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PROGRAMME

09:15–09:30	Welcome by O. Rukšėnas, President of LNA
09:30–10.15	**Ewelina Knapska.** OF MICE AND MEN. UNDERSTANDING SOCIAL LEARNING (Nencki Institute of Experimental Biology, Poland)
10:15–10:45	**Birgit Derntl.** EMOTIONAL HORMONES: HOW SEX HORMONES AFFECT WOMEN'S BRAIN AND BEHAVIOR (University of Tübingen, Germany)
10:45–11:15	**Andero Uusberg.** COGNITIVE MECHANISMS OF EMOTIONAL REAPPRAISAL (University of Tartu, Estonia)
11:15–11:45	**Rasa Mončiunskaitė.** DOES THE CONTRACEPTIVE PILL ALTER FEMALE AFFECTIVE PROCESSING? (Vilnius University, Lithuania)
11:45–13:00	Lunch / Posters
13:00–13:45	**Frances de Blasio.** EEG-ERP BRAIN DYNAMICS IN THE EQUIPROBABLE AUDITORY GO/NOGO TASK (University of Wollongong, Australia)
13:45–14:15	**Thomas Koenig.** BRAIN FUNCTIONAL MICROSTATES: CURRENT UNDERSTANDING AND FUTURE PERSPECTIVES (Translational Research Center, University Hospital of Psychiatry, University of Bern, Switzerland)
14:15–14:45	**Roma Šiugždaitė.** TRANSDIAGNOSTIC BRAIN MAPPING IN DEVELOPMENTAL DISORDERS (University of Cambridge, United Kingdom)
14:45–15:15	**Guy C. Brown.** HOW THE BRAIN EATS ITSELF: MICROGLIAL PHAGOCYTOSIS OF LIVE NEURONS (University of Cambridge, United Kingdom)
15:15–16:00	Break / Posters / LNA annual meeting
16:00–16:30	**Kaiser Karim.** CONSISTENT AND SCALABLE HUMAN IPSC-DERIVED CELLS FOR IN VITRO CNS DISEASE MODELLING AND DRUG DISCOVERY (Bit.bio)
16:30–17:00	**Jay Gopalakrishnan.** HUMAN BRAIN ORGANOIDS: FROM DEVELOPMENT TO DISEASE MODELING OF COVID-19 (University of Dusseldorf, Germany)
17:00–17:30	**Dieter Henrik Heiland.** HUMAN TISSUE MODELING FOR SPATIOTEMPORAL INVESTIGATION OF BRAIN TUMOR DEVELOPMENT (University of Freiburg, Germany)
17:30–18:00	**Anton Bespalov.** DRUG DISCOVERY TODAY: HOW TO BET ON THE RIGHT HORSE? (PAASP, Germany)
18:00–18:20	Concluding remarks, discussion, awards

ORAL PRESENTATIONS

POSTER PRESENTATIONS

POSTER PRESENTATIONS

POSTER PRESENTATIONS

POSTER PRESENTATIONS

ORAL
PRESENTATIONS

OF MICE AND MEN. UNDERSTANDING SOCIAL LEARNING

E. Knapska

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Social learning, i.e., learning the value of stimuli and actions from others, is adaptive and often crucial for survival by helping an individual to avoid harm and maximize rewards. How social learning is implemented in the brain is unclear, though. Do we have neural circuits dedicated to social interactions? Or do we repurpose the domain-general neural circuits? In order to learn, social animals, including humans, have to interact with others. Disentangling complex social interactions into the prime factors, i.e., social motivation and social information processing allows for dissecting the underlying neural circuits. We focused on the neural circuits in the central amygdala (CeA), a region critically involved in generating motivated behaviors and orchestrating emotional responses. We have identified the neural circuitry in the CeA along with their cortical projections, which strongly modulate social motivation, showing that social reward partially shares domain-general circuits and partially involves social-specific pathways. Further, we studied processing of emotions perceived socially. We have discovered that animals respond differently to social cues about imminent vs. remote threat. We found that they are able to select appropriate defensive strategies in a novel environment depending on emotional cues from a conspecific, showing that animals efficiently process social information and are able to decipher important information analysing basic socio-emotional cues. We identified different neural circuits for processing of socially perceived imminent vs. remote threat and showed that social information about threat is partially processed through the same systems as non-social information. In line, human fMRI studies have demonstrated that socially perceived threat involves a set of brain regions analogous with those described in rodents, supporting the idea that the basic neural mechanisms for processing of social information are conserved across species. Further, to study social learning in more naturalistic conditions, in which animals are embedded in the complex social structures and often interact nonrandomly with group members, we have developed the Eco-HAB system. The Eco-HAB is an automated system for tracing social behaviors and learning of mice living in a group under semi-naturalistic conditions, which allows for measuring voluntary behaviors. Using the Eco-HAB, we show profound effects of social information about reward on behavior of animals in both familiar and novel environment. Mice effectively learn from olfactory social cues and use that information to localize the reward. Importantly, the animals display individual variability in social interactions, which seems to be important for information spreading. Thus, tracking individual differences in social interactions and learning within the social networks is crucial to understand the mechanisms underlying healthy and impaired social functioning.

EMOTIONAL HORMONES: HOW SEX HORMONES AFFECT WOMEN'S BRAIN AND BEHAVIOR

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Women undergo a sequence of different hormonal transitions during their reproductive years. These hormonal fluctuations provide specific neuroendocrine conditions that modulate brain structure and function across a woman's lifespan. The trophic effects of gonadal hormones emerge early in brain development and remain relevant throughout adolescence and adulthood. Besides an extensive reorganization of the brain during puberty, neural alterations have also been observed in response to even subtle changes in endogenous or exogenous sex hormone levels later in life. Many of these actions occur in brain regions crucial for a variety of cognitive and emotional behaviors. Consequently, hormonal transition periods and even subtler fluctuations during the menstrual cycle or hormonal contraception may predispose women to mental disorders which will be discussed in the talk.

COGNITIVE MECHANISMS OF EMOTIONAL REAPPRAISAL

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Reappraisal, or changing how one thinks about an emotional situation, is an effective strategy for regulating unwanted emotions and other affective states. Existing reappraisal research has struggles with characterizing the cognitive mechanisms involved in a given instance of reappraisal. In this talk, I present a recently proposed framework that applies appraisal theory to resolve this problem. The framework distinguishes two kinds of reappraisal: reconstrual or changing the mental models that are activated to explain a situation; and repurposing or changing the goals that are activated to evaluate this situation. The framework goes on to characterize instances of reappraisal as a collection of shifts along appraisal dimensions. I illustrate these ideas with recent findings from self-report studies.

DOES THE CONTRACEPTIVE PILL ALTER FEMALE AFFECTIVE PROCESSING?

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Sex steroids are closely linked to women's emotional well-being. Mounting evidence from electrophysiological studies suggest that hormonal fluctuations during the menstrual cycle can modify emotional stimuli processing. However, it remains unclear how oral contraceptives (OC), being one of the most popular birth control methods globally, influence brain reactivity towards affective stimuli. The aim of the study was to evaluate the influence of OCs on female emotional processing in a cohort of healthy females of reproductive age. In attempt to determine OC effect on the brain, we chose electroencephalography (EEG) method due to high temporal resolution that allows for a precise discrimination of rapid affective-cognitive processes. Also, neural correlates related to affective processing (e.g. late positive potential, LPP) are well established. The subjects were 19-38 years old, 37 naturally cycling women and 33 antiandrogenic OC users. Women were instructed to passively watch color images ranging from neutral everyday objects and scenes − such as household furniture and landscapes − to rare or exciting scenes − such as mutilated bodies and erotic nudes. We conducted event-related potential (ERP) analysis to define the electrophysiological reactivity to visual emotional stimuli between the groups. The differences in ERPs between OC and NC women were most pronounced in parieto-occipital and centro-parietal areas. Lower ERP and lesser bioelectrical brain activity among OC users indicate diminished brain activity to all visual emotional stimuli. On average, LPP mean amplitude of OC women was lower than NC in all stimuli categories including neutral. Differences of mean LPP amplitudes between each emotional stimulus category and neutral images confirmed lowered OC women response to arousing images with significantly suppressed reaction to highly unpleasant stimuli. Taken together, the results suggest altered affective picture processing among OC users with significantly blunted brain activity to the highly unpleasant images. Based on these findings, we speculate that the usage of OC may have effect on female affective cognition, emotion, mood and general psychological well-being.

EEG-ERP BRAIN DYNAMICS IN THE EQUIPROBABLE AUDITORY GO/NOGO TASK

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Background and aim:

Electroencephalography (EEG) and event-related potentials (ERPs) remain prominent measures within the neurosciences, each having amassed significant volumes of research within their largely independent literatures. Substantive interrelations between the ongoing EEG activity and ERP component outcomes are now widely acknowledged, following the pioneering brain dynamics work of Başar beginning some four decades ago. While several technical and analytical obstacles have impeded our elucidation of the mechanisms underlying such EEG-ERP dynamics, identification of the robust pattern/s of these dynamics will further our understanding, and may offer biomarkers for use in detecting pathological deviation. The present study reviews a series of investigations aimed to identify such normative patterns and their consistency in healthy ageing.

Materials and methods:

EEG-ERP dynamics investigations in the equiprobable auditory Go/NoGo paradigm are reviewed in healthy young (M_{age} ~20 years) and older (M_{age} ~68 years) adults. This variant of the Go/NoGo provides an optimal signal-to-noise ratio for each of the conditions, and the proposed sensory and cognitive processes involved have been mapped for this task in a sequential processing schema.

Results:

Preferential occurrence of prestimulus brain states in the traditional delta band has been observed, and prestimulus delta amplitude contributions appear to show the most robust impact on the ERP component outcomes. Findings in the remaining EEG bands are more complex; assessment of the dynamic contributions of prestimulus theta and alpha brain states appears sensitive to the quantification methodology utilised, while prestimulus beta states show little consistent impact.

Conclusions:

Prestimulus delta brain states and their dynamic contributions to the processing outcomes in the equiprobable auditory Go/NoGo task appear to be optimal candidate markers of normative function. The increased availability and implementation of advanced quantification techniques and analytic methods add great promise for the future of brain dynamics research, and the pursuit of electrophysiological biomarkers of health and dysfunction.

BRAIN FUNCTIONAL MICRO STATES: CURRENT UNDERSTANDING AND FUTURE PERSPECTIVES

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The phenomenology of the spatial dynamics of resting state EEG can be described surprisingly well in terms of microstates; i.e. as a non-random and non-overlapping sequence of a few and transiently stable prototypical scalp field configurations. From a physical point of view, this observation can only be reasonably explained by the assumption that within a single microstate, the predominant part of the EEG sources oscillates either in phase or in antiphase to the other sources. According to Fries (2005) model of communication through coherence, such relatively slow in- and antiphase oscillations temporally align or misalign neuronal excitability and can therefore drastically alter the flow of information among brain regions. Thus, from a mechanistic point of view, the switching between microstates may represent a global, flexible and adaptive gating of communication between large-scale networks. As microstates may dynamically switch these relationships through the gating of information flow, microstates may dynamically and adaptively modify the quantity and quality of conscious experience. In my contribution, I will carefully review the methodology, the empirical findings and the theoretical background behind the microstate model, critically evaluate the claims that have been made based on it, and outline its possible extensions into the time-frequency domain.

TRANSDIAGNOSTIC BRAIN MAPPING IN DEVELOPMENTAL DISORDERS

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Between 14%–30% of children and adolescents worldwide are living with a learning-related problem sufficiently severe enough to require additional support. Their difficulties vary widely in scope and severity and are often associated with cognitive and/or behavioral problems. In many cases, children who are struggling have either no diagnosis or receive multiple diagnoses. The aim of this work was to investigate how does the developing brain give rise to these difficulties?

Structural neuroimaging, cognitive, and learning data were collected from 479 children (299 boys, ranging in age from 62 to 223 months), 337 of whom had been referred to the study on the basis of learning-related cognitive problems.

Machine learning identified different cognitive profiles within the sample, and hold-out cross-validation showed that these profiles were significantly associated with children's learning ability. The same machine learning approach was applied to cortical morphology data to identify different brain profiles. Hold-out cross-validation demonstrated that these were significantly associated with children's cognitive profiles. Crucially, these mappings were not one-to-one. The same neural profile could be associated with different cognitive impairments across different children. One possibility is that the organization of some children's brains is less susceptible to local deficits. This was tested by using diffusion-weighted imaging (DWI) to construct whole-brain white-matter connectomes. A simulated attack on each child's connectome revealed that some brain net-works were strongly organized around highly connected hubs. Children with these networks had only selective cognitive impairments or no cognitive impairments at all. By contrast, the same at-tacks had a significantly different impact on some children's networks, because their brain efficiency was less critically dependent on hubs. These children had the most widespread and severe cognitive impairments.

Based on our results, we propose a new framework in which the nature and mechanisms of brain-to-cognition relationships are moderated by the organizational context of the overall network.

HOW THE BRAIN EATS ITSELF: MICROGLIAL PHAGOCYTOSIS OF LIVE NEURONS

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Neuronal synapses, dendrites, axons and cell bodies can be phagocytosed by microglia a) physiologically during development, and b) pathologically in brain pathologies. We have been investigating what regulates microglial phagocytosis of neurons, and whether it contributes to neurodegeneration[1,2]. In neurodegenerative diseases, such as Alzheimer's disease, there is brain atrophy, i.e. loss of brain tissue including neurons, that occurs with cognitive decline, suggesting the possibility that blocking neuronal loss may halt progression of the disease.

P2Y6 is a microglial receptor for the nucleotide UDP released by stressed neurons, and is required microglial phagocytosis of neurons[3]. We found that inhibition of P2Y6 prevented microglial phagocytosis of live neurons induced by amyloid beta, tau, cytokines or endotoxin in co-cultures of neurons and glia[4]. A P2Y6 inhibitor also prevented neuronal loss induced by injection of endotoxin in rat striatum in vivo[4]. Recently (unpublished) we found that knockout of P2Y6 in mice prevents in vivo loss of neurons and/or memory induced by: a) chronic peripheral endotoxin, b) ventricular injection of amyloid beta, and c) the chronic tauopathy of the P301S mouse.

These results indicate that excessive microglial phagocytosis may contribute to neurodegeneration, and can be prevented by blocking the microglial P2Y6 receptor.

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2. Pampuscenko K, Morkuniene R, Sneideris T, Smirnovas V, Budvytyte R, Valincius G, Brown GC, Borutaite V (2020) Extracellular tau induces microglial phagocytosis of living neurons in cell cultures. J Neurochem. 154:316-329.
3. Koizumi S, Shigemoto-Mogami Y, Nasu-Tada K, Shinozaki Y, Ohsawa K, Tsuda M, Joshi BV, Jacobson KA, Kohsaka S, Inoue K (2007) UDP acting at P2Y6 receptors is a mediator of microglial phagocytosis. Nature 446:1091-5.
4. Neher JJ, Neniskyte U, Hornik T, Brown GC (2014) Inhibition of UDP/P2Y6 purinergic signaling prevents phagocytosis of viable neurons by activated microglia in vitro and in vivo. Glia 62:1463-75.

CONSISTENT AND SCALABLE HUMAN IPSC-DERIVED CELLS FOR IN VITRO CNS DISEASE MODELLING AND DRUG DISCOVERY

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Advances in cellular reprogramming have opened up new doors for studying human health and disease, drug discovery, and the development of cell therapies. Widespread use of human-induced, pluripotent stem cell (hiPSC)-derived, mature cell types however, is restricted by complex differentiation protocols and inefficient reprogramming methods. bit.bio opti-ox cellular reprogramming technology overcomes these restrictions by enabling the precisely controlled expression of transcription factors, and as a result, deterministic induction of a new cell identity. The resulting mature hiPSC-derived cells are functional within days and provide high quality cellular models with simple protocols.

Using opti-ox reprogramming, bit.bio has generated consistent and homogenous cultures of glutamatergic neurons (>80% VGLUT1/2) and GABAergic neurons (VGAT1, GABA), which show homogenous molecular phenotype at single cell transcriptomics resolution. Reprogramming is consistent and synchronised, giving fully differentiated functional neurons in only 14 days. opti-ox technology can generate functional cells with high consistency at scale from human iPSCs, including those carrying disease-specific mutations, offering novel avenues for the development of human in vitro models to support CNS research and drug discovery.

About bit.bio:

bit.bio is an award-winning human synthetic biology enterprise based in Cambridge, UK. bit.bio's mission is to code cells to advance the wellbeing of humanity. To do so, we apply the principles of computation to biology. Our current focus is to develop a scalable technology platform capable of producing consistent batches of every human cell. This has the potential to unlock a new generation of medicine: it will enable research and drug discovery to move on from inappropriate models and work with the cells that actually are affected by human disease. A scalable platform of consistent cells will also be the basis for a new generation of cell and tissue therapies.

For more information visit bit.bio

HUMAN BRAIN ORGANOIDS: FROM DEVELOPMENT TO DISEASE MODELING OF COVID-19

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Stem cell-derived human brain organoids are a new class of reductionist experimental systems that provide unprecedented opportunities to study the complexity of brain development and diseases. In my seminar, I will describe how patient-specific brain organoids have successfully modeled microcephaly mechanisms, identifying a critical role for primary cilia in neural stem cell homeostasis. Targeting cilia, we could trigger the differentiation of patient-derived glioma stem cells and establish how the human brain organoids have served as a native 3D substrate model glioma invasion. Finally, I will describe the initial findings of SARS-CoV-2-mediated neurotoxic effects in cortical neurons of brain organoids.

HUMAN TISSUE MODELING FOR SPATIOTEMPORAL INVESTIGATION OF BRAIN TUMOR DEVELOPMENT

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Glioblastoma are highly malignant tumors of the central nervous system. Several approaches were established to model glioblastoma growth, heterogeneity and development using animal/murine models. Unfortunately, the transferability from murine models to human were found to highly limited due to the fact that glioblastoma were artificially induced which resulted in a lack of heterogeneity and subclonal architecture. Over the recent years, we developed an immune-competent human neocortical slice model as a framework for glioblastoma research. We established multiple approaches for cell manipulation and loss-of-function models such as integration of autograft-lymphoid cells or depletion of myeloid cells to allow a broad field of application. Using our model, we addressed central questions on the role of microenvironmental impact during tumor development or evolution of anti-tumor-immunity. Through the combination of high-dimensional data acquisition and integrative analysis tools, we were able to reconstruct microenvironment-driven fate decisions in tumor development or map alterations in tumor-associated T cell activation. We believe that human-originated models have the potential to replace mouse models and improve our understanding of human brain health and disease.

DRUG DISCOVERY TODAY: HOW TO BET ON THE RIGHT HORSE?

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Background and aim:
Success rates in modern drug discovery and developed are constantly decreasing. In several therapeutic areas such as neuroscience, the alarmingly low rate of positive results in clinical proof-of-concept and late-stage development trials has triggered a marked reduction in ongoing and emerging activities and is calling for urgent corrective measures.

Materials and methods:
Several large-scale analyses and collaborative efforts have been undertaken to udentify the root causes of low productivity.

Results:
In this presentation, the Astra-Zeneca's 5R framework (right target, right tissue, right safety, right patient, and right commercial potential) along with the collaborative efforts such as the EQIPD consortium, the largest private-public partnership dedicated to quality of nonregulated biomedical research.

Conclusions:
Prospective application of the 5R framework requires knowledge not only about the framework but also organization and individual scientists' effort to adhere to bets possible research pravtice in order to support each of the "R"s with robust and reliable data.

POSTERS
PRESENTATIONS

CONTROL OF GLIOBLASTOMA CELL FOCAL ADHESION, MIGRATION AND PROLIFERATION BY ECM PEPTIDES

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Tumour is highly responsive to it's microenviroment, and the lack of reliable and simple in vitro models of cancerous tissue hinders effective reaserch and development of new potential drugs and treatments. We have applied a new 2.5 D in vitro glioblastoma models on synthetic extracellular matrix mimicking hydrogels from collagen like peptide (CLP) attached to polyethylene glycol (PEG-CLP), and its conjugates with RGD or IKVAV peptides recapitulating activity of fibronectin and laminin, respectively. We compare focal adhesion formation, migration and proliferation of glioblastoma cells of human and rodent origin on hydrogels with different ECM peptides.

The peptides were synthesized, conjugated to PEG, tested by 1H NMR assay, and crosslinked with DMTMM. Spheroids of glioblastoma HROG36 (human) and C6 (rat) cells were formed by hanging drop method and placed on hydrogels. Cell proliferation was determined by Presto Blue kit and fluorescent plate reader, migration was assessed by light microscopy, and focal adhesion - by immunocytochemistry and fluorescent microscopy. Images were processed and analysed by ImageJ software.

In both glioblastoma cell lines, PEG-CLP-RGD significantly increased the number of focal adhesion points but decreased the size of the connections, compared to PEG-CLP. A decrease in focal point size was also induced by the IKVAV peptide. The changes were accompanied by increase in projected cell area and decrease in cell shape index. PEG-CLP-RGD stimulated both migration and proliferation of HROG36 cells. PEG-CLP-RGD and PEG-CLP-IKVAV slightly increased C6 cell migration, however, only PEG-CLP-IKVAV significantly stimulated proliferation of this cell line.

In conclusion, C6 cells have distinct behavioral response to CLP-, RGD- and IKVAV-induced focal adhesions. Also, PEG-CLP hydrogels prove themselves as a simple to use ECM-mimicking platform for studying the influence of environmental signaling on cancer cells.

PERCEIVED LENGTH OF DIFFERENT SHAPES

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Background and aim:

Perception of spatial dimensions of visual objects depends on their shape and surface properties[1]. Rectangular objects, or simply a contour, appear longer than an empty space of the same length that was simultaneously shown next to the stimulus. According to our latest psychophysical data, other geometric shapes (triangles, ovals, or rhombuses) also cause misperceptions of size, but obviously of different strengths and even signs[2].

Materials and methods:

In the present experiments with the length adjustment procedures, subjects adjusted the empty space of the stimulus to equal the length of the test object. The judgment errors indicated the strength and sign of the object size illusion. Six geometric shapes were tested: a simple line, rhombus, oval, rectangle, and two equilateral triangles with the vertex of one directing toward the stimulus center and with that of the other pointing toward the one of the stimulus ends. Filled and empty stimuli were used.

Results:

The strength of the illusion and the order of the strengths were different among observers. However, some general regularities have been determined. The vertex of both the empty and filled triangle pointing toward the stimulus center was the most powerful shape to induce the illusion of extent. The triangles of the lateral orientation were two-three times less effective than those directed to the center. The rhombus shape was the weakest stimulus type. The rectangles and ovals were about of the middle strength. The lateral orientation triangles and rhombuses might produce the illusion of the negative sign. The filled shapes provided a somewhat stronger illusion than the empty contours.

Conclusions:

The data obtained support the assumption that the contours of the visual objects are the main primary determinant of the illusion of the object size.

[1]   A. Bertulis, T. Surkys and A. Bielevičius, Oppel-Kundt illusion balance; ACTA Neurobiologiae Experimentalis. 2019, December.

[2]   A. Bielevičius, A. Bertulis, I. Česnavičienė, J. Loginovič, T. Surkys, Perception of object length; LNA conference, 2019, November.

THE BASIC PROPERTIES OF CHIRP-EVOKED HAPTIC STEADY-STATE RESPONSES: SCALP TOPOGRAPHY AND SPECTRAL SENSITIVITY

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Background and aim

Chirp-evoked haptic steady-state responses are a frequency-domain response in the EEG signal that is produced by oscillatory signals with frequency changing monotonically in time. The aim of this study was to explore the properties of the steady-state response evoked by chirp-modulated haptic stimuli in 1-35 frequency range.

Thirty volunteers participated in two experiments. In the first study we compared responses to chirp-modulated stimuli with linear and logarithmic frequency progression within 1-35 Hz range. In the second study only chirp-modulated stimuli with linear progression were used. In both experiments subjects performed an active oddball task, and counted target stimuli (0.2 probability), consisting of constant frequency stimulation stimuli (25 Hz). EEG phase-locking factor and evoked amplitude responses were analyzed.

In the first study we observed stronger responses in linear chirps condition than in logarithmic condition. In both studies we observed maximal responses at two distinct scalp locations centered respectively at parietal and frontocentral channels respectively, with maximal response between 20 and 30 Hz.

Our studies demonstrate that chirp-evoked haptic steady-state responses represent a robust indicator of somatosensory processing. Further studies in special populations may prove their usability for diagnosis of somatosensory processing disruptions.

10-WEEK YOGA PRACTICE IMPROVES MOTOR LEARNING BY ATTENUATING BRAIN-DERIVED NEUROTROPHIC FACTOR LEVELS IN OLDER ADULTS

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Background and aim:

Higher concentration of brain-derived neurotrophic factor (BDNF) level is related to enhanced neuroplasticity and neurogenesis, which can affect motor learning. Nevertheless, previous studies observed that yoga can increase BDNF level, no studies have examined the effects of yoga on motor learning. Thus, the aim of this study was to investigate the effects of 10-weeks of regular yoga practice on motor learning in older adults.

Materials and methods:

Thirty-three healthy subjects aged 66.9 ± 6.0 years were enrolled for this study and randomly allocated to two groups. In experimental group subjects (n=18) had to participate in yoga practice for 10 weeks, 2 times/week, 90 min/session. In control group subjects (n=15) were asked do not change anything in their living habits. Before and after 10 weeks, blood samples were collected to determine BDNF concentration level. In addition, subjects had to perform a speed-accuracy reaching task using a Dynamic Parameter Analyzer (DPA–1) with nondominant hand. A single block of 20 trials was performed before the yoga practice and five blocks of 20 trials were performed after the yoga practice.

Results:

Yoga practice decreased reaction time at 2nd to 5th block ($p < 0.05$) and movement time at 1st to 5th block ($p < 0.05$), whereas in the control group only movement time decreased at 5th block ($p < 0.05$) compared to baseline block value. A faster reaction time at 2nd to 5th block ($p < 0.05$) and shorter movement time at 1st to 5th block ($p < 0.003$) was observed in yoga group compared with the control group. Furthermore, BDNF level increased ($p < 0.05$) in experimental group while it remained unaffected in control group. The changes in BDNF were negatively correlated with change in reaction time improvement during motor learning task ($r = –0.45$, $p < 0.05$).

Conclusions:

Yoga-induced increase in peripheral BDNF level is related to improved learning of speed-accuracy motor task in older adults.

ASSOCIATIONS AMONG PATTERNS OF INTERNET USE AND DEPRESSION, ANXIETY AND IMPULSIVITY IN A SAMPLE OF NON-CLINICAL INTERNET USERS

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Background and aim:

The increasing availability of the Internet resulted in a reported prevalence of problematic internet use (PIU) from 0.8% to 26.7% in different populations. PIU is strongly linked with mental disorders including depression, anxiety, OCD, ADHD, Social Phobia, and impulsivity. As the amount of time spent online is insufficient to indicate problematic behavior, we are seeking to define the internet-related behaviors as a continuum, ranging from healthy to problematic or excessive by investigating non-clinical population. With this study we seek to evaluate the relationship between Internet use patterns and symptoms of depression, anxiety, and levels of impulsivity in a sample of non-clinical Internet users.

Materials and methods:

A total of 107 young adults (55 male), the mean age 25.53 ± 4 years participated in the study and filled the questionnaires. Internet usage patterns were assessed using Internet Addiction Test (IAT) and short version of Problematic Internet Use Questionnaire (PIUQ-9). A set of tests was used to evaluate the psychological wellbeing: Barratt Impulsiveness Scale (BIS-II), Beck Depression Inventory (BDI-II) and Beck Anxiety Inventory (BAI).

Results:

Spearman's correlation test revealed a strong correlation between the scores of IAT and PIUQ ($r = 0.702$, $p < 0.001$). IAT correlated with BDI-II ($r = 0.223$, $p = 0.021$), BAI ($r = 0.245$, $p = 0.011$) and BISII ($r = 0.190$, $p = 0.499$). In addition, PIUQ correlated with BDI-II ($r = 0.240$, $p = 0.013$) and BIS-II ($r = 0.245$, $p = 0.011$).

Conclusions:

Results revealed the correlations between the scores of Internet Addiction Test and scores of depression, anxiety, and impulsivity while Problematic Internet Use Questionnaire scores are associated with depression and impulsivity in the non-clinical population. The preliminary experiment data is consistent with the results from previous reports.

INFLUENCE OF SOCIAL MEDIA SOUNDS ON PHYSIOLOGICAL PARAMETERS AND WORKING MEMORY

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Background and aim:

Social media (SM) became an integral part of our daily lives. It is used to communicate, share content, and follow world events. People spend on average 2.5 hours' a day on SM. However, the data of SM impact on human physiology and cognition is scarce. The aim of this work is to investigate the effect of SM sounds on heart rate (HR), heart rate variability (HRV) and working memory.

Materials and methods:

The study contains two tasks: passive listening and working memory. First, 5 min duration electrocardiogram (ECG) and breathing rate were recorded in three conditions with sound (neutral, unpleasant, and SM sounds) and in silence. Next, a working memory task was carried out using three auditory stimuli: silence, neutral (60Hz) and Facebook Messenger sounds. In addition, participants filled in questionnaires about SM usage, anxiety, general health etc. Preliminary data of 28 participants (27.0±10.4 years) is presented.

Results:

Majority of the participants (n=22) check SM several times a day, some (n=7) - several times an hour. Participants (n=21) tend to mute SM sounds more than 6 hours per day. Women (n=16) tend to spend more time on SM compared to men (n=12).

We noticed that in all sound conditions average HR was lower (70±10 bpm) than in silence (72±11 bpm) among both men and women. In sound conditions HRV (RMSSD) among women increased and was the highest for SM sounds, while for men the opposite: HRV decreased and in SM condition was the lowest. A noticeable variation of ECG parameter values was related to individual, sex, and age differences.

In the working memory task average performance accuracy in the presence of neutral sound (66±11%) was significantly lower (p<0.01) than in silence (71±12%) or SM condition (72±14%). Meanwhile, the reaction time in the presence of SM sound (0.78±0.16s) was significantly shorter (p=0.02) than after hearing neutral sound (0.80±0.16s) or in silence (0.81±0.16s).

Conclusions:

Large variation of cardiovascular parameters points that sample size should be significantly increased for an evaluation of SM sound effects on cardiovascular parameters. The presence of SM sound did not worsen the performance on the working memory task.

SYNAPTIC PLASTICITY IN CLUSTERED DENDRITIC SYNAPSES ON A HIPPOCAMPAL CA1 PYRAMIDAL NEURON

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Background and aim:
Synaptic plasticity, such as long-term potentiation (LTP) and long-term depression (LTD), has been believed to underlie the biological basis of learning and memory in the brain. In the hippocampal CA1 area, Schaffer collateral-pyramidal cell synapses can undergo NMDA-dependent LTP and LTD following high or low neuronal activity, respectively. The aim of this study was to evaluate the effect of the synaptic cluster properties on synaptic plasticity in a CA1 pyramidal neuron using a computational modeling approach.

Materials and methods:
We used a detailed compartmental model of a hippocampal CA1 pyramidal neuron (Migliore et al., PLOS Comp Biology 2018) and a NMDAr-dependent voltage-based model of synaptic plasticity to study the development of synaptic strengths in the individual Shaffer collateral synapses clustered or distributed randomly across the stratum radiatum region of the cell dendrites. Fifty synapses were stimulated simultaneously applying the protocols most widely used in experimental studies of synaptic plasticity: low-frequency (LF) stimulation at 1 Hz for 900 s for LTD induction and high-frequency (HF) continuous 100 Hz tetanization for 1 s repeated at 1 s interval for LTP induction.

Results:
Spatially clustered synapses (cluster radius 20 μm) underwent LTP following the HF stimulation and LTD after the LF stimulation, with 76% and 74% of synapses having been potentiated or weakened, respectively. Increased radius of the synaptic cluster (50 μm) promoted LTD induction for both HF and LF stimulation protocols, while the randomly distributed synapses remained unmodified.

Conclusions:
Structural organization of the multiple excitatory synaptic inputs shapes synaptic modifications in a CA1 pyramidal neuron.

Funding:

DOMINANT RESTING EEG FREQUENCY AS AN INDICATOR OF THE NEUROBEHAVIORAL STATE IN PROLONGED DISORDERS OF CONSCIOUSNESS

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The prolonged disorders of consciousness (PDOC) remain a challenge for an accurate clinical diagnosis, mainly due to a very scarce or ambiguous behavioral responsivity. Behavior-based diagnostic approaches often lead to misdiagnosis, often reaching as high as 40% cases. Objective methods for PDOC diagnosis are based on measurement of brain activity and may be treated as a support for a better diagnosis, independent of motor restrictions.

In this study we used a robust method of resting EEG spectral decomposition to identify specific spectral properties for different types of PDOC. 60 patients and 37 healthy volunteers took part in this study. Patient group consisted of 22 unresponsive wakefulness patients, 25 minimally conscious patients and 13 patients emerging from the minimally conscious state.

Ten-minutes of resting EEG was acquired during wakefulness and then segmented into 2-second fragments, which were transformed into frequency domain using FFT. Subsequently, frequency spectra were decomposed and parameterized using FOOOF method by Haller et al. (2018). Provided by this method, the maximal peaks in 1-14 Hz were identified in the centro-parietal region. The neurobehavioral capacity of patients and PDOC diagnosis was assessed using Coma Recovery Scale - Revised (CRS-R).

We observed that the maximal peak frequency in the 1-14 Hz range successfully predicted both neurobehavioral capacity of patients as indicated with CRS-R total score as well as PDOC diagnosis.

Our study shows that a spectral decomposition with a simple algorithm of the resting EEG signal from centro-parietal electrodes might be a valuable support for behavioral diagnostic techniques.

MONITORING THE AUDITORY TEXTURES PROCESSING IN HUMAN CORTEX TO DISTINGUISH STATES OF CONSCIOUSNESS

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Background and aim:

One of the most challenging clinical issues regarding patients with persistent disorders of consciousness (PDOC) is to reliably estimate their residual conscious perception of the environment. This requrires measurement that directly assess their cortical state, e.g. in reaction to stimuli. Auditory stimulation in combination with neural recordings is a promising technique towards objective estimation of conscious awareness. In this study, we investigated the potential of complex acoustic stimuli to elicit EEG responses suitable for objectively classifying a wide range of subject groups (5), from unconscious to responding.

Methods:

We presented naturalistic auditory textures to subjects, which changed their statistics at an unexpected point in time (0.75s, 1.6s and 3s). Active listeners were asked to indicate the change by button press, while all other groups (awake passive, asleep, minimally conscious state (MCS), and unresponsive wakefulness syndrome (UWS)) listened passively. Sleep data were aquired during deep NREM sleep (N2, N3 phases early in the night). The evoked potential at stimulus onset and change in stimulus statistics were next quantified, as well as the descriptional complexity of neural response during the change of stimulus statistics.

Results:

Detection of the change in statistics requires the formation of internal model of its spectro-temporal structure. On the group level, we found that onset and change potentials classified patients and healthy controls successfully but failed to differentiate between the UWS and MCS groups. Conversely, complexity of the neural representations (measured using Lempel-Ziv complexity) allowed reliable differentiation between UWS and MCS even for individual subjects, when compared with the classical behavioral scale (Coma Recover Scale -Revised, CRS-R).

Conclusion:

Overall, our results suggest that the processing of statistical stimuli varies with the state of consciousness, thus potentially allowing a discrimination of the consciousness level in noncommunicative patients.

MONITORING OF CRITICAL FLICKER FREQUENCY DURING 4-MONTH ISOLATION IN A SPACESHIP MOCK-UP (THE SIRIUS-19 PROJECT)

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Background and aim:
The work was conducted during the project SIRIUS-19[1]. The goal of the project was to imitate a flight to the Moon, landing on its surface and going back. Our group monitored vision of the crew during all duration of the project, in particular, by measuring critical flicker frequency (CFF). It is obvious that for the safety of the long-term flights there should be no significant changes in the parameters of the visual system state. Some previous investigations confirmed good stability of the human visual system in conditions of the long-term isolation. The aim of this paper was to consider the results of measuring CFF – the parameter characterizing not only vision but also a general capacity for work.

Materials and methods:
The experimental group consisted of 6 adults (3 males, 3 females, mean age (SD) 34.3(6.3)) who were isolated in a mockup for 4 months with a busy astronaut-like schedule, artificial lighting conditions and restricted communication with people outside. The control group consisted of 6 adults (3 males, 3 females, (SD) 33.7(7.4)), who maintain their usual lifestyle. CFF for red light was measured each 2 weeks, during 4 months, twice a day (in the morning and in the evening), monocularly, for each eye. The average values of CFF obtained in 6 trials (3 times increasing and 3 times decreasing flicker frequency) were calculated for the analysis.

Results:
In both groups, the data of the three first and three last measurements were compared. In the experimental group, the statistically significant increase was found in the later part of the isolation period (Wilcoxon test, $z = -2.357$, $p = .018$); in the control group, no significant difference was found.

Conclusions:
We have revealed a small statistically significant increase of CFF in the group isolated for 4 months inside a spaceship mock-up. Though this difference appeared to be not clinically important, further investigation of the CFF dynamics in such conditions seem to be necessary in view of more prolonged flights.

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[1]   https://www.nasa.gov/content/sirius

ARE COGNITIVE FUNCTIONS ASSOCIATED WITH PSYCHOMOTOR FUNCTIONS IN STROKE PATIENTS?

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Background and aim:

Stroke is one of the most leading cause of death and long-term disability worldwide. Stroke patients often experience cognitive and psychomotor dysfunctions which significantly affect daily activities. Many studies confirm the importance of cognitive functions for successful movement capabilities. However, some studies results indicate that cognitive functions have minimal influence on psychomotor functions. It is not clear if better cognitive functions related to better psychomotor functions or not. The aim of this work was to evaluate the link between cognitive functions and psychomotor functions in stroke patients.

Materials and methods:

The subjects were 22 stroke patients, 11 females, 11 males. Age range was between 61 and 89 (M=78,09; SD=8,6). Cognitive functions (attention, memory, verbal fluency, language, visuospatial abilities) measured with The Addenbrooke's Cognitive Examination –III (Hsieh, Schubert, Hoon, Mioshi, Hodges, 2013). Psychomotor functions were evaluated by the Finger Tapping Test (Reitan, 1959). Language and the total ACE-III score varied between different education groups. To evaluate correlations between language as well as the total ACE-III scores and psychomotor functions were calculated Partial correlation coefficients. Relationships between the other cognitive (attention, memory, verbal fluency, and visuospatial abilities) and psychomotor functions were evaluated by Spearman's correlation coefficients.

Results:

The results indicated that the total psychomotor function score positively correlated with attention (r=0.48, p=0.03), visuospatial abilities (r=0.5, p=0.02) and the total ACE-III score (r=0.49, p=0.03). Moreover, right hand psychomotor function was positively associated with attention (r=0.46, p=0.03) and visuospatial abilities (r=0.48, p=0.02).

Conclusions:

The results of the study demonstrate that better psychomotor functions are associated with better cognitive functions in stroke patients. As well as, better psychomotor functions are associated with separate cognitive dimensions such as attention and visuospatial abilities.

AMBLYOPIA AND ECCENTRIC FIXATION

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Background and aim:

Amblyopia or 'lazy eye' is impaired or dim vision without obvious defect or change in the eye. It is often associated with abnormal visual experience, most commonly strabismus, anisometropia or both, and form deprivation. The main task of amblyopia treatment is to ameliorate etiological factors to create a clear retinal image and, to ensure the participation of the amblyopic eye in the visual process. The treatment of amblyopia and eccentric fixation is usually associated with problems in the therapy. Eccentric fixation is present in around 44% of all patients with amblyopia and in 30% of patients with strabismic amblyopia. In Latvia, amblyopia is carefully treated in various clinics, but eccentricity diagnosis is relatively rare. Conflict which has developed relating to the relationship between the visual disorder and the degree of eccentric fixation in amblyopia should to be rethoughted, because it has an important bearing on the cause and treatment of amblyopia, and the role of the eccentric fixation in this case.

Materials and methods:

Visuoscopy is the most used method for determination of eccentric fixation. With traditional visuoscopy, a fixation target is projected onto the patient retina, and the examiner asks to look straight directly at the center of the target. An optometrist then observes the point on the macula used for fixation. This objective test provides clinicians with direct observation of the fixation point of the eye. It requires patients to voluntarily fixate the target and assumes the foveal reflex accurately demarcates the center of the foveal pit. In the end, by having a very simple method to evaluate fixation, it is possible to indirectly evaluate treatment improvement, as eccentric fixation is always associated with reduced visual acuity.

Results:

So one may expect that if eccentric fixation in amlyopic eye is found with visuoscopy, then visual acuity should be less than 1.0 (in decimal units). With occlusion or another amblyopia therapy, one would expect both visual acuity and fixation to improve simultaneously, that is fixation would become more central.

Conclusions:

Improvement in fixation pattern by treatment is an indirect measurement of improvement of visual acuity. Evaluation of eccentric fixation in the child may be helpful in identifying amblyopia in children prior to measurement of visual acuity. This is very important because the earlier amblyopia is diagnosed – the better the chance of improving visual acuity.

NOVEL VISUAL ACUITY CHARTS WITH MODIFIED 3-BAR OPTOTYPES: APPROBATION IN CATARACT PATIENTS

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Background and aim:

Two novel charts for visual acuity (VA) assessment with modified 3-bar optotypes were created. The aim of the work was to compare the novel charts and two standard charts (ETDRS and E-chart) in cataract patient examination.

Materials and methods:

The novel charts were implemented in proportional (IITP-PD chart) and in linear (IITP-LD chart) designs and both charts included modified 3-bar optotypes. These charts were compared with standard ETDRS and E-chart.

Far monocular unaided vision (3 m distance) was assessed in 79 cataract patients aged 45-90 yrs (mean (SD) age 75.2 (9.3) yrs). Each chart was used twice for each subject (test and retest). The interval between test and retest varied from 1 to 24 hours (depending on patient's condition and preference). The Bland-Altman analysis was used to analyze repeatability and between charts agreement.

Results:

It was found that all charts have similar repeatability, with 95% limit of test-retest agreemet: 0.29, 0.33, 0.37, and 0.40 logMAR for IITP-LD, ETDRS, E-chart, and IITP-PD, respectively.

The median VA values for combined test and retest data appeared to be 0.40, 0.40, 0.49, and 0.49 logMAR for IITP-LD, IITP-PD, ETDRS, and E-chart, respectively, i.e. the data obtained with both IITP charts corresponded to better VA (i.e. overestimation).

The factors affecting measurements were: difficulties in discriminating left and right orientations in E-chart, systematic confusion of certain letters in ETDRS, and higher guess level for the optotypes in IITP charts. The latter factor was compensated by increasing number of the optotypes in each line.

Conclusions:

The IITP charts are comparable in repeatability with ETDRS and E-chart though novel charts slightly overestimate VA in comparison with those charts. Nevertheless, IITP charts have the following benefits: they are easier to understand and to respond, do not require knowing of the alphabet or discriminating right-left directions.

MOLECULAR SUBTYPING OF GLIOBLASTOMAS USING PCA ANALYSIS OF GENE EXPRESSION DATA

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Background and aim:

Glioblastoma (GBM) is the most common and aggressive malignant brain tumor in adults. Histologically similar but very different at the molecular level GBMs were classified into several subtypes according to its molecular signature. Different researchers are currently indicating different numbers of GBM subtypes. The aim of this study was to reveal the overlap of the GBM subtypes between the Phillips et al. (2006) and Verhaak et al. (2010) subtyping and define the number of GBM subtypes for further research.

Materials and methods:

We used the gene expression data of the GBM tumors (N=528) from the Cancer Genome Atlas (TCGA) database. The most informative 300 genes out of the 12 000 ones were selected applying the Chi-Square Test feature selection method. The principal components (PCAs) were extracted, and the Neural subtype (Verhaak, 2010) was compared with the Mesenchymal, Classical and Proneural subtypes (Phillips et al., 2006) using two-sample Hotelling T2 test and independent two-sample t-test. Finally, the Euclidean distance was calculated to estimate the separability of these four GBM subtypes.

Results:

Statistically significant differences in the means of the extracted 20 PCA (explaining 71% of the data variance) were observed between the Neural subtype (Verhaak et al., 2010) and all three GBM subtypes - Mesenchymal, Classical and Proneural subtypes defined by Phillips et al. (2006): Hotelling T2=429.95, $p<0.001$; Hotelling T2=225.22, $p<0.001$; Hotelling T2= 298.92, $p<0.001$ accordingly. The Neural subtype (Verhaak et al., 2010) shows statistically significantly different PCA1 and PCA2 mean values than Mesenchymal, Classical and Proneural subtypes (Phillips et al., 2006). Euclidean distance between the centers of the Neural subtype (Verhaak et al., 2010) and Mesenchymal, Classical, Proneural subtypes (Phillips et al., 2006) are accordingly 2.326, 1.366 and 2.069. Mesenchymal, Classical and Proneural subtypes defined by both Phillips et al. (2006) and Verhaak et al. (2010) overlap and do not differ statistically significantly in the means of the extracted PCAs.

Conclusions:

Our results suggest that the Neural subtype (Verhaak et al., 2010) represents a group of the glioblastoma tumors having its unique genetic signature that differs statistically significantly from the Mesenchymal, Classical and Proneural subtypes (Phillips et al., 2006). GBM heterogeneity at the molecular level is certainly important for the disease initiation, course, and patient outcome.

EXOSOMES FROM TLR3 AGONIST POLY I:C-STIMULATED AIRWAY CELLS INITIATE INFLAMMATION IN THE CNS

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Background and aim:

Viral upper respiratory tract infections are the most common among the contagious diseases. Exosomes from virus-primed airway cells may contain viral genetic material and/or immune response-related inflammatory factors. Exosomes can easily pass blood-brain barrier and thus, transmit the inflammatory signal to brain, however, this posibility has not yet been studied.

The aim of this work was to investigate whether exosomes from virus mimetic TLR agonist poly I:C-affected airway cells can induce inflammatory response in CNS.

Materials and methods:

Exosomes were isolated from airway epithelial cells by Total Exosome Isolation Kit. Exosomes were characterized by morphology (transmission electron microscopy), by size (dynamic light scattering) and by CD9 and CD63 markers (ELISA). Exosomes were intranasally introduced to Balb/c mice or applied on cultured microglia. Exosome internalisation in culture was assessed by fluorescence, and in brain tissue slices – by confocal microscopy. Caspase 1 was evaluated by luminescence method. Microglial and brain tissue mRNA expression was assessed by RT-PCR.

Results:

Intranasally applied airway exosomes penetrate brain within 1-3 hours, and are internalised primarily by microglial cells, as was confirmed both in vivo and in vitro. Poly I:C-primed airway exosomes significantly increased activity of inflammasome (caspase 1) and expression of PTGS2 and TNF-α in cultured microglia. TNF-α expression was also elevated in brain tissue after poly I:C-primed airway exosome treatment. Neither inflammatory cytokine expression, nor caspase 1 activity was affected by exosomes from untreated airway cells.

Conclusions:

Consequently, exosomes from TLR3 agonist poly I:C-affected airway cells can enter brain and induce inflammation in CNS.

THE INVESTIGATION OF THE GLYCOBIOLOGY OF GLIOBLASTOMA MICROENVIRONMENT

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Background and aim:

Sialic acids are a component of glycocalyx and changes in their expression are associated with malignant properties of cancers, including invasiveness and metastatic potential. Human glioblastoma (hGB) cells express very high levels of cell-surface terminal sialic acids that possibly reduce cell immunogenicity by masking cell face antigens. However, there is insufficient data on the actual levels of sialylation and sialidases in hGB. We aim to validate a recently established human organotypic brain slice culture technique for glycobiology research and to characterise the sialylation levels in hGB.

Materials and methods:

Bioorthogonal CLICK chemistry was adapted to assess the sialylation levels ex vivo and in vitro. Calcium imaging was used to investigate glioblastoma cells network activity. Multi-electrode array technique was used to evaluate extracellular electrical activity. Expression level of genes involved in glioblastoma cells sialylation was evaluated by RNA-sequencing.

Results:

Bioorthogonal CLICK chemistry is applicable for human organotypic brain slice culture model and glioblastoma cells. Preliminary data shows a high level of cell-surface terminal sialic acids expression in glioblastoma cells. Inhibition of sialic acid synthesis and sialidase activity in these cells affects calcium signalling and extracellular electrical activity.

Conclusions:

Human organotypic brain slice culture technique can be used as a novel framework for glycobiology research allowing to metabolically label sialic acid moieties and characterise changes in glycocalyx. Furthermore, data obtained from glioblastoma cell cultures confirms that these cells express high levels of cell-surface terminal sialic acids and suggest an important role for sialic acids in glioblastoma signalling and network activity.

PSYCHOPHYSICAL STUDY OF FEATURES OF THE ILLUSION OF INTERRUPTED SPATIAL EXTENT

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Aim:

The aim of the study was to further develop a quantitative model of the illusion of interrupted spatial extent and test it to account for the effects caused by stimuli containing distracting line-segments of various lengths and positions.

Methods:

Illusion was studied as a function of the distance between the distracting lines and the lateral terminator of the reference spatial interval of the three-dot stimulus. Data obtained in three different series were fitted with relevant functions of the model.

Results:

It was shown that the model satisfactorily describes all changes in the illusion magnitude for stimuli with a distracting line located either inside the interval, as well as for a stimulus with two lines located symmetrically relative to the lateral terminator. In addition, the model was successfully applied to fit the experimental data previously obtained for conventional Oppel-Kundt stimuli.

Conclusions:

A good correspondence between the experimental and theoretical results supports the suggestion that the context-evoked augmentation of neural excitation can determine the occurrence of the illusion of interrupted spatial extent.

NLRP3 INFLAMMASOME ACTIVATION BY VIRAL OLIGOMERIC PROTEINS IN MICROGLIA

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Background and aim:

Inflammasomes – intracellular protein complexes, which are important components of the innate immune system. The best described inflammasome is NLRP3, which contains three major components – nucleotide-binding and oligomerization domain-like receptor, apoptosis-associated speck-like protein (ASC) and procaspase-1. NLRP3 inflammasome activation results in release of inflammatory cytokines, like IL-1β, and inflammatory cell death – pyroptosis. Activation of NLRP3 inflammasome is associated with various diseases, including gout and Alzheimer's disease. Our previous study showed that NLRP3 inflammasome is activated by soluble amyloid beta oligomers.

The aim of this work is to extend the latter research and determine if viral oligomeric proteins of different structure activates NLRP3 inflammasome.

Materials and methods:

The subject was primary microglia cell culture isolated from C57BL/6 newborn mice. Cells were treated with various viral oligomeric proteins: filaments forming measles and mumps viral proteins; spherical viral-like particles of these polyomaviruses – Karolinska Institutet polyomavirus (PyV), Washington University PyV, John Cunningham PyV, Merkel cell PyV. MCC950 was used to inhibit NLRP3 inflammasome activation. After treatment cell viability was measured using LDH assay. Secretion of inflamatory cytokines IL-1β and TNFα was detected by ELISA. Formation of NLRP3 inflammasome components – ASC specks was visualized by imunocytochemistry.

Results:

We did not detect any effect of measles and mumps viruses' proteins on NLRP3 inflammasome activation. However, VLPs of polyomaviruses induced NLRP3 inflammasome activation in microglia cells.

Conclusions:

We showed that NLRP3 inflammasome is activated by spheres forming VLPs of polyomaviruses. In addition, filaments forming proteins of measles and mumps viruses did not activate NLRP3 inflammasome. Our results demonstrate that viral proteins can activate inflammasome depending on their structural properties.

IS TAICHI / QIGONG EXERCISE BETTER THAN OTHER EXERCISES ON BODY AWARENESS AND PSYCHOLOGICAL WELL-BEING: A COMPARISON STUDY

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Background and aim:

Taichi and Qigong are typical mind-body exercises which might improve body awareness and psychological well-being. However, it is very little known about Taichi/Qigong (T/Q) effects on body awareness and psychological well-being compared to other exercises (OE). Therefore this study aimed to compare the practitioners of T/Q and the practitioners of OE on body awareness and psychological well-being.

Materials and methods:

117 replies to questionnaire were collected in Lithuania (male 31 %, female 69%, age 42±14 years), which were divided into three groups: T/Q (n=14), T/Q plus OE (n=54), OE (n=49). Two questionnaires were used in this research: Body Awareness Questionnaire (Shields, Mallory & Simon, 1989) (Cronbach alfa – 0.87) and Lithuanian Psychological Well-being Scale (LPGS – J, Kairys, Bagdonas, Liniauskaitė, Pakalniškienė, 2013) (Cronbach alfa – 0.88). A list of questions about physical activity and sociodemographic information were also presented to the respondents. Data analysis was based on Kruskal-Wallis, 1-way ANOVA and Pearson correlation tests.

Results:

There weren't significant differences between the three groups on body awareness (p=0.4) and the general psychological well-being (p=0.06). However, the tendency that practitioners of T/Q exercise alone had slightly higher scores than T/Q plus OE and OE of body awareness was noticed. On the contrary, T/Q group demonstrated slightly lower psychological well-being scores than other groups.. A significant difference between groups was found only in one subscale of psychological well-being named "Control" (p=0.017) with a mean score of 26.25 for T/Q group, 30.2 for T/Q plus OE group, and 29.9 for OE group. The exercise frequency (times/week) was positively correlated to general psychological well-being (r=0.2, p=0.05). No correlation between T/Q exercise experience and body awareness or psychological well-being was found.

Conclusion:

To conclude, our research reveals that Taichi/Qigong exercises are not better than other exercises on body awareness and psychological well-being. But it is worth noticing that the group practicing only Taichi/Qigong consisted only of 14 respondents and should be expanded in further researches.

SPONTANEOUS EYE BLINK RATE AS AN INDICATOR OF DOPAMINERGIC TRANSMISSION IN PROBLEMATIC INTERNET USE

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Background and aim:

Problematic Internet use (PIU) is a modern global social problem generally understood as inability to control use of the Internet and causing negative consequences in individual's daily life. It is already shown that excessive use of the internet shares some common mechanisms with substance use disorders (SUD). SUDs are related to the altered dopaminergic transmission and Spontaneous Eye Blink Rate (sEBR) is considered as an indicator of dopaminergic tone. Due to the action of substances used or psychological disorders, dopaminergic activity in the brain can be decreased or increased which results in a lower or higher sEBR, respectively. sEBR has not yet been studied in the context of PIU and our aim of this research is to examine if there are any changes of sEBR associated to the internet use patterns.

Materials and methods:

26 young adults (14 women and 12 men, mean age 25.9 SD 3.86) participated in the study. Based on the scores of Internet Addiction test (IAT) participants were divided into two groups of 13 people each: high IAT (score > 30), indicating problematic internet use and low IAT (score < 30), indicating non-problematic internet use. Electrooculography (EOG) was used to measure eye movements during resting state task (duration of the task was 5 minutes). Recordings were reviewed and then calculated with BLINKER.

Results:

IAT scores on both groups differed significantly - 18.6, SD 2.56 in low IAT group and 33.3, SD 2.46 in high IAT group. A group with high IAT showed significantly lower sEBR (11.16 blinks/min, SD 8.72) than low IAT group (17.5 blinks/min, SD 6.37). Correlation between IAT scores and sEBR did not reach significance, but a negative trend was observed (Spearman's rho = -0.35, p = 0.08).

Conclusions:

Preliminary data shows that participants with high IAT scores tend to have a lower spontaneous eye blink rate than participants with low IAT scores, suggesting sEBR can further be investigated as one of dopaminergic transmission indicators in problematic Internet use associated conditions.

THE EFFECT OF VIRUS MIMETIC POLI I:C-PRIMED AIRWAY EXOSOMES ON MICROGLIAL ENERGETIC METABOLISM

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Background and aim:

Viral infections of upper respiratory tract can induce airway epithelial exosomes with inflammatory cargos including even viral particles. Exosomes are shown to easily cross blood brain barrier; thus, they might transmit inflammatory signal from periphery to the brain. Activated immune effector cells undergo immune-metabolic transition characterised by shift from mitochondrial to glycolytic ATP production and increase in reactive oxygen species (ROS). However, it is not known whether virus-primed airway exosomes might trigger similar changes in microglia.

The aim of this study – to investigate the effect of virus mimetic polyinosinic polycytidylic acid (poly I:C)-primed airway exosomes on human microglial cell energetic metabolism.

Materials and methods:

Exosomes were isolated from poly I:C-primed human bronchial epithelial cell (HBEC-3) culture medium by Total Exosome Isolation Reagent, and characterized by particle size (Zetasizer) and specific exosomes markers (ELISA). Poly I:C encapsulation in HBEC-3 exosomes was monitored by using dihydrorhodamine-conjugated poly I:C and fluorescent plate reader. Exosome internalisation by microglia (HMC-3) was identified by light and fluorescent microscopy. Mitochondrial and glycolytic activity of microglial cells was assessed by Seahorse XFp metabolic analyser. Intracellular ROS were determined by 2',7'-dichlorofluorescein diacetate assay and mitochondrial superoxide – by MitoSOX™ Red followed by fluorescence imaging and analysis by Image J software. Statistical data analysis was performed by IBM SPSS Statistics 20 software.

Results:

HBEC-3 exosomes were internalized by microglial cells after 2 hours after treatment. Mitochondrial function of microglial cells was significantly inhibited and glycolysis activated after 24-hour treatment with virus-primed HBEC-3 exosomes. This was accompanied by increase in the production of intracellular and mitochondrial ROS. Such effects were not observed in HMC-3 cultures treated by exosomes from HBEC-3 cells not affected by poly I:C.

Conclusions:

Poly I:C-primed airway exosomes induce transition of energy production phenotype from mitochondrial to glycolytic and stimulate ROS production in microglial cells.

MMP-9 DEFICIENCY IMPROVES POST-STROKE RECOVERY RATE

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Background and aim:

Cerebral ischemia is one of the most common causes of mortality worldwide. Ischemic brain displays enhanced activity of matrix metalloproteinase-9 (MMP-9), an extracellularly acting protease, implicated in pathological remodeling processes of the nervous tissue. The aim of the present study was to establish focal middle cerebral artery occlusion (fMCAo) protocol, evaluate the MMP-9 activity changes after ischemic stroke and verify the impact of MMP-9 deficiency on long term survival and recovery process.

Materials and methods:

All experiments were performed in C57BL/6 mice. Regional cerebral blood flow was monitored using Doppler control. The effectiveness of stroke was verified by TTC and Nissl staining. Changes in MMP-9 activity were assessed in ipsi- and contralateral cortex and hippocampus by gel zymography. For evaluation of the influence of MMP-9 on recovery rate, mice lacking MMP-9 (MMP-9 KO on C57BL/6 background) and wild type (MMP-9 WT) littermates were used. During first week a postoperative care and feeding protocol was applied. Animal weight was controlled during 30 days post-stroke. Additionally, we performed focal neurological deficit evaluation using experimental stroke scale, inclined plane test and nest-building activity.

Results:

Advanced neurodegeneration was observed 30 days post-ischemia. Pronounced increase in MMP-9 activity was observed during first 24 hours post-stroke in ipsi- but also contralateral cortex. Lack of MMP-9 did not diminish the mortality of the animals. MMP-9 KO group was characterized by smaller weight loss and lower focal neurological deficits post-stroke recovery compared with MMP-9 WT. Moreover, nest building rate was faster in MMP-9 KO as compared to WT, while the maximum slope angle (inclined plane test) in MMP-9 KO was significantly higher during first 3 weeks post-ischemia compared to WT.

Conclusions:

Our study indicates that MMP-9 deficiency improves recovery rate and reduces long-term detrimental effects of the ischemic stroke.

THIRD STAGE OF 40 HZ AUDITORY STEADY-STATE RESPONSE REVEALED WITH STIMULI OF DIFFERENT LENGTH

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Background and aim:

There is a need for objective neurophysiological biomarkers for diagnostics and monitoring of neuropsychiatric disorders. It is proposed that the 40 Hz auditory steady-state response (ASSR) could be such a marker since altered power and phase precision of the response were reported in schizophrenia (SZ), depression and developmental disorders. However, there is no consensus on the best assessment practice of ASSRs.

An important characteristic of the procedure is the duration of auditory stimulus. It has been shown that SZ patients have an enhanced ASSR to longer than 1500 ms stimulations and reduced responses to 500 ms stimulations compared to healthy subjects. However, the effect of auditory stimulus duration on ASSR parameters has never been specifically addressed in healthy population. The purpose of our study was to systematically evaluate how stimulus duration influences 40 Hz ASSRs.

Materials and methods:

40 Hz click trains of 500, 1000, 1500 and 2000 ms were used to elicit ASSR in 14 healthy subjects. To ensure subjects attention towards auditory stimulation participants were asked to silently count occasionally presented single clicks. Intertrial phase coherence (ITPC) was used to evaluate ASSR. ITPC values were averaged over separate time periods to assess different stages: early-latency part (0-100 ms); late-latency part (100-500 ms); steady-state part (500-1500 ms); and pre-offset response (last 400 ms of stimulation).

Results and Conclusions:

The earlier research showed that ASSRs can be divided into early- and late- latency responses which are generated by different neural networks. However, our results with longer than 500 ms stimuli revealed that ASSRs can be divided into three stages. The third stage (steady-state period) follows the late-latency response and lasts until the end of stimulation. ITPC during steady-state period is weaker than during the late-latency part and this difference is independent of stimulation length.

MEASURING COMMUNICATION OF INTENDED AFFECT IN EXPRESSIVE PIANO PERFORMANCE FOR FUTURE APPLICATION IN BRAIN-COMPUTER MUSIC INTERFACING

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Background and aim:

The increased accessibility and mobility of EEG equipment and online signal processing techniques have provided the opportunity to collaboratively develop a Brain-Computer Music Interface (BCMI) system capable of supporting affective communication during Embodied Music Interaction. The resulting BCMI system is aimed to function consistently across different individuals and environments, overcoming current technological and contextual limitations. At this stage, we aim to identify parameters within behavioural data to inform future steps and present only a fraction of the results related to the self-evaluation responses.

Methods:

A procedure was designed to collect synchronised EEG data, audio recordings, and self-evaluation responses of 10 academic musicians at different levels of experience performing a piano playing task. A piano score with a 30 second duration, instructions, and self-rating steps were synchronised with EEG recording. The task entailed 200 repetitions by each participant over 4 sessions. By means of improvised variations on the score, communication of 1 of 5 distinct emotion descriptors - Neutral, Distressed, Excited, Depressed and Relaxed - was instructed at each repetition. After each repeat, participants self-evaluated communication of valence and arousal, rating each dimension from 1-9.

Results and conclusions:

Participants' ratings of their own performances were consistent with their intentions. For estimations of valence, a significant interaction between session, run and level of experience was observed indicating inconsistency between ratings of experienced and less experienced participants within the middle of the first session. For arousal estimations, interaction between session, run and emotion was significant, pointing to more neutral arousal levels indicated during the beginning of session 1. The analysis of EEG data will follow focusing on feature extraction in relation to the performance of each emotion and mapping these to control parameters of audio or visual BCMI output.

VISUAL HALF-FIELD PARADIGM: HOW WE CAN USE THIS TOOL TO DETERMINE THE LATERALIZATION OF WORKING MEMORY AND FOREIGN LANGUAGE PROCESSING?

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Background and aim:

The visual half field paradigm is a well-established measure to evaluate functional hemispheric laterality of cognitive functions. It is well known that visual stimulus can be processed more efficiently if it is projected directly to the specialized hemisphere. Verbal stimuli presented in the right visual field (RVF) are processed faster and more accurately, indicating that left cerebral hemisphere (LH) is dominant in language processing. However, knowledge about lateralization of foreign language is limited. Even less is known about lateralization of visual working memory (VWM). We investigated hemispheric asymmetry of foreign language and VWM processing by assessing participants' behavioural metrics (response accuracy, reaction time, laterality index), evaluating links between language and VWM, the effect of handedness and sex.

Materials and methods:

81 volunteers (27 men) performed the translingual lexical decision task (TLDT), VWM task and completed the Edinburg Handedness Inventory. Each trial in TLDT consisted of two 100 ms duration stimuli, either word or non-word, that were presented simultaneously for both the RVF and LVF. Participants had to decide whether a meaningful word was presented in the LVF or RVF or non-word in either side. In VWM task, trials consisted of four types of displays: a fixation display, a cue display (arrow indicating in which VF the change may appear), a memory sample display (from 3 to 5 letters in each VF), and a memory test. Participants had to recall and decide if there was a change of letter in the RVF or LVF depending on the cue.

Results:

Accuracy in TLDT task was higher for RVF/LH than LVF/RH ($p < 0.05$). In the VWM task, memory capacity and accuracy were higher and reaction was faster in the RVF/LH than in LVF/RH ($p < 0.05$). The greater memory capacity was linked with higher accuracy in both visual fields in VWM task ($r > 0.64$, $p < 0.001$) and higher accuracy in the LVF/RH in TLDT ($r = 0.24$, $p = 0.03$). However, there was no significant relationship between laterality index in TLDT and VWM task.

Conclusions:

We showed that the left hemisphere dominates for foreign language and VWM processing. There was no direct correlation between laterality indexes in language detection and VWM tasks.

AGE-RELATED DIFFERENCES OF PORCINE ATRIAL INTRACARDIAC GANGLIA

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Background and aim:

Intracardiac ganglia (ICG) is important component of the regulation of heart rhythm and contractile properties. Neurochemical phenotype and morphology of ICG neurons play important role in this regulation. For example, adrenergic system is known to increase heart rhythm and younger animals usually demonstrate higher heart rhythm compared with older. However, the knowledge whether this translates to ICG neuronal phenotype is limited. We investigated if age-related differences of adrenergic and nitrergic phenotypes exists in porcine atrial ICG.

Materials and methods:

Hearts from 11 adult pigs and 8 newborn piglets were used in the study. Whole-mount preparations of epicardium from five atrial regions were double labelled for choline acetyltransferase (ChAT) and tyrosine hydroxylase (TH) or nitric oxide synthase (nNOS) using immunohistochemical procedures and imaged using confocal microscope.

Results:

Newborn piglet atrial ICG contained markedly more biphenotypic neurons positive for both ChAT and TH (ChAT+/TH+) (16.2 %) than adult pig (3.6 %) and those positive only for TH (ChAT-/TH+) (12.8 % and 0.1 %, respectively). Comparing abundance of small intensely fluorescent (SIF) cells, positive for TH, clusters also revealed age-related differences. 20.8 % of newborn piglet and 4.5 % of adult pig atrial ICG contained at least one SIF cells cluster. Differences of nitrergic phenotype were not so marked, as neurons positive for nNOS constituted 6.9 and 3.7 % of all neurons within younger and older animals, respectively.

While ChAT+/TH+ and ChAT+/nNOS+ neurons were evenly distributed across newborn piglet atrial regions, adrenergic phenotype was more abundant within right atrium and nitrergic within dorsal atrial regions of adult pig.

Overall, adult pig possessed more than twofold bigger neurons compared with younger conspecifics. ChAT+/TH-, ChAT+/nNOS+ and ChAT+/TH+ neurons of newborn piglet and ChAT-/nNOS and ChAT+/nNOS+ neurons of adult pig atrial ICG were the biggest.

Conclusions:

These findings show that abundance of adrenergic neurons and clusters of SIF cells in porcine atrial ICG decreases with the age which is consistent with the decreased heart rhythm in older animals and size of neurons increases unevenly depending on phenotype.

INVESTIGATION OF THE EFFICIENCY OF MICROGLIAL EXOSOMES AS A DRUG DELIVERY SYSTEM

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Background and aim:

Glioblastoma is the most aggressive form of brain cancer with poor survival. In vitro studies showed that doxorubicin is toxic to glioblastoma cells, however, it cannot cross the blood-brain barrier. Immune cell-derived exosomes are nanosized membrane vesicles, able to recognise cancer cells and cross the blood-brain barrier, thus, can be used as anticancer drug delivery system. Microglia are the main immune cells of the brain, and exosomes of these cells have not yet been explored as drug vehicles. This study aimed to investigate the effects of natural and doxorubicin-loaded microglial exosomes on glioblastoma cells.

Materials and methods:

Exosomes were measured and counted by dynamic light scattering, visualised by transmission electron microscopy, and marker-identified by ELISA. The uptake of exosomes into human glioblastoma cells was visualized by fluorescence microscopy. Electroporation was used to load microglial exosomes with doxorubicin. Viability of human glioblastoma cells HROG36 was tested by PrestoBlue fluorescent assay and plate reader, apoptosis and necrosis levels were assessed by staining with Hoechst/propidium iodide and Cell Event Caspase-3/-7 Detection reagent followed by fluorescence microscopy.

Results:

The size range of isolated microglial exosomes was 60-90 nm, their morphology corresponded to a typical exosome and they were positive for exosome marker CD9. Exosome uptake studies revealed that exosomes can be internalized by glioblastoma cells in 2 hours and remained inside the cells for at least 24 hours. Doxorubicin-loaded exosomes reduced the viability of glioblastoma cells more efficiently compared to the same amount of free doxorubicin. Moreover, natural microglial exosomes exhibited a cytotoxic effect against glioblastoma cells.

Conclusions:

The study suggests both naïve and doxorubicin-loaded microglial exosomes as potential therapeutics for glioblastoma treatment.

ANTIOXIDANT ENZYME STATUS IN MOUSE BRAIN AND LIVER: THE EFFECTS OF LONG-TERM SUPPLEMENTATION WITH ALUMINUM OR SELENIUM

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Background and aim:

The aim of this work was to investigate the effects of Al or Se on the "primary" antioxidant defense system (the enzymes catalase, superoxide dismutase and glutathione reductase) in cells of mice brain and liver after long-term (8 weeks) exposure of drinking water supplemented with $AlCl_3$ (50 mg or 100 mg Al/L of drinking water) or Na_2SeO_3 (0.2 mg or 0.4 mg Se/L of drinking water).

Materials and methods:

The experiments were done on 4-6-week-old BALB/c laboratory mice (male) weighing 20-25 g. The activities of the antioxidant enzymes (CAT, SOD and GR) in homogenates of mice brain and liver were determined spectrophotometrically. The concentration of protein in the organ's homogenates were measured by Warburg-Christian method. Results were expressed as the mean ± SEM.

Results:

Results have shown that higher dose of Se increased the activities of SOD and CAT in mouse brain and liver. Exposure to lower dose of Se resulted in an increase of CAT activity in mouse brain, but did not show any statistically significant changes of SOD activity in both organs. Meanwhile, the administration of both doses of Al caused no changes in activities of these enzymes in mouse brain and liver. The greatest sensitivity to the effect of Al or Se was exhibited by GR. Exposure to both doses of Al or Se resulted in statistically significant increase of GR activity in both brain and liver.

Conclusions:

Exposure to drinking water supplemented with Na_2SeO_3 (0.2 mg or 0.4 mg Se/L of drinking water) resulted in an increase of antioxidant potential in mouse brain and liver through enhancing the activities of SOD, CAT and especially GR, which plays a pivotal role in maintaining the redox state of the cell. Exposure to both doses of $AlCl_3$ (50 mg or 100 mg Al/L of drinking water) resulted in statistically significant increase only in brain and liver GR activity, but caused no changes in activities of SOD and CAT.

BEAUTY AS A FACTOR OF INTERNET ADDICTION

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Background and aim:

In this study, our aim is to examine the influence of beauty on internet user inclination toward active viewing of images. The investigations of eminent representatives of neuroaesthetics S. Zeki, A. Chatterjee, V. Ramachandran et al. revealed, respectively, the reaction of some areas of the brain to the experience of beauty. Special attention is paid for the active role of the reward and pleasure centers of the brain in the cases of aesthetic experience of beauty.

Materials and methods:

Review of the latest observations and innovations in neuroaesthetics. Qualitative meta-analysis.

Results:

Presented below are two basic neurological assumptions related to a better understanding of the role of beauty as a determinant for internet addiction.

1. Taking into account that our brain automatically responds to beauty by linking vision and pleasure, this quality is exploited by many images provided by internet. For instance, attractive faces activate parts of our visual cortex in the back of the brain (fusiform gyrus, lateral occipital complex) as well as parts of our reward and pleasure centers in the front and deep in the brain (ventral striatum, orbitofrontal cortex, ventromedial prefrontal cortex) which just underpin the experience of beauty. Moreover, e.g., experience of music lights up the parts (different groups of cells) in medial orbitofrontal cortex (mOFC) as well as in adjacent cingulate cortex. If person experiences an uncontrollable repetition compulsion to view attractive (beautiful) digital images, including pornography, he/she earlier or later might be condemned for behavioral addiction.

2. The whole complex of the most lookable images is significantly enlarged by such quality of visual perception of beauty as abstraction. Recently, more and more results have been proved that when we experience beauty, regardless of whether it was from auditory or visual source, we always get activity in the mOFC that is a part of the reward and pleasure centers of the emotional brain. Consequently, the user of internet gets a very big possibility to choose multiple attractive photos, pictures, music, moves or short films supplemented by pleasant conversations and text messages. Thus, in today's imagery saturated world consumption of beautiful images in most cases becomes immoderate or excessive. As a result, such habit model of internet user can cause some serious problems of behavioral addiction.

Conclusions:

The neurological evidence suggests that idea of beauty can be considered in many aspects as a determinant for internet addiction which, respectively, might become a hindrance for the user of internet to have social relations, to learn or to work. If somebody wishes to safe personal independence from internet, they certainly have to monitor their media habits and reasonably reduce their liking for glamorous images.

MAGNO- AND PARVOCELLULAR SYSTEMS AND COGNITIVE FUNCTIONING IN SCHIZOPHRENIA

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Background:
The both the magnocellular and parvocellular systems (mechanisms of global and local analysis) is the basis for building a complete and realistic picture of the world, planning, choosing appropriate strategies in solving problems and regulating behavior. The magnocellular and parvocellular neural systems are differently sensitive to spatial frequency: the magnocellular system – to low spatial frequencies, parvocellular system – to high frequencies.

Materials and methods:
We used the visocontrastometry and methods of experimental psychological assessment of mental disorders – the Poppelreiter figure, Incomplete figures, TMT, 10 words test, Elimination of excess, Comparison of concepts, Similarity. Mathematical statistics were calculated with the STATISTICA10 using the Mann-Whitney test, the Spearman correlation analysis and regression analysis. The study included 68 patients with schizophrenia; the average age 34±12 years (51 male, 21 female). The participation went on terms of voluntary informed consent of the patient him/herself.

Results:
It was shown that all memory indicators, including delayed reproduction, have a statistically significant direct correlation with contrast sensitivity in the low spatial frequency range that the magnocellular system is specific (global analysis). The delayed reproduction was correlated with contrast sensitivity in the high spatial frequencies range (r=0,60), that is specific by the parvocellular system (local analysis). The results of the regression analysis indicate about a high coefficient of determination of memory indices and contrast sensitivity in the range of low and high spatial frequencies. At the same time, the greatest contribution to the effectiveness of delayed reproduction is made by the contrast sensitivity in the high spatial frequency range. A direct correlation was established between contrast sensitivity in the range of low (r=0,75), medium (r=0,56) and high (r=0,40) spatial frequencies with the number of correctly completed images in the "Incomplete images" and, accordingly, the inverse correlation with the number of incorrectly completed images (low (r=-0,81), medium (r=-0,64) and high spatial frequencies (r=-0,57)). In addition, the contrast sensitivity in the low spatial frequency range shows a pronounced direct connection with the number of recognized images in the Poppelreiter figure (r=0,50).

Conclusions:
Activity of magnocellular system is associated with peculiarity of working memory, the properties of attention, abstraction processes. Decrease of activity of the parvocellular system is accompanied by a violation of the selectivity of attention, abstraction and categorization, selection of significant signs in the perception of visual information.

MENTAL REPRESENTATION OF NUMBERS CAN BE TRAINED WITH THE COMPUTER MATHEMATICAL GAME IN CHILDREN WITH DEVELOPMENTAL DYSCALCULIA – PRELIMINARY RESULTS

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Background and aim:

Various neuroimaging, behavioral and clinical studies revealed a crucial role of parietal cortex in processing of numbers. Atypical development and structure of thus region results in developmental dyscalculia. Many studies confirmed the benefits of a cognitive training using computer games and the modern technology in math education and therapy of dyscalculia observed both on behavioral and neuronal level. The aims of our premilinary study was to examine the effect of such training with computer math game on the level of basic mathematical abilities in children with dyscalculia as well as to compare their numerical competences with healthy control group.

Materials and methods:

Forty-two children participated in the study. They were divided into 2 groups: 1st group – children diagnosed as dyscalculic (DD, N=21) and 2nd group (N=21) were typically developed children (TDG). We measured basic numerical abilities in both groups. Then, 7 participants from the 1st group were training with "Kalkulilo" game. Training took 5 hours, divided into 10 sessions. After training we measured the level of basic mathematical abilities again.

Results:

The results showed in DD group, as compared to TDG, lower percent of correct responses and increased reaction time in numerosity estimation, number comparison and numerical Stroop tasks as well as worse precision in number line estimation tasks. Furthermore we demonstrated the positive effect of training on the level of number competences in comparison of numbers presented in different.

Conclusions:

Due to the small study sample the conclusions based on the obtained results are preliminary, however they suggest clear differences between groups and promising effect of cognitive training in DD children. Moreover we can concluded that "Kalkulilo" may be a valuable tool not only in math education but also it could be helpful e.g. in overcoming the cognitive deficits observed in dyscalculia.

INTELLICAGE TRAINING SYSTEM TO STUDY BINGE-LIKE ALCOHOL DRINKING AND TRANSITION TO ADDICTION IN MICE

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Background and aim:

Alcohol use disorder (AUD) is a neuropsychiatric disease that combines behavioral, psychosocial, and neurobiological aspects. Modeling the complexity of AUD requires a compilation of different behavioral animal models. More sophisticated models capture addiction-related behavioral aspects, such as alcohol craving, compulsive seeking and intake, dependence, and relapse. Models of heavy alcohol use and binge alcohol drinking patterns, which can emerge prior to the onset of dependence, focus on pharmacological relevant blood ethanol concentration without getting insight into behavior. The aim of the present study was to design a binge-like alcohol drinking model adapted for IntelliCage training system.

Materials and methods:

Here we used IntelliCage training system to model different aspects of both binge alcohol drinking in mice and further selected addiction-like behaviors in the same subjects. IntelliCage is a fully automated home cage allowing studying long term activity (up to many weeks) and consumption patterns in mice living in a social group. Each mouse is implanted with subcutaneous transponder and can be monitored and characterized individually. To model binge-like drinking we adapted "drinking-in-the-dark" model.

Results:

Mice were allowed to consume voluntarily alcohol but only for limited time during the dark phase of their cycle. We monitored alcohol consumption and activity of animals. After this training, some mice acquired addiction-like traits such as increased craving or motivation to obtain alcohol when access to alcohol was limited or required additional effort. We estimated alcohol consumption that was relevant for binge-drinking protocols.

Conclusions:

Our study provides a framework to examine different aspects of heavy drinking and its long term behavioral implications that may lead to addiction.

THE LINK BETWEEN THE INDIVIDUAL DIFFERENCES IN AUDITORY STEADY-STATE RESPONSE AND EXECUTIVE FUNCTIONS

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Background and aim:
The auditory steady-state response (ASSR) represents the synchronized neural activity elicited by a periodic auditory stimulus. Research demonstrates potential link between gamma-band ASSR and cognitive functions, yet there is a gap in consistency of these results. We aim to examine the relation between the gamma-range ASSRs and executive functions.

Materials and methods:
The data was collected from 46 subjects of both genders using 64 channels EEG. Before recording, the Global-Local (GL), Digit span backward (DSb), Bivalent shape (BST) and Tower of London (ToL) tasks were performed. The stimulus applied during the recording consisted of single clicks presented in a log manner within a changing (by 1 Hz) frequency window starting at 30 Hz, increasing to 60 Hz, and then going back to 30 Hz. Following pre-processing and time-frequency transformation, the peaks of the individual gamma frequency (IGF) were extracted from phase-locking index (PLI).

Results:
Both individual gamma frequencies and corresponding PLI maximums correlated between chirp-up and chirp-down parts ($p < 0.05$). Moreover, for both chirp parts there were matching negative correlations between the PLI maximums and the performance time on the GL ($p < 0.01$) and BST ($p < 0.05$) tasks as well as positive correlations with the number of correct answers on the GL task ($p < 0.05$). Finally, there was a positive correlation between the PLIs of the increasing frequency part of the chirp and move time on the TOL task ($p < 0.05$) and a negative correlation between the decreasing part of the chirp and the DSb capacity ($p < 0.05$).

Conclusions:
Our preliminary findings suggest that both changing frequency parts of the chirp stimulus are similarly entraining the brain activity as the response values are correlated. Furthermore, the correlations shown with the GL and BST tasks might suggest the relation between the ASSR phase-locking and certain executive functions, where lower phase synchrony would indicate slower information processing and lower number of correct answers. However, the associations found with the frequency peaks are contradictory.

THE EFFECT OF WORKER BEHAVIOURAL STATUS AND INTRA-TRACHEAL ADMINISTRATION OF INOTOCIN ON BEHAVIOUR OF WORKERS OF THE ANT FORMICA CINEREA DURING DYADIC NESTMATE RESCUE TESTS

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Background and aim:

The aim of this work was to investigate the effects of intra-tracheal administration of inotocin, an insect orthologue of the neurohormone oxytocin, on behaviour of workers of the ant Formica cinerea during dyadic nestmate rescue tests. Oxytocin is known to influence social behaviour of many animals including humans, but the role of inotocin in the mediation of insect behaviour remains very little known.

Materials and methods:

We used as subjects foragers of F. cinerea collected in the field and then kept in laboratory nests. We used both extranidal workers (= foragers that continued to engage in outside-nest activities) and intranidal ones (=.foragers that switched to staying in artificial nest chambers). We administered intra-tracheally to the tested ants either 2 x 0.2 µl of 0.6% saline or 2 x 0.2 µl of inotocin (1 µg /1 µl) dissolved in 0.6% saline. Each of these ants, the rescuers, was then subjected to a 10 min confrontation with a nestmate victim immobilized in an artificial snare (the so called dyadic nestmate rescue test). Each test was video recorded. The behaviour of 41-44 rescuers was analyzed in each of the four experimental groups.

Results:

Inotocin administration was followed by significant shorterning of the latency from the start of the test to the onset of the so called company keeping behaviour (a close physical contact of the rescuer with the victim). However, that effect was observed only in the case of extranidal workers. The rate of occurrence of numerous other behaviour patterns carried out close to the victim was also significantly higher in extranidal workers than in intranidal ones.

Conclusions:

Inotocin administration exerted a stimulatory effect on pro-social behaviour displayed by the tested ants in response to an endangered nestmate. However, that effect was present only in the case of extranidal workers. Many other responses to the victim were also more strongly expressed in extranidal ants than in intranidal ones.

SELF-EFFICACY AMONG ATHLETS – SPOTTING THE DIFFERENCES

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Self-efficacy, as defined by Albert Bandura, is a belief about one's competence to cope with difficult or new situations, overcome difficulties and get the desired results of one's actions. Previous research showed significant correlation between sport and self-efficacy (Inoue et al., 2015; Laborde et al., 2015; Eime et al., 2013). An athletes' perceived self-efficacy may be reinforced by a vicarious experience while they're watching other successful athletes. It can be also reinforced by the verbal persuasion of authority, which can be a coach. Other sources are social learning and personal experience. The aim of the study was to measure self-efficacy among the athletes and spot anticipated differences. High level of self-efficacy was hypothesised. As the same experience may have various effects on people, individual differences were expected.

116 athletes in the age from 18 to 40, including 67 males and 46 females, from both individual and team sports were examined using Generalised Self Efficacy Scale. They also answered additional questions about practiced sports, training experience, eventual breaks and the reasons behind them, injuries and sports achievements.

Data analysis showed that athletes who have experienced some injuries in the past perceive themselves as more self-efficient (M=32,75 SD=3,15) than those who haven't (M=31,11 SD=3,69) t(113)=-2,53 p=0,013. There was positive correlation between self-efficacy and the amount of sports achievements. The main effect of the gender revealed higher self-efficacy among women (M=32,76 SD=0,76) than men (M=30,69 SD=0,63). The interaction of gender and the training experience was detected F(1)=4,51 p=0,036. Women's percieved self-efficacy was increasing faster and was higher than men's while the training experience was short. However after minimum 3 years of training experience, those differences seem to fade.

As the results concerning injury show, experience may be perceived and interpreted in various ways. Something that for some people may seem like a failure, could actually reinforce one's self-efficacy.

NEUROELECTRIC MICROSTATES AND SUBJECTIVE EXPERIENCE: A PILOT STUDY ON FIVE MICROSTATE CLASSES

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Background and aim:

One of the options to evaluate resting-state electroencephalogram (EEG) is to apply microstates approach where the recorded oscilations are defined as „states" of the signal that evolve over time. These brain electrical microstates qualify for basic building blocks of mental end emotional processes, and their temporal properties can be modulated by various conditions and subjective experience.

In the previous study, using 4 canonical microstates (A, B, C, D), Pipinis et al. (2016) showed correlation between contribution of microstate C and somatic aweraness. However, based on methodological literature, when only 4 microstates are used, spatially similar but functionaly different microstates are merged into a single microstate class C. In this pilot study, we aimed to capture activity of more microstates and relate them to different subjective expereinces during resting state.

Materials and methods:

5 min. eyes-closed resting state EEG data from 46 participants were collected using 64 channels EEG. After the recording, participants filled in Amsterdam Resting-State Questionnaire (ARSQ). EEG was subjected to microstates analysis where topographies at Global Field Power (GFP) peaks were submitted into k-means algorithm. Based on Silhouette value, the optimal number of clusters was identified as 5. Duration, occurrence, contribution and transition probabilities were calculated for each of 5 microstates. Spearman correlation between microstates parameters and scores on ARSQ categories were calculated.

Results and Conclusions:

Extracting more than 4 microstates classes we showed that spatially similar topographies, microstate C and microstate E, display distinct correlation patterns with different subjective experiences during the resting state. Furthermore, we showed correlation between activity of microstate C and E. Our result confirms that the optimal number of clusters should be estimated for each dataset using optimization criteria, rather than choosing a fixed number based on literature.

INHIBITOR OF ATP SYNTHASE BEDAQUILINE IS ABLE TO REDUCE ISCHEMIA – REPERFUSION CAUSED BRAIN INJURY

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Background and aim:

Ischemic stroke is one of the leading causes of death and disability in developed countries and available treatments are limited to a small percentage of patients. Novel neuroprotective drugs are currently studied extensively because they have potential to improve functional recovery from stroke thus improving quality of life for patients. Since ischemia – reperfusion (I/R) injury is closely related to mitochondrial dysfunction and the opening of mitochondrial permeability transition pore (mPTP), mitochondria are an attractive target for neuroprotective strategies. In this study, we sought to investigate whether inhibition of ATP synthase – a major component in energy metabolism also involved in the opening of mPTP – can protect against brain I/R injury. Thus, we tested the effect of ATP synthase inhibitor bedaquiline (BDQ) on the outcomes of I/R (infarct area, neurological impairement and mitochondrial functions) in rats.

Materials and methods:

Rats were subjected to 60 min of middle cerebral artery occlusion (MCAO) vith endovascular suture following with 24 h reperfusion. Single dose of 2mg/kg BDQ (or vehicle) was given to the rats 60 min before MCAO surgery. After reperfusion rats were killed by CO_2 gas and brains were removed. We evaluated the size of infarct by 2,3,5-triphenyl-tetrazolium chloride staining in coronal brain slices. Neurological impairment was investigated using the original Longa et al methodology. Mitochondrial respiration was measured using high-resolution respirometry and calcium retention capacity (CRC) was measured using fluorescent dye Calcium Green 5N.

Results:

Our results indicate that a single dose of BDQ is able to reduce infarct size by half and reduce the neurological impairment score by 36%. Mitochondrial respiration with pyruvate, malate and succinate as substrates was reduced in the MCAO group compared to control by 38 % and BDQ improved respiration to control levels. CRC in the MCAO group was reduced by 45 % compared to control, however BDQ did not improve CRC.

Conclusions:

Inhibition of ATP synthase with BDQ has neuroprotective effect against I/R injury through its action on mitochondria however it does not inhibit I/R-induced opening of the mPTP.

FRONTAL ALPHA ASYMMETRY IN EMOTION REGULATION

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Background and aim:

Frontal alpha asymmetry (FAA) is defined as the difference between right and left alpha activity over frontal regions of the brain. Recent studies show that resting state FAA could predict emotion regulation difficulties. In the present study, we aimed to examine how resting state frontal alpha activity is related to emotion regulation as a trait and a state.

Materials and methods:

34 women (27.8 ± 4.5 years) were instructed to just view or use reappraisal strategy to downregulate or upregulate negative emotions towards low and high intensity negative images. Participants rated the perceived negativity after each image using Visual Analog Scale. Resting state electroencephalogram (EEG) was recorded for 3 minutes before and after the emotion regulation task. Absolute alpha scores were calculated for left (F3) and right (F4) frontal electrodes. FAA index was calculated using the formula Ln(F4)-Ln(F3). Greater FAA indicates higher left side frontal activity. Participants' habitual use of reappraisal and suppression strategies was evaluated using the Emotion regulation Questionnaire. Alexithymia was assessed using Toronto Alexithymia Scale.

Results and Conclusions

The preliminary analysis of the study results revealed that: i) participants preferred cognitive reappraisal strategy for emotion regulation over expressive suppression, and none of them were alexithymic; ii) women had diverse FAA index, indicating mixed predominant frontal activity between study participants; iii) perceived negativity values were lower in down regulation, and higher in up regulation compared to view condition; iv) the change of perceived negativity values in down regulation condition correlated negatively with the FAA index, suggesting that the higher left frontal activity is related to better down regulation of negative emotions using reappraisal strategy; v) FAA tended to correlate negatively with alexithymia scores, indicating that alexithymia was more expressed in individuals with more active frontal right.

THE EFFECT OF WHOLE-BODY HYPERTHERMIA ON COGNITIVE FUNCTIONING IN OLDER AND YOUNG MEN

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Background and aim:

Due to the thermoregulatory of our body, we can maintain consistent body temperatures around 35.5 °C and 37 °C and keep physiology homeostasis. However, numerous evidence illustrated that older adults are lower in core body temperature (rectal; Tre) than the young adults. In line with this, age-related response to heat stress might be delayed in aged adults. We tested the hypothesis that severe whole-body hyperthermia (Tre increased about 2.5°C) may lead to a greater depression in cognitive functioning in older men than in young men.

Materials and methods:

Eleven young (19–21 years) and nine older (61–80 years) healthy subjects volunteered for this study. They were immersed in approximately 43° C waist line hot water(HI) until young men Tre to 39.5 °C, older men Tre to 39°C, separately. To access cognitive performance (short term memory, visual recognition memory and executive function), the Automated Neuropsychological Assessment Metric (ANAM4, Oklahoma, USA) was used.

Results:

Though no significant hyperthermia-induced test durations and memorable figures in forced-choice recognition memory test were observed, a decrease number of memorable figures was found to be greater in older than in young men. In older men, whole-body heating was accompanied by a significant decrease in mean reaction time in unpredictable task switching of the odd/even numbers, in parallel with a greater increase in repeating numbers. In young men, mean digit length was dropped significantly in the forward digit-span task whereas it was no significant difference in the older men.

Conclusion:

Despite delayed and weakened thermoregulation and age-related decline in cognitive function, executive functioning in whole-body severe hyperthermia is increased apparently in healthy aging.

CONVOLUTIONAL AUTOENCODERS FOR TEXTURE ANALYSIS AND VISUAL SALIENCY MODELING

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Background and aim:

Our work is devoted to creating the neural network models of the Second Order Visual Mechanisms (SOVM). These mechanisms detect spatial modulations of contrast, orientation and spatial frequency in an image. The main goal of this work was to train fully convolutional autoencoders for decoding these modulations.

Traditionally, SOVMs are seen as a mechanisms for texture segmentation. Currently, SOVMs are of interest to researchers in the context of studying visual attention and developing saliency models. Areas of spatial heterogeneity are potential targets of attention and/or fixational eye movements. SOVM models can be used to identify these targets in an image.

Materials and methods:

Keras library and Python language were used in the modeling. The training was conducted on modulated textures synthesized from Gabor micropatterns. The spatial-frequency spectra of these artificial images were broadband and similar to spectra of natural images. The modulation frequency was high and varied slightly. Models were trained to extract the modulating function values from training textures.

Results:

We obtained good learning accuracy for convolutional autoencoders specific to modulated feature. Kullback-Leibler divergence (KL) and Pearson's correlation coefficient (CC) were used as learning quality metrics. We got KL=0.007 and CC=0.946, KL=0.006 and CC=0.962, KL=0.009 and CC=0.933 for autoencoders which are specific to contrast, orientation, and spatial frequency modulations respectively.

Conclusions:

The fully convolutional architecture of our models makes it possible to process images of different sizes. The high modulation frequency to which the network is tuned makes it easier to process images at different spatial frequencies using a simple resize operation. Preliminary results show that our models can be used as inputs to network that generate salience maps. Our models have a few parameters and can be easily adapted to run on inexpensive neural processors.

THE EFFECT OF POST-STROKE METFORMIN TREATMENT USING PERMANENT MIDDLE CEREBRAL ARTERY OCCLUSION IN RATS

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Background and aim:

Stroke is the second leading cause of death worldwide, but the treatment has limited effectiveness. Thus, the development of new neuroprotective agents or combined therapies is imperative. It was shown that pre-treatment with metformin (Met) has neuroprotective effect against ischemia induced brain damage, but the post-conditional effect of Met requires further investigation. The aim of this study was to evaluate the impact of Met treatment on infarct size and microglial activation after permanent middle cerebral artery occlusion (pMCAO).

Materials and methods:

Adult male Wistar rats (N=23) were divided into 3 groups: rats receiving intraperitoneal Met injections (50 mg/kg/day) or equal volumes of saline injections (pMCAO group) and the control sham-operated (skin incision only, without occlusion of MCA). Rats were sacrificed after 48h post-occlusion. Injection of Met or saline was initiated immediately after pMCAO and was repeated every day until sacrifice, which was 2 times based on time of stroke. Then rat brain was sliced. The infarct size was measured by TTC staining. Total number of microglia was evaluated using isolectin-IB-4 conjugated with AlexaFluor488 and activated microglia was labeled immunohistochemically using anti-IBA-1 antibody. Average cell numbers were calculated at the 5 randomly selected microscopic fields of the contralateral, ipsilateral striatum using ImageJ software.

Results:

The infarct size after pMACO was $20\pm2\%$ of infarct size and after treatment with Met was similar to note in the pMCAO group. In the pMCAO group a total number of microglia was 78 ± 3 cells/field and number of activated microglia was 44 ± 3 cells/field. The number of isolectin-IB-4 and IBA-1 positive cells decreased up to 39 ± 4 and 18 ± 3 cells/field after treatment with Met, respectively ($p<0.005$).

Conclusions:

Post-stroke Met treatment in pMCAO rat model has no effect on infarct size, while it reduces pMCAO induced microglial proliferation and activation.

CBDA CONTROL OF NEURONAL HYPEREXCITABILITY AND THE OVERALL THERAPEUTIC POTENTIAL OF ACIDIC CANNABINOIDS

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Background and aim:

In cannabis, the most prevalent phytocannabinoids Δ9-tetrahydrocannabinol (THC) and non-psychotropic cannabigerol (CBG) and cannabidiol (CBD) are biosynthesized and accumulated as in their acid forms – THCA, CBGA, and CBDA. The acidic cannabinoids commonly undergo non-enzymatic decarboxylation into their neutral forms during extraction, storage, or heating processes. In comparison to THC and CBD, acidic cannabinoids remain understudied. This poster summarizes and highlights recent literature and original experimental evidence on biological actions of non-psychoactive acidic cannabinoids.

Methods:

In our experiments, in vitro electrophysiology was used to study effects of acidic cannabinoids on neuronal excitability and seizure-like activity in juvenile (P20-P30) rat brain slices. Whole cell recordings were performed in the hippocampal CA1 pyramidal cells. Seizure-like activity was induced using low magnesium model of seizures.

Results:

We report new original experimental findings on the effects of the acidic cannabinoids on the in vitro neuronal synaptic transmission using whole-cell neurophysiology in juvenile rat brain slices. CBDA was equally as effective as CBD at controlling neuronal excitability and seizure-like activity.

Conclusions:

We emphasize that overall in vivo and in vitro data on activity of non-psychotropic acidic cannabinoids is promising. Further studies are warranted and necessary to unravel their full therapeutic potential in humans. Like other cannabinoids, acidic cannabinoids may become increasingly more important components of the future cannabis-based nutraceutical and pharmaceutical formulations.

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