. rtPCR results showed that melatonin MT2 receptors are expressed in neutrophils and endothelial cells.

Our results demonstrate that melatonin via MT2 receptor negatively regulates fMCP induced neutrophils migration to peritoneal cavity.
INFLUENCE OF STIMULUS DURATION ON THE RAT VISUAL CORTEX VISUALLY EVOKED POTENTIALS TO VISUAL STIMULUS ONSET AND OFFSET

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Luminance and duration are among the most important parameters of visual stimulus influencing response. It is known that increasing stimulus intensity causes shorter latency, faster rise time, higher amplitude and visual evoked potential (VEP) complexity. But visual evoked potentials are mostly investigated using light flash (up to 10 ms duration), whereas in natural conditions stimulus duration usually is longer.

Aim of our work was to investigate effect of stimulus duration on the latency and amplitude of visual evoked potentials to stimulus onset and offset.

18 rats were used in this study. Under general anesthesia with urethane one epidural electrode was implanted above rat visual cortex. Stimulation was performed by VisStim 1.0 and PsychoPy2 1.74.01 software. Stimulus intensity ranged from 16 lx to 221 lx, duration – from 50 ms to 500 ms. Two types of stimuli were used – light and darkness. Stimulus duration and intensity were changed pseudo – randomly so that stimuli of each intensity were presented at each duration for 100 times, in total 54 combinations. At the end of experiment animal was euthanized.

We analyzed amplitude and latency of the waves elicited by stimulus onset and offset.

The main findings:
1. Increasing stimulus duration:
   a) Increases latency of positive waves evoked by stimulus onset and reduces latency of negative waves evoked by stimulus offset.
   b) Increases amplitude of positive waves evoked by stimulus onset and negative waves evoked by stimulus offset.
2. Stimulation with short (50 and 100 ms) stimuli elicit only two waves (positive and negative), whereas stimulation with longer stimuli elicit four waves (positive and negative after onset and positive and negative after offset).
TEMPORAL DYNAMICS OF SUBJECTIVE, PERFORMANCE AND CARDIAC MEASURES DURING A SUSTAINED MENTAL ROTATION TASK

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Mental fatigue is a ubiquitous phenomenon and a common complaint in large population groups, but published research results in this field are controversial due to the multidimensional nature of the phenomenon. In the present study we investigated how the duration of a sustained cognitive task influences subjective, performance and physiological measures.

49 subjects (18 males and 31 females) performed 4 blocks of mental rotation task (1600 pairs of figures, ~1.5 h of duration in total). Accuracy (percent of correct responses) and mean response times (RT) were the main performance measures. Participants rated their subjective fatigue, task aversion, motivation and boredom by means of visual analogue scales 7 times during the experiment. Electrocardiogram was recorded during the whole experiment.

With increasing time-on-task, mean RT tended to decrease and accuracy to increase, demonstrating a vivid practice effect, especially at the beginning of the task. At the end of the task, RT measures seemed to approach a plato and accuracy measures began to decrease, showing a possible growing effect of fatigue.

Subjective measures demonstrated a fairly stable increase of subjective fatigue, task aversion and boredom and decrease of motivation during the task.

Heart rate (HR) decreased and heart rate variability (HRV) increased with time-on-task. However, low frequency (LF) component of HRV, usually associated with involvement of sympathetic ANS, tended to increase with time-on-task.

Our results demonstrate a dissociation of performance and subjective measures during a sustained cognitive task. Although subjective measures showed a fairly stable increase of subjective fatigue, performance accuracy increased and mean response times decreased during the task.
Multiple results from studies of the geometric illusions of the Müller-Lyer type support a suggestion that these perceptual distortions of length can be considered to be a consequence of mutual displacements of stimuli terminators. According to “centroid” hypothesis, the visual system is unable to determine the position of stimulus terminators independently from the adjacent contextual flanks, and the judgments of separation between the terminators are biased towards the distances between the centroids of the flanks. Recently, in order to account for the data obtained in experiments with different modifications of illusory figures, a quantitative model of centroid extraction has been developed.

The aim of the present work was to verify one of the crucial assumptions underlying the “centroid” approach in the modeling of illusions of extent, i.e., to check whether the magnitude of illusion for stimuli consisted of three clusters of terminator/flank may be considered as the result of summation of contributions from each contextual distractor. We have performed a psychophysical study with three-spot stimuli supplemented by contextual vertical stripes. In three different series of experiments either one stripe (left, central, or right), pairs of stripes (left-central, right-central, or left-right), or three stripes were presented.

It was shown that the summation of the experimental data for stimuli with reduced number of contextual flanks is commensurate with the magnitude of the illusion derived from judgments of extent for full versions of the illusory figures. Thus, the results obtained are consistent with the “centroid” explanation of illusions of extent which implies algebraic summation of contributions from each contextual distractor.
PERCEIVED SHIFTS OF TERMINAL SPOTS IN THE OPPEL-KUNDT ILLUSORY PATTERN

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The Oppel-Kundt illusion is characterized by perceived distortions of extent: in the visual field, an interval filled with vertical stripes equally spaced is judged as longer than an empty interval of the same physical length. In our experiments, the perceived length distortions of the Oppel-Kundt type were studied. The positional shift of the stimulus terminals was measured. On the monitor screen, the Oppel-Kundt type horizontal stimuli formed of spots were viewed. Each stimulus comprised of three parts: an empty space in the middle and two filled intervals on the flanks, which length and number of filling spots could vary. At a certain distance below or above the stimulus, the separate test interval formed of two spots was shown. The subjects adjusted the test interval length to be equal to the perceived extent of the stimulus empty space. The errors of subjects’ measurements were considered as the illusion strength. The pilot experiments indicated that, for all subjects and all stimuli, the unfilled interval spaced between filled flanks appeared shorter than the test interval which had no flanks. It was also demonstrated that the illusion strength increased with increasing density of filling but did not vary significantly with varying of the filled flanks length. The data obtained support the suggestion that the perceptual positional shifts of the terminal spots into the unfilled stimulus part trigger the sensory illusion on extent of the Oppel-Kundt type.
SEMA3A AND NGF IN REGENERATION OF SENSORY AXONS

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Regeneration of nervous system is complex and complicated process that involves neuron survival after injury as well as elongation of neurites and their guidance to final targets. Dorsal root ganglion (DRG) sensory neuron axon growth is highly impeded when they encounter neuronal growth cone-collapsing factor semaphorin3A (Sema3A) in both regeneration of adult nervous system and development of nervous system in embryonic stages. On the other hand, precise guidance of axon is mediated by many factors and increasing evidence shows that DRG axon development in both pathological and physiological conditions can be stimulated by nerve growth factor (NGF).

The aim of this study was to evaluate the potential of increased NGF concentration to abolish Sema3A induced inhibitory responses in regenerating fifteen days old mouse embryo (E15) DRG axons in vitro. Development and regeneration of DRG axons was evaluated in Neurobasal-based medium supplemented with different NGF concentrations (0; 1; 10; 50 and 100 ng/mL) that are close or higher than present in physiological conditions of mouse serum (8.6-10.1 ng/mL). Moreover, we have evaluated influence of constant presence of Sema3A (10 ng/mL) on NGF-dependent axon development. The interplay of these signaling molecules was evaluated at axon survival, elongation and growth cone guidance levels, by measuring axon outgrowth and evaluating axon number per DRG explant. The measurements were performed after 16 hours of explants incubation in the presence or absence of Sema3A at different NGF concentrations. Axon growth cone collapse rate was determined in the presence of NGF after 1 hour of Sema3A treatment following 23 hours growth in vitro.

We found that increase of NGF concentration increased survival of DRG neurons (axon number) independently of presence or absence of Sema3A. Moreover, increase of NGF concentration abolishes Sema3A-induced inhibitory effect on axon outgrowth while has no effect on Sema3A-induced collapse rate.

Overall our results support hypothesis that NGF has therapeutic properties in nervous system regeneration promoting axon growth while having only limited effect on impeding Sema3A-dependent guidance.
THE NEUROCHEMICAL PATTERN OF THE CARDIAC NERVE GANGLIONATED PLEXUS ON THE RABBIT HEART BASE

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The purpose of this study was to investigate the neurochemistry of the epicardiac ganglionated nerve plexus in the whole-mount preparations of the rabbit atria. The cardiac nerve structures were revealed by the immunofluorescence labeling for the general neuronal marker PGP 9.5, the choline acetyltransferase (ChAT), the tyrosine hydroxylase (TH) and the neuronal nitric oxide synthase (nNOS) in whole-mount atrial preparations derived from 15 young rabbits.

Somata of intrinsic cardiac neurons (ICNs) displayed the immunoreactivity for PGP 9.5, ChAT and nNOS. The majority of ICNs were immunoreactive for ChAT (52±11 %), the small population of the ICNs (19±16 %) exhibited the immunoreactivity for nNOS and 30±5 % of the ICNs were biphenotypic for ChAT and nNOS. The mean number of ChAT-IR neurons was statistically significantly higher than the mean number of both nNOS-IR and the biphenotypic neurons (P < 0.05). ChAT-IR neurons were surrounded by the baskets of ChAT-IR varicose nerve terminals. nNOS-IR nerve fibers did not form pericellular complexes with neurons. Singular varicose TH-IR nerve terminals were observed within ganglia. The extrinsic cardiac nerves entering the heart base were predominantly composed of the TH-IR nerve fibers that spread in the left atrium. The sparse ChAT-IR nerve fibers proceeded on the heart base. There was no nNOS-IR nerve fibers within nerve bundles.

We concluded that the rabbit cardiac ganglionated nerve plexus do not have TH-IR ICNs within ganglia and the mesh work of the extrinsic nNOS-IR nerve fibers. The immunochemical pattern of CGNP revealed in the present study will facilitate further investigations of the autonomic control of the rabbit heart.
Alzheimer disease (AD) is one of the most common dementia disorders in the elderly. According to the main hypothesis on AD, the deposition of Aβ oligomers in the brain plays the central role in disease pathology. One of the most promising treatments for AD is considered to be immunotherapy with Aβ antibodies. However, the toxic effects of the antibodies remain unclear. The aim of this study was to investigate effects of immune complexes of anti-Aβ1-42(#11E12)/Aβ1-42 on viability of neurons in mixed neuronal–glial cerebellar granule cell (CGC) cultures.

Our results show that after 24h incubation of cells with multimeric immune complexes the number of microglial cells significantly increased and the number of viable neurons was reduced in cultures while Aβ1-42 oligomers and anti-Aβ1-42 antibodies added separately were non-toxic to neurons. Similar result was obtained with complexes of #11E12 antibody and Aβ1-40 which were highly toxic and caused neuronal death. In contrast, Aβ1-40 added alone did not cause any significant neuronal death. All complexes of F(ab’)2 fragments of antibodies and their antigens had no effect on neuronal viability or glial proliferation. Furthermore, fragmented Aβ1-42 peptides (Aβ1-6, Aβ1-13) did not change the number of neurons in CGC culture and had no effect on number of microglia. In conclusion, our data show that 1) multimeric antibody–antigen complexes cause neuronal death in mixed neuronal–glial cultures, which is dependent on activation of Fc receptors in microglial cells; 2) oligomeric/multimeric structure of antigen is essential factor in neurotoxicity of antibody–antigen complexes.
NEUROIMUNOHISTOCHEMISTRY OF THE RABBIT CARDIAC CONDUCTIVE SYSTEM

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Rabbit is a widely used animal model in physiological studies of autonomic control of cardiac conduction system (CCS). However, the neural components of rabbit CCS is not fully determined using immunohistochemical techniques.

Aim of the study - to identify the dominating type of nerve fibers in rabbit CCS.

CCS components and neural structures were identified applying multiple immunohistochemical labeling of hyperpolarization activated cyclic nucleotide-gated potassium channel 4 (HCN4, marker of cardiac conductive myocytes), protein gene product 9.5 (PGP 9.5, general neural marker), choline acetyltransferase (ChAT, cholinergic marker), tyrosine hydroxylase (TH, adrenergic marker), substance P (SP, peptidergic or sensory marker), neuronal nitric oxide synthase (nNOS, nitrinergic marker) and in whole mounts and tissue sections of atria, interatrial and interventricular septa and around the orifice of atrioventricular valves.

SAN contained a dense meshwork of nerve fibers with predominance of CHAT (53.28±0.22 %) and TH (46.72±0.22 %) positive nerve fibers. The dominance of CHAT(+) nerve fibers were significantly higher over TH(+). SP and nNOS fibers were in minority. SAN area also contained a small quantity of (discrete or gathered in small clusters) CHAT(+), nNOS(+) and bi-phenotypic neurons. CHAT(+) and TH(+) nerve fibers were predominant in the atrioventricular node (AVN) as well. Around the orifice of both tricuspid and bicuspid valves a small number of the HCN4(+) cells was observed. These areas were densely innervated by CHAT(+), TH(+) and sparse SP(+), and nNOS(+) nerve fibers as well.

CCS in rabbit contains a dense pattern of nerve fibers with a clear predomination of cholinergic and adrenergic fibers. Small number of cholinergic, nitrinergic and bi-phenotypic neurons is present in the rabbit SAN area.
EFFECT OF N-STEAROYLETHANOLAMINE IN DIFFERENT DOSES ON BEHAVIOR OF RATS AFTER CHRONIC ALCOHOLIZATION IN “OPEN-FIELD”

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The aim of this study was to compare the behavioral changes in rats in the case of chronic alcoholism and usage of stearoylethanolamine (NSE).

In this investigation 96 white male rats (weight: 150-200 g) were tested, previously differed by their behavior in the “open field” test. The number of central and peripheral squares which was crossed (horizontal locomotor activity), lifting of the posterior paws (vertical locomotor activity), research activity, duration of grooming (emotional activity) were measured. The chronic alcoholic intoxication was made in 2 steps: 1) animals had the free choice between 15 % ethanol solution and the water during 14 days; 2) animals were receiving ethanol as the unique source of liquid during 1 month. NSE water solution was being delivered per os using plastic tube (5 mg/kg and 0.1 mg/kg) during 7 days. The substance was synthesized in the Department of Biochemistry of lipids. After the first test in “open field” all animals were divided into 6 groups: I – intact animals; II – animals that receive NSE (0.1 mg/kg); III – animals that receive NSE (5 mg/kg); IV – animals with the model of 30 days chronic alcohol intoxication; V - animals that during the last 7 days of forced alcoholization were receiving NSE (0.1 mg/kg); VI – animals that during the last 7 days of forced alcoholization were receiving NSE (5 mg/kg). After alcoholization and administration of NSE the “open field” test was made for the second time.

NSE in the dose of 0.1 mg/kg did not affect the behavior of rats in the open field; NSE in the dose of 5 mg/kg reduced locomotor activity and increased emotional activity. Application of NSE in both doses did not alter motivation to consume ethanol. NSE in the dose of 0.1 mg/kg in tandem with alcohol reduced locomotor activity and increased emotional activity of rats in the “open field” in different way comparing with usage of the same dose of NSE.
DISTINCTION BETWEEN PHYSICALLY POSSIBLE AND PHYSICALLY IMPOSSIBLE ACTIONS DISCLOSED BY SEM

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Mirror neuron system is known to be involved during imitation and observation of actions (Iacoboni et al 1999). Observation of grasping movement consistently implicates such brain areas as intraparietal sulcus (IPS) and dorsolateral prefrontal cortex (DL-PFC). When visual areas receive inputs from the retina, motion sensitive neurons through dorsal pathway send information to parietal and motor regions. IPS has visual control of grasping and manipulation of hand movements. While previous research clearly showed a sensitivity of the automatic imitation system to biological plausibility and attributed intentionality, the findings of (Liepelt and Brass, 2010) show its insensitivity to physical plausibility. We hypothesize that observation of actions is mediated by the mirror neuron system differently according to physical plausibility of the movement.

We performed an fMRI experiment with 2 blocks of short videos. During one block 20 participants were observing a hand of avatar that is grasping various objects; during another the hand was performing a grasping movement with the same objects just in physically impossible manner.

In our study we looked at brain regions that are part of mirror neuron system and causal relationships between them using structural equation modeling (SEM).

We found that during observation of an impossible movement there is strong connection between IPS to DL-PFC. That was not found for possible movement. This strong involvement of the frontal areas talks about integration of sensory information, movement selection in a presence of conflict and about organizing movement sequence in order to reproduce it. We conclude that part of mirror neuron system that was investigated mediates not intentions but physical plausibility (kinematics) of the movement.
DIFFERENCES OF FRONTAL LOBE HEMISPHERIC ACTIVATION DURING THE WISCONSIN CARD SORTING TEST: A fNIRS STUDY

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Functional Near-Infrared Spectroscopy (fNIRS) is an optical brain spectroscopy and imaging method using near infrared light to measure changes of chromophore concentration during task performance. Brain activity, with following hemodynamic response (HR), is associated with a number of different processes in human brain and some of them can be assessed using optical techniques.

The aim of this work is to acquire and compare hemodynamic responses from two different devices in order to support or refute hypothesis of activation differences in frontal lobe hemispheres during cognitive task performing.

Possibility of hemispheric activation differences during cognitive task performance has been mentioned by authors who represent their results collected from fMRI and PET studies with healthy volunteer subjects.

Non-commercial fNIRS continuous wave device with 2 channels was designed and used for previous frontal lobe studies in Department of Neurobiology and Biophysics. The pilot experiments were performed with a validated and tested in clinical studies Wisconsin Card Sorting Test (WCST), which significantly activates the frontal lobe during all performance duration. Furthermore, WCST is also used to diagnose frontal lobe disorders. To validate data obtained from our prototpe device, WCST were performed with commercial continuous wave 16 channels forehead sensor from Biopac, fNIR400.

The results collected from both fNIRS devices are comparable and show that small differences in activation of both hemispheres during cognitive task may exist in healthy humans.