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ABSTRACTS

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I. ORAL PRESENTATIONS

Scientific session "NEUROANATOMY, NEUROPHARMACOLOGY AND NEUROTOXICOLOGY"

OP1. CHEMICAL NEUROANATOMY OF THE RAT CAROTID BODY

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Background: The carotid body (CB) is a small, paired, neural crest-derived neuroendocrine structure that helps for the maintenance of the chemical composition of arterial blood by a control of ventilation. The CB parenchyma is organized in clusters of cells called glomeruli, which are in close association with a profuse network of capillaries, and afferent sensory fibers joining the glossopharyngeal nerve. The most abundant cell type in the CB glomeruli are the neuron-like glomus or type I cells, which are enveloped by processes of glial-like sustentacular or type II cells.
Methods: The expression of putative neurotransmitters and their receptors in the rat CB was investigated at light microscopical level using immunohistochemistry.
Results: Our immunohistochemical studies revealed that glutamate-like immunoreactivity was associated with glomus cells, intraglomerular and periglomerular nerve fibers within and around the cell clusters and to a lesser extent with sustentacular cells. Many glomus cells and nerve fibers showed GABA-like immunoreactivity in the rat CB. Immunohistochemistry also revealed that type I cells displayed immunoreactivity for several biogenic amines. In particular, all the glomus cells were immunostained for tyrosine hydroxylase (TH), a rate-limiting enzyme of catecholamine synthesis. Most TH-immunoreactive cells also contained histidine decarboxylase, the histamine synthesizing enzyme, vesicular monoamine transporter 2, which is highly specific for histamine, and synaptosome-associated protein of 25 kDa that is a component of the neuroendocrine exocytosis apparatus. In addition, we were able to find that glomus cells were richly endowed with H1 and H3 histamine receptors. Moreover, some of them possessed 5-hydroxytryptamine immunoreactivity. At the light microscopic level, we observed some glomus cells typically aggregated in clusters and containing substance P (SP), vasoactive intestinal polypeptide (VIP) and methionine enkephalin (met-Enk). Furthermore, many nerve fibers penetrating the CB and enveloping the glomus cells, and some blood vessels were immunopositive for SP, VIP, met-Enk, neuropeptide Y and calcitonin gene-related peptide.
Conclusion: A striking feature of the CB is the presence of a wide variety of endogenous neuroactive substances, including the classical neurotransmitters and neuropeptides that have been proposed to play a role in the chemoreception processing.
This work was supported by the European Social Fund and Republic of Bulgaria, Operational Programme "Development of Human Resources" 2007-2013, grant BG051PO001-3.3.06-0048.

OP3. EFFECTS OF ANGIOTENSIN SYSTEM ON SEIZURE ACTIVITY, BRAIN DAMAGE AND DIURNAL BEHAVIOURAL CHANGES IN THE KAINATE MODEL OF TEMPORAL LOBE EPILEPSY: LONG-TERM INTRACEREBROVENTRICULAR INFUSION OF ANGIOTENSIN II

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Introduction: The brain renin-angiotensin system (RAS) has been suggested to be involved in pathogenesis of epilepsy [1, 2]. Our previous studies revealed that Angiotensin (Ang) II has anticonvulsant effects in acute seizure models [2]. However, data on its role in experimental models of epilepsy are missing. In the present study, we tested whether post-treatment with Ang II after kainate (KA)-induced status epilepticus (SE) can affect epileptogenesis, concomitant behavioral changes and brain damage.
Methods: Male adult Wistar rats (two-month-old) were repetitively injected with Kainate acid (KA) (2,5 mg/kg, i.p.) until induction of status epilepticus (SE). On the 5th day after SE, the rats were intracerebroventricularly (i.c.v.) infused via osmotic mini-pumps with Ang II (1.52 μg/ml/day for 28 days). The animals were divided into four experimental groups (n=10-14) as follows: Group I: control sham rats treated with vehicle (C-sham); Group II: control rats treated with AngII (C-Ang); Group III: sham rats treated with KA (KA-sham); Group IV: rats treated with KA+Ang II (KA-Ang). The KA-treated rats were video-recorded for up to three months for detection of spontaneous motor seizures (SMS). Locomotor activity (open field test, OF), anxiety (elevated plus-maze, EPM) and depressive-like behavior (sugar preference test, SPT) were evaluated during the last week of drug. Neuronal damage (major cell loss) in hippocampus was analyzed by hematoxylin.
Results: Long-term i.c.v. exposure to Ang II decreased the latency for onset of the first SMS and increased frequency of SMS two months after SE. Ang II infusion exacerbated the KA-induced hyperactivity in OF and caused depressive-like behavior in SPT. The reduced anxiety of KA-treated rats was alleviated by Ang II exposure. However, Ang II partially restored the neuronal damage in the hippocampus, mainly in the CA1 area.
Conclusion: Whereas the long-term i.c.v. infusion of Ang II after the KA-induced SE aggravated epileptogenesis and worsened behavioral changes including hyperlocomotion and depression it caused a neuroprotection in the CA1 area of the hippocampus. Our present results and previous findings on the effects of long-term AT1 receptor suggest that most of these responses are mediated through AT1 receptors activation in a phase-dependent mode and further confirm the hypothesis that these receptors have a pivotal role in the development of epilepsy.

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OP4. EFFECTS OF ANGIOTENSIN SYSTEM ON SEIZURE ACTIVITY, BRAIN DAMAGE AND DIURNAL BEHAVIOURAL CHANGES IN THE KAINATE MODEL OF TEMPORAL LOBE EPILEPSY: LONG-TERM LOSARTAN TREATMENT

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Introduction: The brain renin-angiotensin system (RAS) has been suggested to be involved in pathogenesis of epilepsy [1, 2]. Recently, we have shown that the blockade of AT1 receptor might be useful as an adjuvant treatment strategy for the prevention of oxidative stress and neurotoxicity caused by status epilepticus (SE) in rats. [3]. The purpose of the present study was to further assess the efficacy of long-term treatment with losartan (10 mg/kg), the selective AT1 receptor antagonist, during kainate (KA)-induced epileptogenesis inWistar rats.
Methods: Male adult Wistar rats (sixty-day-old) were repetitively injected with Kainate acid (KA) (2,5 mg/kg, i.p.) until induction of status epilepticus (SE). Losartan treatment (10 mg/kg/day in dringking water) started after onset of SE and continued for 4 weeks. Animals were randomly divided into four groups: Cveh (controls treated with vehicle, n = 10); C-los (rats treated with losartan, n = 10); KA-veh (rats treated with KA and vehicle, n = 13); KA-los (rats treatedwith KA and losartan, n=12). The KA-treated rats were video-recorded for up to three months for detection of spontaneous motor seizures (SMS). Locomotor activity (open field test, OF), anxiety (elevated plus-maze, EPM) and depressive-like behavior (sugar preference test, SPT) were evaluated 9 weeks after SE, when all rats had developed chronic epileptic state. Neuronal damage (major cell loss) in hippocampus was analyzed by hematoxylin.
Results: AT1 receptor antagonism increased the latent seizure-free period and decreased the frequency of spontaneous motor seizures. Losartan positively affected epilepsy-provoked behavioral changes, including impulsivity, low anxiety level and depression in a phase-dependent manner and restored the changes in diurnal fluctuation of motor activity. Long term Losartan treatment exerted neuroprotection selectively in the CA1 area of the hippocampus in the KA-treated rats.
Conclusion: Our findings suggest that the AT1 receptor antagonist exerts disease-modifying effects during KA-induced epileptogenesis and neuronal damage in CA1 hippocampal area, attenuated some of the behavioral changes and restored diurnal variability in locomotor activity.

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OP5. DESCENDING REFLEX MOTORITY OF COLONIC LONGITUDINAL MUSCLE – EXCITATORY AND INHIBITORY NEUROTRANSMITTER ACTIVITY IN RAT MODEL

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The neurotransmitter systems defining the colonic motor activity and the role of colon as storage or conduit intestinal organ are a matter of study. The pacemaker mechanisms for generation and propagation of the colonic motor complexes are preserved in isolated preparations in *in vitro* conditions indicating that the nerve pathways underlying the peristaltic ascending and descending motority are contained in the gut wall. Spontaneous or electrically-induced local and descending motor activity in the longitudinal axis of isolated colonic segment-model preparation were recorded in partitioned organ bath as a display of excitation of local nerve networks and descending reflex pathways. Spontaneous motority of the longitudinal muscle layer was characterized by irregular high-amplitudes contractions, but not relaxations, suggesting higher contractile activity than relaxation ability. Electrical field stimulation (0.8 ms, 40 V, 5 Hz, 20 s) applied to the distal or to the proximal part of the segment-preparations induced sensitive to the blocker of neural conductance tetrodotoxin (0.1 μM) local or descending contractions indicating the nerve-mediated origin of the responses. The local contractions were more expressed than the descending ones ($p<0.05$) showing that the nerve excitation declined depending on the distance away from the point of electrical stimulation application. The descending contractile responses decreased by amplitude and a relaxation revealed on the background of atropine (0.3 μM). The contractions were decreased more, but not eliminated, and the relaxation were enhanced when the antagonist of NK1 receptors spantide was (0.1 μM) additionally added to the bath solution, thus demonstrating that cholinergic and tachykininergic neurotransmissions are responsible, at least in part, for the descending contractile reflex motority. L-NNA (0.5 mM), an inhibitor of nitric oxide synthase, increased the descending contractile responses during atropine treatment and decreased the relaxation while L-Arginine (0.5 mM), a substrate of nitric oxide synthesis, decreased the contractile activity and deep the relaxation. These results indicated that in the rat-model excitatory cholinergic and tachykininergic and inhibitory nitrergic neurotransmitter activity control the descending reflex motority of colonic longitudinal muscle.

OP6. NEUROTOXICOLOGY STUDIES IN INSTITUTE OF NEUROBIOLOGY

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Some of the most valuable neuroscience research achievements are selected (40 years survey):

Saccadic eye movement, LSD25 and visual illusions

Can we explain the visual disturbances (illusions) in human after intake of LSD (potent agonist of central serotonin receptors) by some changes in peripheral visual functions? The velocity of saccadic eye movement in 4 males and 1 female subject before and after LSD

intake was not changed showing the central visual perception as the action place (*Mitrani, Mateeff et al.* 1972).

Social isolation syndrome and benzodiazepine receptors

Three-month isolation housing of Wistar rats induced in some of them aggressive behavior in respect to mice (muricide behavior). It was shown for the first time that this was accompanied by drastic decrease in the affinity and numbers of benzodiazepines binding sites in certain brain structures (cerebral cortex, hippocampus, midbrain and cerebellum) (*Petkov and Yanev* 1982). Benzodiazepines do not exert antiaggressive effects in Wistar isolated rats but inhibit the aggressive behavior of isolated mice. This could be explained by the fact that the decreased number of benzodiazepines binding sites in isolated aggressive mice was restored after benzodiazepines (medazepam) administration (*Tyutyulkova, Gorancheva et al.* 1986).

Pesticides, prenatal exposure and postnatal neurotoxicity

Albino rats antenatally treated with the dithiocarbamate fungicide Basfungin in doses which cause no great structural anomalies in the development of the brain and of the other organs and systems of the foetus, have shown dose-dependent decrease in the reactivity of central nervous system in the basic and the first generation. Less affected were male animals (*Mirkova and Yanev* 1976).

Phosphodiesterase inhibitors and blood brain barrier

The aporphine alkaloid Glaucine and its derivatives were shown to be high efficient inhibitors of phosphodiesterase activity in different organs including brain (*Petkov and Stancheva* 1980). Pretreatment of rats with Glaucine potentiate the increase of dopamine brain levels after consecutive l-DOPA administration by 30% (*Petkov, Yanev et al.* 1982). This fact could be explained by some changes in blood brain barrier permeability for l-DOPA based on the recent findings for specific tissue localization and selective inhibition by glaucine derivatives of phosphodiesterase IV isoform.

Xanthates and neuroprotection

From the first findings that different derivatives of potassium salts of dithiocarbonic acid (xanthates) inhibit hexobarbital metabolism in rat liver (*Mitcheva, Yanev et al.* 1976), the selective and powerful mechanism-based inhibitor of CYP 2B6 n-octylxanthate (C8) was developed (*Yanev, Kent et al.* 1999). This permits the use of C8 as efficient neuroprotective agent for some neurotoxins which requires CYP2B6 metabolic activation (chlorpyriphos, (*Khokhar and Tyndale* 2014).

Coda: "Share your knowledge with others. Thus achieve immortality." (*Dalai Lamas***)**

Scientific session "PSYCHOPHYSIOLOGY"

OP7. PERFORMANCE FLUCTUATIONS: A SIGNATURE BEYOND EXECUTIVE CONTROL

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The maintenance of stable goal-directed behavior is a hallmark of conscious executive control in humans. Here, we revisit this notion and demonstrate two sub-conscious sources of performance variability thus opening a look beyond executive control.

One source is related to the default mode network that, in contrast to attentional network, manifests intrinsic oscillations at very low (<0.1 Hz) frequencies. We analyzed the time dynamics of performance accuracy in attention deficit/hyperactivity disorder (ADHD) to

search for periodic fluctuations of error occurrence in the multisecond scale. Identifying periodic error fluctuations with a frequency <0.1 Hz in ADHD would provide a behavioral evidence for such interferences. Performance was monitored during a visual flanker task in 92 children (7- to 16-year olds), 47 with ADHD, combined type and 45 healthy controls. Using an original approach, the time dynamics of error occurrence was analyzed in the frequency and time–frequency domains in order to detect rhythmic periodicity. Major results demonstrate that in both patients and controls, error behavior was characterized by multisecond rhythmic fluctuations with a period of approx. 12 s, appearing with a delay after transition to task. Only in ADHD was there an additional 'pathological' oscillation of error generation, which determined periodic drops of performance accuracy each 20–30 s. Thus, in patients, periodic error fluctuations were modulated by two independent oscillatory patterns. The findings demonstrate that: (i) attentive behavior of children is determined by multisecond regularities; and (ii) a unique additional periodicity guides performance fluctuations in patients.

In another experiment, a visual serial reaction time task (SRTT) was trained by 108 subjects. Task structure comprised blocks with a hidden regularity of stimulus sequence (regular blocks) and blocks with random stimulus presentation (random blocks). Training was performed under implicit conditions, i.e., subjects were not aware about stimulus order in regular blocks. After an 8-h retention period, gain of explicit knowledge (ExK) about hidden regularities was tested. Strikingly, individuals gaining ExK about abstract regularity at test manifested a substantially different processing of regular sequences already at training characterized by increased performance variability and high error rate. Since these signs of 'distractability' in explicit solvers were not detected for random stimulation, a trait-dependent sensitivity to regularities is plausible, which modifies task processing strategy. It is suggested that explicit solvers have the ability to create rapidly an implicit representation of higher order regularities. At a fragile stage, this representation may induce inappropriate pre-activations interfering with task performance, but its subsequent stabilization promotes insight.

These observations may re-conceptualize the understanding of attentive behavior beyond the executive top-down control. They reveal new origins of psychopathological behaviors and extend our understanding of insightfulness. Increased behavioral variability in both normal and pathological conditions merits a new look.

OP8. REDUCED INTER-REGIONAL SYNCHRONIZATION OF OSCILLATORY THETA NETWORKS DURING ERROR MONITORING IN AGING

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Behavioural monitoring is accompanied by an increased activation of the mid-frontal brain encompassing the supplementary motor cortex and anterior cingulate cortex (Ridderinkhof et al., 2004). In the current research, it was hypothesized that this monitoring-related activation reflects the functioning of a distributed oscillatory network operating in the theta frequency range, which connects motor, sensorimotor, and pre-motor cortical regions with the mid-frontal brain. To explore the functional efficiency of a distributed theta network in aged individuals during performance monitoring, response-related potentials were recorded from young and older adults while they performed a choice-reaction task. Trials from correct and

error responses were analyzed at bi-lateral and mid-line fronto-central, central, and centro-parietal electrodes in the time-frequency domain. Spatial synchronization of response-related theta oscillations between FCz and other cortical regions was assessed by measuring phase-locking value (PLV). PLV was significantly larger over the hemisphere contra-lateral than ipsi-lateral to the responding hand and was maximal for pairs of electrodes at sensorimotor and motor regions. These lateral and regional asymmetries point to the existence of a functional connection between the medial frontal cortex and activated motor areas during response generation. Error responses were associated with a reduction of FCz-PLV at sensorimotor and motor cortical regions indicating reduced connectivity. However, only in older subjects, was the error-related reduction of FCz-PLV significant. It is concluded that increasing age in humans impairs error processing by suppressing the connectivity between medial frontal and sensorimotor regions.

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OP9. EXCESSIVE DAYTIME SLEEPINESS AND COGNITIVE DEFICIT

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The Syndrome of Excessive Daytime Sleepiness (EDS) acquires vivid attention – and apprehension – in recent days due mostly to its imminent relationship with another category – the quality of life. The extent of daytime sleepiness directly affects vigilance level and hence, performance. The initial vague feelings of tiredness and early morning headache are supplanted by heightened irritability, absent-mindedness, diminished libido, gaining of weight, and general fatigue. Medical specialists rarely estimate the principle cause and later on, with appearance of hypertension, edemas, obstructed breathing stray even further away from the righteous treatment. All these might eventually lead to unexpected strokes and heart attacks. In the meantime, the affected population continues to perform everyday routines and this accounts to about 30% of road accidents due to drowsy driving and falling asleep on the wheel. Occupational hazards and health insurances have cost the US budget more than $ 6 billion in 2011 by the mere fact that almost 70 million Americans were suffering the EDS Syndrome. Basically, the major culprits might be described as dissomnia - sleep disturbed breathing (SDB) and insomnia - inadequate sleep hygiene. Both cause sleep fragmentation and EDS. A golden standard for discerning a possible SDB affliction is the all-night polysomnography (PSG). Multiple physiological parameters could be recorded in the course of the sleep, namely: electroencephalographic activity (EEG), eye movements (EOG) and muscle tension (EMG). These three, taken together, are used for evaluation of sleep stages, sleep cycles and sleep architecture. The heart beats and the blood oxygenation are continually monitored as well as breathing efforts and the amount of air that gets through the upper airways. In cases of either upper airway resistance syndrome (UARS) or obstructive sleep apnea (OSA) the SDB provokes innumerable awakenings and total fragmentation of sleep during futile efforts to restore blood oxygen saturation. Since people do not possess a proper sense of whereabouts during bedtime, the ultimate EDS next day may go either unnoticed or unexplained. Neuropsychological testing could reveal the ominous chain of events: short-term and working memory lapses; retarded (inattention) and erroneous (lack of behavioral inhibition) responses; inadequate adaptation to changes in task model; problems in cognitive processing and contextual memory; unstable sustained attention; inadequate planning and

execution of directional behaviour; motivational inability; lack of emotional cohesion and impulsiveness. Actually, 80% of such patients present also with personality changes along the behavioral deficit. The method of choice is application of nasal constant positive air pressure via nCPAP devices that miraculously restore almost immediately all vital signs. The cognitive deficit comes to terms last late. These days particular attention is devoted to insomnias caused by either disorganized sleep pattern or by lack of sufficient sleep time. Those are substantiated by excessive texting, twitting and chatting, so mercilessly imposed upon young generations by modern technologies of Internet and mobiles. Physical harm from electromagnetic radiation is combined with elements of addiction and abstinence, a new malaise of contemporary society.

Reference

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OP10. DIFFERNT EFFECTS OF REM-SLEEP ON NEUROBEHAVIORAL FUNCTIONING IN CHILDREN WITH DEVELOPMENTAL PSYCHIATRIC DISORDERS COMPARED TO TYPICALLY DEVELOPING CHILDREN

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The precise functions of rapid eye movement (REM) sleep are still elusive, particularly in developmental psychiatric disorders. The present study aims at investigating the role of REM sleep in children with a broader spectrum of common psychiatric conditions, compared to typically developing children (TDC). Sixty-six children with attention deficit-hyperactivity disorder (ADHD: n =24), tic disorder (TD: n = 21) and ADHD/TD comorbidity (n = 21), and 22 TDC, matched for age and gender, underwent a two-night polysomnography (PSG), and their psychopathological scores and intelligence quotient (IQ) were assessed. Major PSG findings showed more REM sleep in children with psychiatric disorders than in TDC. Multiple regression analyses revealed that in all children with psychopathology, the elevated REM sleep proportion correlated positively with scores of inattention and negatively with performance IQ. In contrast, in the group of TDC, REM sleep proportion correlated negatively with scores of inattention and positively with performance IQ. Altogether, these results indicate different effects of REM sleep on neurobehavioral functioning, depending on presence or absence of developmental psychiatric disorders.

Keywords: REM-sleep; neurobehavioral functioning; children with developmental psychiatric disorders; TDC

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II. SHORT COMMUNICATIONS

Scientific session "NEUROANATOMY, NEUROPHARMACOLOGY AND NEUROTOXICOLOGY"

SC1. PILOT STUDY OF PREVENTIVE EFFECT OF MYRTENAL ON MEMORY AND ACHE ACTIVITY IN AD EXPERIMENTAL MICE

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Background: The research for biologically active substances for treatment and prevention of neurodegenerative diseases is an important trend in modern experimental neurobiology. Object of this communication is the natural monoterpene myrtenal, having a complex mechanism of action in most of its effects, including on memory functions.
Objectives: The purpose of this pilot study was to investigate the protective effect of mirtenal on memory and acetylcholinesterase (AchE) activity in experimental rodents. We believe that the observed changes in cognitive performance of the animals is related to (AchE) activity in the brain.
Materials and Methods: We studied the effect of myrtenal (20 mg/kg ip) on the memory function in healthy healthy male Albino mice for periods of 5 and 11 days, and scopolamine-induced model of dementia type Alzheimer's disease (AD) (scopolamine 1mg/kg ip, 11 days). The preventive effect of myrtenal was evaluated when compared with referent compounds: galantamine (a well-known anti-AChE agent), and strong antioxidants (lipoic acid and ascorbinic acid). Changes in the cognitive functions were tested using Step through test (for learning and memory - Jarvik and Kopp, 1967) and Hole board test (for exploratory activity - Boissier, Simon, 1964). In parallel, in biological brain were investigated AChE activity levels (Ellman et al., 1961).
Results: In healthy animals treated with myrtenal we observed positive short-term effects (after a 5-day treatment) on memory.

Treatment with myrtenal of dement mice produced a significant restoration of cognitive function (with 30%). Established preventive effect of myrtenal was comparable with the effect of galanthamine. Administered together myrtenal and lipoic acid demonstrated better prevention in combination than when administered alone (with 50% increased memory). This was confirmed by the results of anticholinesterase activity, which show significant inhibition of AChE activity by combining myrtenal with lipoic acid (25% vs controls). While the combination myrtenal and vit.C showed adverse unexpected effects - stimulating the cholinesterase activity with no effect on memory.

Conclusion: Myrtenal demonstrated significant pharmacological effect on memory in healthy and AD animals. Combination of myrtenal and lipoic acid decreased significantly AChE activity and increased cognitive function in AD mice.
Key words: Alzheimer's disease, myrtenal, cognitive functions, AchE activity

SC2. ACYLPEPTIDE HYDROLASE AS A BIOMARKER OF EXPOSURE TO ORGANOPHOSPHATES

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Organophosphorus (OP) chemicals have been in use for over 50 years and their acute toxicity is relatively well understood. Chronic low-level exposure to OPs has been implicated as a causal factor in a variety of different forms of human ill-health involving the nervous or immune systems. These effects appear to occur at exposure levels too low to be attributable to inhibition of acetylcholinesterase activity. It is well known that the major mode of action of these compounds is by covalent phosphorylation of the active site serine of serine hydrolases. This results in slowly reversible or irreversible inhibition of the target enzyme. The principle target is acetylcholinesterase, however a whole range of other serine hydrolases are active in the nervous, immune systems and blood and therefore present possible targets. Such possible target is acylpeptide hydrolase (APH). The aim of this presentation is to review data for APH activity after OP exposure as well as some own in vivo and in vitro experiments with OP nerve agents and pesticides.

N-Acylpeptide hydrolase (EC 3.4.19.1) catalyzes the hydrolysis of N-acylated peptide substrates of various sizes and with different types of acyl groups (acetyl, chloroacetyl, formyl, and carbamyl) to generate an acylamino acid and a peptide with a free NH. The enzyme help the post-translational acetylation of intracellular proteins and peptides. It is localized in hepatocytes, brain cells and erythrocytes. It is generally assumed to be an efficient means of protecting these substances from proteolytic degradation in eukaryotic cells, and thus of increasing their half-life. Thus APH and the proteasome act in coordination to clear cytotoxic denatured proteins from cells. APH may be involved in regulation of neuropeptide turnover, which provides a new and plausible mechanism for its proposed cognitive enhancement effect.

APH have been shown to be an essential target for reaction with organophosphates pesticides. Significant inhibition was shown after dichlorvos, naled, and trichlorfon, DFP and only slight inhibition after lethal ip dose of sarin. APH is inhibited by both chlorpyrifos (CPS) and metabolites of tricresyl phosphate (TCP). The purified APH was inhibited by CPO, diazoxon (DZO), paraoxon (PO), PSP, and the classical NTE inhibitor, mipafox.

In in vivo experiments with rats poisoned with high doses of soman and tabun, it was find out that the changes in CHE's activity in blood, liver and brain, were less sensitive than the changes in APH activity. Our data are the first evidence which shown selective, significant and long lasting (up to 80% from the control at day 7^{th}) inhibition of Er-APH activity after tabun poisoning and only slight decreased (15%) after 24h of soman intoxication. APH inhibition was observed also after low non-convulsive tabun doses. In in vitro experiments with human erythrocytes the inhibition potency of different OP pesticides on ACHE and APH activities, were compared.

These data show that blood APH activity would be an appropriate marker for OP chronic exposure.

SC3. XANTHATES (DITHIOCARBONATES): HEAVY METALS CHELATION PROPERTIES AND BIOLOGICAL EFFECTS

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Different salts of aryl and alkyl derivatives of dithiocarbonic acid (known under the trivial names xanthogenates or xanthates) are well known from many years as powerful heavy metals chelators. Based on this chemical property xanthates are used with success in:

- Industrial flotation for production of cooper, zinc and lead.
- Environmental chemistry for removal of traces of heavy metals from wastewaters (mercury) or extraction of cadmium from soil.
- Analytical chemistry for spectrophotometric determination of metals (Cu, Mo, Zn).

In this short review we present data from our laboratory and by other authors for the biological effects of xanthates, which could be explained by chelation of biologically important metal ions in the body. With that their property could be explained:

- The in vivo antidotal effect after poisoning with heavy metals (chelation of mercury, cooper).
- The antiangiogenetic effect for inhibition of tumor growth (due to chelation of zinc in different metaloproteinases).
- CNS effects – inhibition of amphetamine-induced locomotor activity and decrease of brain noradrenaline levels (due to in vivo or in vitro inhibition of dopamine-β-hydroxylase (a cooper dependent enzyme).
- Antioxidant action – chelation of iron; chelation of cooper/zinc in the brain markedly ameliorate β-amyloid accumulation in Alzheimer's disease.
- Antiproliferative (antitumor) action – inhibition of phospholipase C (zinc dependent enzyme).
- Xanthates/heavy metals complexes with well-expressed antitumor action – gold (inhibition of thioredoxin reductase), platinum (thioplatin), palladium, bismuth, nickel; metronidazole/xanthate ^{99m}Tc complex as target delivery to hypoxic tumors.

SC4. CAN ALPHA LIPOIC ACID BE USEFUL IN PREVENTION AND TREATMENT OF ALZHEIMER'S DISEASE?

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Alzheimer's disease (AD) is characterized by the presence of extracellular amyloid plaques and intraneuronal neurofibrillary tangles in the brain. The biochemical analysis of amyloid plaques revealed that the main constituent is fibrillar aggregates of a 39–42 residue peptide referred to β-amyloid protein (Ab). The autooxidation of Ab lead to release of reactive oxygen species (ROS) and reactive nitrogen species (RNS) that initiate and promote the neurodegeneration in basal forebrain cholinergic neurons. The beneficial role of antioxidants administration is an evidence that Ab toxicity is linked with the formation of ROS and consequently with increased oxidative stress. Lipoic acid (LA) has been shown to have a variety of properties which may interfere with the pathogenesis of AD. Aside from its enzymatic cofactor role, in vitro and in vivo studies suggest that LA is a powerful

micronutrient with diverse antioxidant properties. It has been documented that LA scavenges the free radicals, increases the concentration of reduced glutathione, and chelates the redox-active metals, suppressing thus the formation of hydrogen peroxide and reactive hydroxyl radicals via Fenton chemistry. These features of LA promise to be beneficial in treatment and prevention of AD disease.

Key words:
Alzheimer's diseases, oxidative stress, alpha lipoic acid

SC5. PHARMACOLOGICAL EFFECTS OF CERTAIN FOOD ADDITIVES ON CNS

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In the past years is significantly extends the use of food additives and energy drinks, because they help to strength the protection of the organism of diseases, improve physical endurance, stimulate mental activity, saving and attention.

Effects on CNS have food additives, containing Caffeine, Taurine, L-Arginine, L-Leucine, L-Isoleucine and L-Valine.

Caffeine stimulates central nervous system, increases the frequency of cardiac contractions. Taurine is an antioxidant, improves energy processes, stimulates regenerative processes in the tissues, protects eyes from cataracts, reduces cholesterol and stimulates the immune system. Combinations of Caffeine and Taurine lead to synergy of pharmacological effects such as increased physical activity, stimulation of the brain, memory and attention.

L-Arginine increases growth. L-Leucine and L-Valine stimulate production of growth hormones, ensure the organism energy and are needed for mental stress. L-Valine stimulates central nervous system.

High consumption of food additives especially by children and young people may cause undesirable side effects, such as headache, insomnia, dehydration and respiratory disorders. These facts justify an increase in the requirements for the adjustment and control of the quality of these products, in connection with their safety for health and full investigation of their effects on CNS.

SC6. AT_1 RECEPTOR ANTAGONISM ATTENUATES KAINATE-INDUCED NORADRENALINE RELEASE BUT NOT SUSCEPTIBILITY TO STATUS EPILEPTICUS IN SPONTANEOUSLY HYPERTENSIVE RATS

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Introduction: AT_1 receptor antagonists have been suggested as an additional treatment strategy in the management of epilepsy [1]. A hyperactive brain angiotensin (Ang) II system

and up-regulated AT_1 receptors are implicated in the cerebrovascular alterations in a genetic form of hypertension [2]. Uncontrolled hypertension could in turn also be a risk factor for a seizure threshold decrease and development of epileptogenesis [3].

Aim: The present study aimed to assess the effects of the selective AT_1 receptor antagonist ZD 7155 on kainic acid (KA)-induced status epilepticus (SE) development and accompanying changes in the extracellular (EC) hippocampal neurotransmitters levels of noradrenaline (NAD), serotonin (5-HT), dopamine (DA) and GABA in spontaneously hypertensive rats (SHRs) and their parent strain Wistar Kyoto (WKY) rats since monoamines and GABA are well-known neurotransmitters involved both in mechanisms of epilepsy and hypertension.

Methods: Microdialysis probe was inserted into the hippocampus of SHRs and WKY rats. SE was evoked in freely moving rats by a repetitive intraperitoneal (i.p.) administration of KA in subconvulsive doses. In the treatment group, ZD7155 (5 mg/kg i.p.) was co-administered with the first KA injection. Seizure-related behavioural changes were scored and extracellular monoamines (NAD, 5-HT, DA) and GABA concentrations were collected and split for analysis by HPLC analysis.

Results: SHRs exhibited higher susceptibility to SE than WKY rats but the AT_1 receptor antagonist did not alter the development of SE neither in SHRs nor in WKY rats. In *vivo* microdialysis demonstrated significant KA-induced increases of the hippocampal DA levels in SHRs and of NAD, 5-HT and DA in WKY rats, while no alterations in the EC GABA overflow were detected. AT_1 receptor antagonism completely abolished all KA-induced increases of hippocampal monoamine levels in SHRs and WKY rats.

Conclusion: AT1 receptor antagonism, thus, modulated seizure-associated increases in extracellular monoamine levels without affecting seizure development per se. Interestingly, compared to WHY rats, SHRs developed more severe seizures while receiving a lower dose of KA; possibly a less pronounced seizure-associated hippocampal NAD and 5-HT release might partly underlie this phenomenon.

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SC7. PHYSICAL EXERCISE PROGRAM IN SPONTANEOUSLY HYPERTENSIVE RATS IS PROTECTIVE AGAINST KAINATE-INDUCED EPILEPTOGENESIS

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Introduction: Clinical and experimental evidence support the hypothesis that physical exercise has beneficial and protective effect against epilepsy [1,2] and cardiovascular diseases [3]. However, the question of a positive or negative impact of physical exercise on epileptogenesis induced in hypertensive state still remains unsolved and unstudied.

Aim: In the present study, we aimed to explore the effect of physical training in spontaneously hypertensive rats (SHRs) considered as a model of essential hypertension on kainate (KA)-induced epileptogenesis, including concomitant behavioral changes.
Methods: Male adult SHRs (two-month-old) were divided in two main groups. The first group (n=20) was submitted to an aerobic exercise program (training group). The second group (n=16) was maintained in the treadmill for the same time as the training group without being submitted to physical exercise (sham group). After a month, the training group was subdivided in KA-treated group (ex-KA) and vehicle-treated (ex-veh) and the sham group was subdivided in sham-KA and sham-veh group, respectively. Kainate acid (KA) was repetitively injected in a subconvulsive dose until an onset of a sustained status epilepticus (SE). After SE KA-treated rats were video-monitored 24 h/day for detection of the first spontaneous motor seizure (SMS). One month after the exercise program, all groups were submitted to behavioral tests for measuring motor activity (open field, OF), anxiety (elevated plus-maze, EPM) and depressive-like behavior (sugar preference test, SPT). For statistical analysis $p < 0.05$ was accepted as an index of statistically significant difference (Student t-test).
Results: The exercise program decreased susceptibility to KA-evoked epileptogenesis. The ex-KA group required more KA injections to develop SE and showed longer latent period to onset of the first SMS than the sham-KA group ($p<0.05$). In OF test, exercise program increased motor activity in KA-treated SHRs compared to sham-KA rats with significantly increased total distance covered in the field ($p<0.05$). Continuous aerobic training caused anxiolytic effect in ex-KA group compared to sham-KA rats in EPM test. The number of crossings in the open arms of the apparatus as well as the anxiety index were significantly different between the two groups ($p<0.05$). Exercise program suppressed the development of depressive-like behavior after KA-induced SE in SPT ($p<0.05$).
Conclusion: The data presented suggest that physical exercise in a model of hypertension alleviate epileptogenesis and has beneficial effect on some behavioral changes evident after SE.

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SC8. EFFECT OF PINEALECTOMY ON ANXIETY AND DEPRESSIVE-LIKE BEHAVIOR IN WISTAR RATS

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Introduction: Melatonin plays a modulatory role in the control of circadian and seasonal rhythmicity, body temperature, mood, and behavioral performance, possesses antioxidant activity and exerts neuroprotective and anticonvulsant effects [1,2].

Aim: The aim of the present study was analyze the role of endogenous melatonin on emotional behavior associated with anxiety and depressive responses in a model of melatonin deficit in rats.
Methods: Wistar rats were sham-operated (sham) or pinealectomized (PIN) according to the method described by Hoffmann and Reiter [3]. Behavioral tests for motor activity (open field, OF), anxiety (light-dark test, LDT) and depressive-like behavior (saccharine preference test, SPT,) were executed a months after the surgery. After decapitation of the animals, the hippocampi were isolated three months after pinealectomy to explore the release of serotonin (5-HT). Student's t-test was used for statistical analysis. $p < 0.05$ was accepted as an index of statistically significant differences.
Results: Pinealectomized rats showed higher motor activity than sham rats in the OF test with significantly increased total distance covered in the field ($*p<0.05$). Experimentally-induced melatonin deficit caused lower anxiety level measured in the LDT. The number of crossing from dark to light part of the apparatus as well as the time in the aversive light compartment was significantly increased in PIN group compared to sham group ($*p<0.05$). A significant difference between PIN and sham group was detected during the dark phase in the SPT test ($*p<0.05$). Pinealectomy had a tendency to attenuate KCl-evoked [^{3}H]-5HT release from the hippocampus. Thus, pinealectomized rats demonstrated depressive-like behavior which positively correlated with a decreased release of the hippocampal 5-HT compared to sham rats.
Conclusion: Melatonin deficit in the pineal gland caused a hyperactivity, decreased anxiety level and depressive-like behavior. Our results suggest that the concomitant decrease of the hippocampal serotonin might mediate the observed behavioral complications in pinealectomy.
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SC9. SAFETY PHARMACOLOGY: NEW CHALLENGES FOR TESTING THE BIOLOGICAL ACTIVITY OF NEW DRUGS

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Safety pharmacology is those studies that investigate the potential undesirable pharmacodynamic effects of a chemical substance on major physiological functions in relationship to exposure in the therapeutic range and above. It is a natural bridge between experimental and clinical pharmacology and toxicology to achieve the main goal of modern pharmacotherapy – to have more effective and safer drugs.
This review mainly focus on some recent advances in drug discovery and development which speed up with less cost the process of toxicology testing. Some modern approaches to achieve this goal:

1. New achievements in implementing of so called **3Rs principles** for decreased numbers of experimental animals which leads to transition in toxicology toward a more pathway-based *in vitro* and computational approach (covered by FP6/7 project consortium AXLR8).

- ***Replace:*** through successful development of new more informative testing methods such as tissue engineering, cell cultures and stem cell technologies, computer modeling (*in silico*). Further testing of substances applied to the skin in practice will not require the use of experimental animals /cosmetics for example from 2013/.
- ***Reduce:*** re-examining the findings of studies already conducted (e.g. by systematic reviews), by improving animal models, and by use of good experimental design.
- ***Refine:*** this includes better housing and improvements to procedures which minimize pain and suffering and / or improve animal welfare. This is particularly important for testing of substances with potential psychotropic activity.

2. Alternatives: *In vivo* models may, with advances in methods and technologies, be replaced by in vitro techniques, which do not involve live animals, but still require animals to be bred and killed for scientific purposes. In foreseeable future we can use more transgenic species, isogenic strains, new animal models, or other novel test systems and could include a toxicogenomic evaluation of tissue responses over wide dose ranges.

3. Recent developments (few examples):

- From 2008 **acute toxicity** studies are not needed prior to first clinical trials in humans. Instead, information can be obtained from other studies, which are performed at more relevant doses for humans and are already an integral part of drug development.
- New testing methods for better in vitro / in vivo extrapolation were needed to meet increasingly develop **protein based therapies** that specifically target human cells. Bad example is CD28-SuperMAB**,** a humanized monoclonal antibody develop as a strong agonist for the CD28 receptor of the immune system's T cells for treatment of B cell chronic lymphocytic leukemia (B-CLL) and rheumatoid arthritis. Six volunteers were hospitalized in 2006 suffering from multiple organ dysfunction, despite being administered at a supposed sub-clinical dose of 0.1 mg per kg; some 500 times lower than the dose found safe in animals.
- New tests for **pyrogenic** contaminants rely on cultured human white blood cells and might replace two existing, more expensive methods - the Limulus assay and testing on rabbits.
- Cultures of human cord blood and mouse bone marrow cells were develop to detect **low white blood cell counts** — a common side effect of cancer drugs.
- **Targeted synthesis** of more effective and safer new drugs with **predictable metabolism** will be discussed which are based on some achievements of pharmacogenomics and are directed to development of personal pharmacotherapy.

SC10. PHARMACOLOGICAL EFFECTS OF PHYTOADAPTOGENS AND OF THE ANTIOXYDANT COPLEX "NOVOMIN" IN A CASE OF VIGILANT COMA AFTER REPEATED BRAIN SURGERY BECAUSE OF MALIGNANT ASTROCITOMA

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A combined phytoterapeutical approach with the synergistic phytoadaptogen alcohol aqueous extract "Live energy" (BASF, Germany), (Rodiola rosea (Rr), Shisandra, Astragalus membranaceus plus vitamins A, C, B6, PP, folic acid etc), as well as with the selective

antitumor antioxidant complex "Novomin" (1) in the case of a 35 years old patient in a vigilant coma after repeated brain surgery was performed. The onset of the disease was three years ago with the ordinary symptoms of brain tumor (splitting headache, lack of stability, dizzness, impaired vision etc.) and according to the i) pre-and postoperative tomography; ii) the specific course of the disease and iii) the postoperative histological verification, the diagnose "astrocitoma anaplasticum cum recidiva and hydrocephalia" was confirmed. Between March 2005 – May 2006 the patient had been operated five times. Radiological (30 heatings) and chemotherapy treatment with Temodal was completely inefficient. After the 5th surgical intervention (May 2007") the patient fell in a vigilant coma.

Complex phytoterapy with "Novomin" and with "Live energy" started on 18th of May 2007. As a result of experimental and clinical studies (performed on over 2000 experimental animals and 1000 onkopatients , Novomin was developed 20 years ago by Sukolinskii et al, (RAMS) Novomin displays definite antioxidant (protective) effect only in the healthy tissues, whereas in the cancer cells it exerts prooxydant (tumor damaging) effects. Therefore Novomin is the first and so far the only phytopreperation having the so-called alternative effect. It normalizes the metabolic processes in the healthy tissues and simultaneously exerts a strong selective tumor damaging effect on the DNA-level in the cancer cells.

Various phytopreparations from Astragalus memban., Rr and Shisandra has been extensively studied as highly potent adaptogens with various health- and especially brain-protective effects (2, 3). The common result of this complex therapy was the astonishingly fast recovery process and in the course of six months the patient was completely rehabilitated. At the moment he works in a furniture factory, exercises daily and takes part in folk dancing. The retracing with repeated magnetic resonance (July "07 and January '08) manifested the total brain recovery without any malignant recurrence, hydrocephalia or other pathomorpholigical findings.

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SC11. OXIDATIVE STRESS, FREE RADICALS, LIPID OXIDATION AND BIO-ANTIOXIDANTS

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Oxidative stress is associated with increased production of so called reactive oxygen species (ROS), i.e. different active radicals and peroxides $OH^{\bullet}$, $O_2^{-\bullet}$, $LO_2^{-\bullet}$, HOOH, LOOH, or with a significant decrease in the effectiveness of antioxidant defences, such as antioxidant enzymes, glutathione, antioxidant vitamins A, C, E. It is well known that the latter lead to an oxidative degradation of biological macromolecules, changing their properties and thus the cell structure and functionality [1,2].

Free radicals are responsible for the pathogenesis of a wide range of diseases: the most serious and difficult to treat health problems such as cancer and cardiovascular diseases, they

also cause asthma, arthritis, inflammations, neurodegenerative disorders, Parkinson's disease and dementia. Aging is a complex combination of deleterious free radical reactions, which affect cells and tissues [3,4].

Lipid oxidation - free radicals formation in the hydrophobic parts of the biological membranes first initiates radical disintegration of the hydrocarbon "tails" of the lipids. This process is known as "lipid peroxidation" [5].

Bio-antioxidants - i.e**.** biologically active compounds with antioxidant potential - natural and synthetic analogues - have a wide range of applications [6-8]. They are important drugs, antibiotics, agrochemical substitutes, and food preservatives. Many of the drugs today are synthetic modifications of naturally obtained substances. This report presents information about structure-activity and beneficial effects on human health of known and new bio-antioxidants. The following bio-antioxidants are considered: Flavonoids, Chalcones, Cinnamic acids, Simple and bis-coumarins, Curcumin related compounds and Lignans. Comparable analysis with known antioxidants such as Dl-alpha-tocopherol, Galic acid, Butylated hydroxytoluene, Ascorbic acid give us possibility to explain the structure-activity relationship of new bio-antioxidants.

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SC12. OXIDATIVE STRESS AND NEURODEGENERATIVE DISEASES

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Oxidative stress plays a major role in the pathogenesis of a large number of diseases, including neurodegenerative disorders. Brain appears to be vulnerable to oxidative damage. In the beginning, because of brain's abundant lipid content, along with its high oxygen consumption and relatively low antioxidant levels, lipid peroxidation was accepted as primary mechanism for neuronal degeneration (Keller et al. 1998). Reactive oxygen species (ROS) rapidly oxidize cellular lipids, resulting in the formation of numerous lipid peroxidation products in nerve cells, leading eventually to neuronal cell death. Later it has been demonstrated that brain's nuclear DNA (Gabbita et al. 1998) as well as proteins (Butterfield

et al. 2001) were also vulnerable to damage by oxygen-derived radicals. Thus oxidative injury in the brain is recognized as a common pathway of cellular injury both in acute neurologic insults such as ischemia-reperfusion and epileptiform brain activity, and in chronic disease states for instance Parkinson's or Alzheimer's disease (Serra et al. 2001).

Antioxidants are now being looked upon as persuasive therapeutic against neuronal loss, as they have capability to combat by neutralizing free radicals. Diet is major source of antioxidants, as well as medicinal herbs are catching attention to be commercial source of antioxidants at present.

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SC13. NORMAL HUMAN TYPES OF FOOT ARCHES AND STEADINESS OF STANDING BALANCE

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Human foot is a strong and complex mechanical structure, which has evolved a unique design for propulsion and support. Human foot arches are formed by the tarsal and metatarsal bones, multiple ligaments and tendons preserving their integrity. They redistribute body weight on wider surface. Also, their springiness reduces the risk of musculoskeletal wear or damage and allows the elastic deformations of the foot.

On foot arch basis different anatomic variants exist. Pes planus (flat feet or fallen arches) is a condition in which the medial longitudinal arch of the foot is missing and the almost entire sole of the foot contacts with the ground. Pes planus is relatively frequent, approximately 20% of the healthy population. Pes cavus (high arch) is a human foot type in which the sole is distinctly hollow when bearing weight because of fixed plantar flexion of the foot. It is less common than flat feet – approximately 10%. The plantar arch types are closely correlated with foot pronation and supination, which is important for the weight redistribution and absorption during gait and stance.

The normal-arched human foot is compliant also during quiet stance as the foot arch height changes with center-of-body-mass displacement (passive participation in posture). There is also a growing body of evidence that the foot actively participates in maintaining equilibrium as it provides somatosensory information on local deformations and different plantar muscles are recruited in response. However, there is paucity of data, what is the influence, if any, of plantar arch type on the steadiness of balance and postural behavior during quiet stance. Therefore, we did a preliminary investigation to evaluate the need of such studies further.

Three healthy women about the same age (26-34 years) and weight (53-57 kg) were diagnosed by a pedobarographic platform Tekscan as having normal and slightly high and

low arch bilaterally. They had no neurological or orthopedic problems, complaints of pain or other inconveniences, originating from feet, during standing or walking. Their postural steadiness was investigated by the same platform on which they stood with eyes open and eyes closed for 30s. COP (center-of-pressure) sway path was measured.

In the eyes open condition the least COP sway path was found in the person with the normal arch. The subject with pes cavus had a slightly greater COP sway path which implies less steadiness. The greatest COP sway path was found in pes planus, despite the increased contact with the ground. In the eyes closed condition the least COP sway path was found in the person with the normal arch again. The subjects with pes cavus and pes planus had clearly greater COP sway path.

The results suggest that individuals with high and low arch have different postural steadiness, compared to those with normal feet. We suppose that different foot architecture may alter sensory information input from feet, which in turn could lead to adaptation and new postural behavior to be developed. Further studies are required to shed light on this matter.

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SC14. EFFECTS OF TRANSCUTANEOUS ELECTRICAL VAGUS STIMULATION ON THE SCALP EEG AND STEADINESS OF STANDING BALANCE

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The transcutaneous electrical stimulation of auricular branch of vagal nerve (tVNS) was introduced largely for diagnostic and therapeutic purposes. However, the effect of both diagnostic and therapeutic stimulation was not studied with methods of quantitative EEG (qEEG). On the other side there is a fast growing body of evidence for a cortical regulation of the quiet upright stance based on the qEEG and force platform measures. However, there is still paucity of reliable quiet stance specific EEG patterns and such data are missing for the sensory-conflicted stance.

The aims of our preliminary study is to test the effects of tVNS on the qEEG parameters and steadiness of standing balance during stance with eyes open and eyes closed as well as estimation of the distribution of qEEG sources with low resolution tomographic analysis (LORETA).

The experimental subject in sitting position was fitted with 19 EEG electrodes scalp electrodes fixed according to the international 10–20 system. First we recorded 2 min control series (with eyes open and eyes closed) while sitting and standing with feet side-to-side on the pedobarographic platform, that collected standing balance data. Then electrical stimulation was applied in sitting position with custom designed bipolar stimulation electrode: electrical square impulses, 0.1 ms duration, 2 s interstimulus interval, 8 mA stimulus intensity. Evoked vagus potentials were recorded bipolarly from the electrode positions P4–F4. After averaging of 100 potentials the electrode placement was verified and four therapeutic series of 300 impulses in 4Hz trains separated with 30s pauses were applied. After therapeutic stimulation we recorded the same series as control ones and repeated the procedure after 20 min.

The results showed that a positive effect of stimulation, marked by the body sway path diminution occurred only while standing with eyes open, while during standing with eyes

closed, no changes were observed. During standing with eyes open we observed after stimulation a diminution of the spectral power in the theta, alpha1 and alpha2 band ranges while in the delta, beta and gamma ranges an increase of spectral power occurred. In the same time LORETA showed that the EEG sources shift to the right and caudal direction. During standing with eyes closed we observed a diminution of the spectral power in the delta, theta, alpha2 and gamma band ranges after stimulation, while in the alpha1, beta ranges an increase of spectral power occurred. LORETA showed that the EEG sources shifted to the right and cranial direction. The results suggest that the therapeutic tVNS changes the cortical mechanisms connected with the integration of vision for the maintaining of standing balance and its effect is not favorable during the sensory-conflicted stance due to absence of vision.
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SC15. SIMILAR OR DIFFERENT EFFECTS OF GRATING LENGTH AND WIDTH?

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An important question in contemporary visual neuroscience is an assessment of characteristics of mechanisms underlying different aspects of grating detection. Precise assessment of effects of Gabor patterns size and form on visual information processing would shed light on underlying mechanisms' properties. A discrepancy between results of different previous studies exists concerning the summation over the stimulus length or width. Some authors concluded that the effects of grating length and width on contrast thresholds are similar, while the results of other teams provided evidence about strong difference between these effects.
The aim of the present study was to evaluate the effects of Gabor grating width and length at low, medium and high spatial frequencies (SFs) and over occipital, parietal and central cortex in order to reveal properties of the mechanisms underlying the different effect of stimulus width and length as well as the spreading of the effect over different cortical areas.
Visual evoked potentials (VEP's) were obtained to grating stimuli with different SFs, displayed in a Gaussian window. When the Gaussian window is elongated along the grating stripes it is considered like skunk-tails stimuli and when the elongation of the window is perpendicular to the grating direction it is recognised as tiger-tails stimuli (Meese TS, Hess RF, 2007, Vision Research, 47, 1880–1892).
We found that the effects of stimulus length and width depend on theirs aspect ratio and grating SF. When SF was low, 1.45 c/deg, the grating length and width effects were similar at all stimulus sizes and VEP recording positions. At medium and high SFs length and width effects were similar for aspect ratios up to 1:4. At higher aspect ratios, 1:8 and 1:16 grating length produced a greater amplification of the VEP amplitude than the increase of grating width. This effect appeared in earlier VEP component, N1 in the early visual areas and in later component, P1, in the hierarchically higher parietal and central cortical areas.
Our results can explain contradictions between previous results on grating length and width effects and might be interpreted as neurophysiological evidence that the underlying mechanisms are arrays of elongated receptive fields (Foley JM, Varadharajan S, Koh CC, Farias MC (2007) Detection of Gabor patterns of different sizes, shapes, phases and eccentricities. Vision Res. 47 (1): 85-107).

SC16. EFFECTS OF CENTER-SURROUND INTERACTIONS IN MOTION DIRECTION DISCRIMINATION

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Center-surround interactions in the activity of neurons are found at different levels of the visual system. The purpose of the present experiments is to study center-surround interactions in motion direction discrimination. As both speed and direction define the velocity of motion, we have examined the influence of angular differences in motion direction and the speed distribution of the motion signals on direction sensitivity.

The stimuli consisted of band-pass dots presented in two concentric circular apertures positioned at the middle of the computer screen. All elements of the center moved downward with speed of 5.5 deg/s. The dot speeds of the surround motion were drawn from uniform distributions with different range. Five levels of speed range centered at the mean value were used: 0; 0.9; 1.8; 2.8 and 3.7 deg/s. The direction of surround motion was randomly varied between 12 possible directions in the range 0˚ to 360˚ with step of 30˚ counter-clockwise from the vertical downward direction.

The observers' task was to respond whether the direction of the center motion appeared to the left or to the right of the vertical.

We investigated also the effects of surround modulation when center motion represented rotation of a sphere around an axis in fronto-parallel plane. In this case the mean speed of motion was the same, but it was distributed non-uniformly. In addition, the effect of aperture size (diameters between 2.2 and 11.8 deg) on the interaction between the central and surround motion was also studied.

We determined bias and the sensitivity of performance using a single-stimulus two-alternative force choice procedure combined with an adaptive algorithm (QUEST) in which the direction of the center stimulus was varied.

The results show: 1.) surround modulation of perceived motion direction; 2.) largest shift in apparent motion direction when the center and surround motions are orthogonal; 3.) no effect of the speed range of surround motion; 4.) performance improvement as stimulus sizes decrease; 5.) significant reduction of surround modulation for rotating stimuli. These findings contradict some of the known data on center-surround interactions in area MT and imply that the observed effects may not be due to processes in this area. A possibility that surround motion effects occurred at an early stage of processing as V1 is raised.

SC17. DOES PRIMING WITH AGE STEREOTYPES INFLUENCES ADAPTATION OF REACTIVE SACCADES IN ELDERLY?

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It was shown in the literature that some characteristics of ocular saccades as speed and accuracy decrease with aging. Also, the speed and magnitude of arm adaptive change reduced, while aftereffects which reflected sensorimotor recalibration, remained intact. On the

contrary, in our recent study, we established no age-related deficit for saccadic adaptation (Bock et al, 2014). We reasoned that sensorimotor performance in old age is determined not only by biological decay, but also by the actor's confidence in subjects' own capacity. Experimentally was shown, that the positive stereotype improved but negative stereotype deteriorated performance of tasks such as locomotion and handwriting in older age.

Therefore, we propose that negative/positive stereotypes would influence also saccade adaptation, as it would be impaired by negative societal stereotypes towards old age, but not by positive ones. To examine this hypothesis, we aimed at comparing saccadic adaptation in elderly participants primed with positive versus negative stereotypes of old age.

Sixteen subjects (8 women and 8 men) aged 50-65years who were first primed with age stereotypes using an established procedure, the scrambled sentence task (Bargh, Chen, & Burrows, 1996) participated in this experiment. Each person was given 20 lists of five words, and had to select four words from each list to formulate a meaningful sentence; the fifth, non-fitting word had to be crossed out. Semantic test consisted of 20 sentences with 5 words, which had to arrange semantically. One of them hasn't had relation for meaning sentence and had to been crossed. Every sentence was one word, which had meaning for positive or negative age stereotype. For example "mature" and opposite "unstable". Eight subjects received lists with positive stereotypes, and the other eight with negative ones; all were instructed to proceed at their own pace. Thus groups of "positive" and "negative" subjects were composed. The scrambled sentence task was followed by a saccade adaptation task, using procedure for double-step trials, where the target jumped onto the circle, presented on computer monitor shifted along the circle by −15 deg (clockwise) after 200 ms, and returned to the center. Eight age-matched healthy subjects participated as controls in the saccade adaptation task but not in the scrambled sentence task.

We found stronger adaptation after positive priming than after negative one and no difference was established between the latter and control subjects. Aftereffects of adaptation were similar for all examined groups. From this we conclude that positive primes enhanced workaround strategies, but not adaptive recalibration. A lack of negative age priming effect could be explained by its less efficient than priming with positive ones or by negative attitude for aging in older people in Bulgaria that leads to a floor effect. This study suggests also that adaptive performance of older subjects is susceptible to central influence.

SC18. SACCADIC ADAPTATION TO DISPLACED VISUAL TARGET IN OLDER GLAUCOMA PATIENTS: A PRELIMINARY STUDY

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Glaucoma causes peripheral visual field loss that leads to disability in many daily tasks including visual search and saccadic eye movements. It was shown that saccadic eye movements are disrupted in patients with primary open-angle glaucoma (Smith et al, 2012; Lamirel C et al, 2014) but literature is silent whether saccadic adaptation which compensates for different changes in the eyes, is affected by glaucoma. Saccades have shown that were affected by old age. The scant literature about adaptation of targeting saccades in older persons, established that older people with corrected to normal vision adapted similarly to younger people (Bock et al, 2014).

Therefore, we aimed at determining whether saccadic adaptation to target displacement of older people with glaucoma, differed from that of older people with unaffected vision.

Four patients with open angle glaucoma of both eyes aged 55-69 years and four age-related controls with normal or corrected to normal vision took part in this examination.

Adaptation of reactive saccade directions was executed by a modified double-step target paradigm of McLaughlin (1967): target jumped from the center in one of eight randomly selected peripheral locations (divided by 45^{o}) on a circle presented on the monitor screen. 200 ms after target onset movement, it was displaced with -15^{0}, thus inducing a gradual adaptive change in saccadic end points. Data were analyzed by custom-designed interactive software, which determined *saccade direction* as angular difference between first target step and primary saccade and direction and reaction time as an interval between appearance of the target and saccade movement onset.

Patients' data did not present a gradual curve of adaptation that was typical for healthy older subjects. Moreover, three of four patients established as negative as positive displacements during all the course of adaptation. Large interindividual variations in patients' group were found. Reaction time was ~50 ms higher in patients than in healthy subjects.

Our findings suggest that older glaucoma patients probably do not optimally compensate for visual field loss and their saccadic adaptation is removed.

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SC19. MICROPERIMETRY IN PATIENTS WITH CHOROIDAL NEOVASCULARIZATION AND IN PATIENTS WITH IDIOPATHIC MACULAR HOLE

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Introduction: Age related macular degeneration (AMD) and idiopathic macular holes (IMH) are diseases affecting the macula that lead to abnormalities in central vision (acuity, scotoma, metamorphopsia, micropsia, macropsia), which can significantly reduce quality of life. D Charts are a newly developed method of microperimetry **(McGowan et al., 2013**) that measures and monitors metamorphopsia strength in the macular region, aiding the diagnosis, tracing and treatment of patients with macular diseases.

Purpose: To test the ability of D-charts microperimetry to map the visual defects of patients with AMD before and after application of anti-VEGF drug, and before and after surgical treatment of patients with IMH.

Patients and methods: Ten patients were examined for a period of 6 months. The patients were divided into 2 groups –with AMD and with IMH. All patients underwent complete eye examination and optical coherence tomography (OCT), and in patients with AMD, fluorescein angiography (FA) was also done. D-charts microperimetry was conducted before and during the treatment with anti-VEGF drug in patients with AMD and before and after surgery (PPV et gas SF620%) in patients with IMH.

Results: Most patients showed improvement in the test results after treatment; in some, the condition remained stable. D-charts microperimetry showed good correlation between the functional disorders and structural changes in the macula. It is an informative method for diagnosis and monitoring the effects in the course of treatment.
Discussion: D-charts microperimetry is a non-invasive, subjective and repeatable method by which subtle changes in central vision in patients with macular pathology can be maped. Modern technology in conducting microperimetry allows the study of patients with low vision and unstable fixation. This method makes it possible to correlate functional disorders and structural changes, which is not feasible with standard perimetry only.
Conclusion: D-charts microperimetry is a useful method to trace the natural progression of macular diseases, as well as for treatment monitoring. These diseases are socially significant because they affect central vision and lead to a deterioration of quality of life and limited daily activities.

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7. Expanded role for microperimetry in Visual Rehabilitation – by Annie Stuart.
8. Predicting visual outcome after macular hole surgery using scanning laser ophthalmoscope microperimetry – Fujio Amari, Kouichi Ohta, Hidenobu Kojima, Nagahisa Yoshimura

SC20. STRUCTURAL AND FUNCTIONAL OCULAR FINDINGS IN PATIENTS WITH MULTIPLE SCLEROSIS

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Introduction: Multiple Sclerosis (MS) is a chronic, autoimmune disease, leading to demyelination and affecting the central nervous system. Eye involvement is common with optic neuritis being the first sign in many of the patients. Comprehensive eye exam can demonstrate eye disorders and contribute to early diagnosis and is essential during follow up of the patients.
Aim: To present the structural and functional eye disorders, which can be observed and followed with the help of eye exams, including optic coherence tomography (OCT) and computer perimetry in patients with MS.
Patients and methods: We have examined MS patients, divided into three groups: the first group consists of patients, where the disease had started with eye manifestations; the second group includes patients, who had developed eye disorders with time; the third group consists of patients, where no eye disorders were found. A full eye exam was performed in all patients, with a photo documentation, including specialized methods such as OCT and computer perimetry**.**
Results and discussion: Decreased vision and perimeter abnormalities are often first signs of MS. In OCT exams a RNFL thinning was observed in MS patients from all groups with

greater thinning in the second group. Recent studies show that the thickness of the Ganglion Cell/ Inner Plexiform(GCIP) layer is more indicative for the progression of the degenerative disease than is RNFL thickness. During the flares patients are treated mainly with corticosteroids. A systemic therapy with beta- interferon reduces the number of flares and slows the progression of the disease.

Conclusion: OCT imaging combined with functional exams are of great value for the follow up of the disease progression and therapy adjustment. The early performance of common and specialized methods such as OCT and computer perimetry contributes to detecting early and subclinical changes and thus to appropriate treatment.

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SC21. VISUAL DYSFUNCTION IN INDIVIDUALS WITH AUTISM SPECTRUM DISORDER: PERSPECTIVES FOR OVERCOMING DIFFICULTIES

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Autism spectrum disorder (ASD) is a developmental neurological disability characterized by difficulties in social interaction, communication and repetitive behaviors. The term spectrum refers to the tremendous variation in how the condition is manifested. The research of underlying neural dysfunction in autism has been primarily concerned with assessing higher-level cognitive and social abilities. The emphasis on higher-level, symptomatology-related functioning has resulted in the over-looking of atypical perceptual processing in autism. However, abnormal processing of low-level sensory perceptual information is also a characteristic feature of autism. Visual functions like spatial vision, color vision, stereovision, motion perception could be affected in ASD population (Simmons, D.R. et al., 2009, Vision Research, 49 (22), 2705–2739.).Atypical sensory processing is often reported – of either hyper- or hypo-sensitivity to sight, sound or touch. Our purpose is to encompass basic visual dysfunctions in individuals with ASD including visual acuity and to search for correlation with certain atypical features of visual perception.We performed a preliminary study on visual acuity measurement involving 21 children and adolescents at mean age 10.4 years, and adults at mean age 23 years with an existing diagnosis of ASD and 21 age-matched typically developing controls. Visual acuity was measured with Snellen chart without correction. The visual acuity of the children with ASD confirmed the so called “eagle eyed visual acuity” but the results for the adults with ASD questioned it. The ASD adults showed significantly lower

visual acuity than the typically developing adults. This controversy is in line with contradictory results in the literature about the superior visual acuity in adults with ASD. Methodological settings may be responsible for the ambivalent results. In addition, ASD individuals are hard to be examined and this could decrease the authenticity of the data. Moreover, experiments conducted by members of our team (Mihaylova M S et al., 2014,.Perception43 ECVP Abstract Supplement,148.) provided evidence of abnormally high internal noise in the visual domain in ASD population that could be responsible for results' diversity. Based on the collected information we suggest that the higher neural noise and the crowding effect of the conventional Snellen chart could produce difficulties of ASD individuals during visual acuity measurements. We propose searching for more appropriate methods including Vanishing Optotypes with their smaller effect of the number of letter alternatives (lower noise). They may be useful to create letter charts to scale small clinical changes in visual acuity of individuals with ASD. We also plan to evaluate impairments in the color vision, stereovision, ocular motility and to perform fundus examination in ASD population and to try to adapt existing examination procedures when possible to the peculiarities of autistic individuals.

SC22. NEUROPHYSIOLOGICAL BASIS FOR NORMATIVE VALUES ESTIMATION OF A TEST BATTERY STUDYING WRITING ABILITIES IN EARLY SCHOOL AGE

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Original tests for studying the writing abilities in early school age children were created. They include materials appropriate for the age in question and approved by the Ministry of Education in Bulgaria. Since different cortical areas, dependable upon the particular task, are engaged in the process, different aspects of reading and writing were investigated. The test battery incorporates 11 tests: dictation, reading, verbal reading, comprehension, reading of words and non-words, phonological tasks. A representative sample out of 2000 children was analyzed. They were separated in two groups: younger (end of second/beginning of third grade) and older (end of fourth/beginning of fifth grade). In the process of gaining normative values the application of numerous statistical procedures was especially valuable for confirmation of the righteous choice of participating stimuli. The final analyses have shown good internal congruence of the stimuli and the performance speed for completion of tests. This elucidated the extent to which the material was acquired.

Scientific session "PSYCHOPHYSIOLOGY"

SC23. NEUROPHYSIOLOGICAL DEVELOPMENT OF COGNITIVE GENDER DIFFERENCES

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"Which is the smarter gender?" This question has never been answered by comparing intelligence scores and school achievements, or by estimating who performs more intelligent jobs in society (1). A more useful approach is to examine specific abilities and the question then is transformed to "What are the gender differences in cognitive abilities?" Strikingly, similarities are more than differences. Yet, specific gender effects on cognitive achievements and operational effectivity do exist (1). Females have advantage in verbal abilities and memory performance. On the opposite, men excel in visual-spatial and mathematical abilities.

Why do these differences exist? Are there neurophysiological grounds leading to different functioning of the neural system in males and females? Functional magnetic resonance imaging (fMRI) confirms the presence of gender variations in the patterns of neurofunctional activation. Event-related potentials (ERPs) further reveal gender effects on the mode and speed of stimulus information processing in the brain. While these observations provide evidence for the neurophysiological origins of cognitive gender differences, it remains not well known if these are genetically inherent, appear in the course of development, or emerge following life-styles across adulthood.

To approach this question we studied auditory ERPs and event-related oscillations (ERO) in 7-16 year-old children (boys and girls) in different conditions: passive listening, sensorimotor integration, working memory activation and selective attention (2,3). It was established that at the behavioral level, the speed of sensorimotor processes did not depend on gender. Yet, younger (7-8 year-old) girls demonstrated better memory than boys, who achieved the results of girls at later age of 9-10 years. Further, gender affected the neural level of information processing. Although neurophysiological networks existed equally in both genders as reflected by spontaneous EEG activity, these networks functioned differently during stimulus processing: 9-16 year-old girls processed more intensively and faster physical stimulus characteristics than boys as indexed by larger amplitudes and shorter latencies of the early ERPs. This was due to the ability of girls to synchronize more efficiently EEG oscillations during stimulus processing.

Perhaps none of the genders is smarter than the other. But here we show that neurophysiological processes develop differentially in boys and girls during childhood and adolescence. At least for the auditory modality, 7-8 year-old girls outstrip boys in neurocognitive (performance in working memory condition) and 9-16 year-old girls – in neurofunctional (ERP components and network synchronization) development.

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SC24. SPATIAL FREQUENCY DISCRIMINATION AND THETA BRAIN ELECTRICAL ACTIVITY

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In human primary visual cortex besides to orientation columns exists also spatial frequency (SF) columns. The visual information for different spatial frequencies is processed

partially from different neuronal ensembles. There are literature data demonstrating that contrast stimuli with different SF can elicit different visual Event Related Potentials (vERPs). The effect of SF on difference is not the vERPs extensively researched.

In this work we studied the changes of the amplitudes and latencies of vERPs components and Event Related Synchronization/Desynchronization (ERS/ERD) caused by the SF difference between the test stimuli as well as to look for correlation between these changes and the transition from "coarse" to "fine" discrimination in dependence on the SF difference.

We recorded the EEG activity in three task conditions as follows: Motor reaction in response of 5.8 cycles degree-1 and 2.9 cycles degree-1 grids; Motor reaction in response of 4.14 cycles degree-1 and 2.9 cycles degree-1 grids; Motor reaction in response of 3.41 cycles degree-1 and 2.9 cycles degree-1 grids with right index finger and left index finger respectively.

Our results showed that with discrimination difficulty increasing the P3 amplitude of vERPs components decreased. Also with discrimination difficulty increasing the P3 latency of vERPs components increased in P3 and O2 electrode positions. The longer values of P3-component latency at smaller SF-differences might be interpreted as a sign that this difference prolongs the cognitive processing time. The ERS in theta frequency band changes also with SF-difference (discrimination difficulty) change.

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SC25. AUDIO-VISUAL ENTRAINMENT APPLICATION IN SMART ENVIRONMENT FOR USERS' PSYCHOPHYSIOLOGICAL RESPONSE METHODOLOGICAL STUDY

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The audio-visual entrainment today is entering modern smart environment as a tool for augmenting cognitive capabilities, stress control and even entertainment. A number of questions are posted as a result of these, regarding the necessity of creating specialized methodology for studying users' psychophysiological response and building digital society resilience.

In support of the resilience problem solution a research model for audio-visual entrainment stimulation has been experimentally tested in different context and users' response for the last five years.

A set of linear and non-linear methods are provided for achieving quantitative measurement of smart environment multimedia influence on users' response through: postural dynamics, brain activity and galvanic skin response during different experimental task conditions.

Additional psychometric measurements of users are included for motivation and preliminary readiness assessments, concerning the studied context.

Accent is also given to possible interpretations of users' emotional and behavioural response correlations with the entrainment stimulation.

The obtained results provide a solid base for studying and assessing modern digital society and new technologies influence on users, encompassing: augmented/simulated environments, smart devices and social networks.

By these, a significant support is given to the digital society resilience building for new and emerging human-machine interaction threats answering.

The study results are due to the successful realization of the following grants: EU Network of Excellence in Managing Threats & Vulnerabilities for the Future Internet – SysSec, www.syssec-project.eu; National Science Fund, Ministry of Education & Science: Cortical Regulation of the Quiet Stance during Sensory Conflict, TK 02/60, www.cleverstance.com; A Study on IT Threats and Users' Bahaviour Dynamics in Online Social Networks, DMU 03/22, www.snfactor.com.

SC26. CEREBRAL PALSY – A CHALLENGE TO THE KNOWLEDGE, SKILLS, SOCIAL ATTITUDES AND COMMITMENT OF STUDENTS IN THE SPECIALTY OF "REHABILITATION"

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According to the WHO definition, cerebral palsy is poly etiological, non-progressive disease of the central nervous system, occurring as a result of a prenatal, perinatal and postnatal factors. The frequency of CP in Bulgaria is 2,0 – 2,5/1000 newborns. Treatment of children with cerebral palsy involves a complex, multifaceted and multistage medical pedagogical rehabilitation, but is mainly focused on improvement of the functional organization in CNS, which is achieved by systematic and continuous rehabilitation. This is the disease with the largest number of methods of physical therapy established over the years, until in 2010 a Consensus for diagnostics, treatment, rehabilitation and service of children with cerebral palsy was accepted.

The process of rehabilitation is getting the most difficult after the age of 7-8 years. Every parent of a child with CP has to tear their time between difficult contacts with medical institutions, social services and schools. This leads to a deterioration in the quality of the rehabilitation. The number of specialized hospitals in Bulgaria is not sufficient, as well as the number of trained professionals.

Until effective communication and cooperation between social services, education and health institutions is activated, teachers at the Medical College decided to draw the students' attention to the problem of the continuous rehabilitation and to create a professional and responsible behavior toward these children. Over the past three school years – since 2012, we deliberately worked with children with CP in the age range of 6-18 years. We set three very important and interrelated tasks:

1. To help children fulfill their daily duties by adjusting their muscular tonus, improving the coordination and the volume of motion and improving the postural control.
2. To improve the practical skills of the students.
3. To create the opportunity of socialization and diverse communication of children with cerebral palsy with different people.

The available tests for the assessment of children with cerebral palsy are used for getting the results.

In conclusion it was considered that from working with children of this age diverse and effective theoretical and practical skills are acquired. On the other hand, children are showing higher motivation on performing the exercises. Unfortunately, the potential of students for performing this most difficult and unattractive rehabilitation is not fully exploited.

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III. POSTER PRESENTATIONS

Scientific session "NEUROANATOMY, NEUROPHARMACOLOGY AND NEUROTOXICOLOGY"

PP1. ROLE OF CANNABINOID CB1 RECEPTORS ON NOCICEPTION IN RATS WITH DEPRESSION-LIKE STATE

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The aim of the study was to investigated the involvement of cannabinoid CB1 receptors in nociception of male Wistar rats with a model of depression (bilateral olfactory bulbectomy - OBX). The OBX method in rats has been proposed as an animal model of chronic depression. In the OBX rat some of the neurochemical and behavioral changes are similar to those observed in depressed patients.

The cannabinoid CB1 receptor agonist HU-210 and antagonist SR 141716A were microinjected i.c.v. on the developed rat depression model.

Methods: Experimental model of depression - bilateral olfactory bulbectomy (OBX)**.** Bilateral OBX was performed according to the method described by Kelly et al. (1997). Animals were anesthetized with Calypsol (50 mg/kg i.p.) and placed in a stereotaxic apparatus (Stoelting Co., USA). The surgical procedure involved drilling two burr holes 2 mm in diameter with coordinates 8 mm anterior from bregma and 2 mm lateral from the sagittal suture (according to the stereotaxic atlas of Pellegrino and Cushman). The bulbs were aspirated with a stainless dull needle tube attached to a vacuum pump. A sham operation was performed in the same way as in the olfactory bulbectomy without the removal of the olfactory bulbs. 15 days after

the OBX surgery when the model of depression has been developed the animals were anaesthetized with Calypsol (50 mg/kg i.p) and placed in stereotaxic apparatus (Stoelting Co., USA). A stainless steel guide cannula was implanted in the left lateral ventricle according to the Stereotaxic atlas of Pellegrino and Cushman (P = 8.0; L = 1.3; h = -3.8). The HU-210 and SR 141716A were dissolved *ex tempore* in saline. The volume of the solutions was 1 μl injected over a period of 1 min and the injection cannula was left in place for additional 30s. Nociception was examined by applying mechanical pressure on the left hind paw of the rat (analgesy-meter test, Randall-Selitto).
Results: HU-210 (5 μg) significantly increased the pain threshold in OBX rats i.e. decreased the pain sensitivity as compared to saline-treated OBX controls and to sham-operated controls, suggesting an implication of CB1 receptors in nociception of OBX rats. SR 141716A (3 μg) did not affect the nociception in OBX rats.
Conclusion: These results suggest that stimulation of CB1 receptors in rats with a model of depression exerted antinociceptive effect.
Acknowledgements: This study was supported by Grant MU-Varna

PP2. HIPPOCAMPAL LATERALIZATION IN COGNITIVE FUNCTION IN RATS

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The aim was to study the effects of neuropeptides angiotensin II (AT II), cholecystokinin-8 (CCK-8) and vasoactive intestinal peptide (VIP) microinjected unilaterally (left or right) into the hippocampal CA1 area on learning and memory (shuttle-box) of rats. Using stereotaxic apparatus (Stoelting, USA) guide cannulas were implanted bilaterally into the hippocampal CA1 area in accordance with the coordinates from the stereotaxic atlas of Pellegrino&Cushman (P = 3.8 mm, L = ± 2.0 mm, h = -3.0 mm). The neuropeptides were dissolved separately ex tempore in saline and 1μl of drug solution (pH 7.4) was infused over a period of 1 min into left- or right-side of studied brain structures. After surgery the animals were allowed 7 days to recover before the behavioural studies. During the recovery period the rats were handled daily. It was found that ANG II (50 μg) facilitated learning and memory microinjected into the left CA1 area as compared to the controls and to the right-side. The combination (losartan100 μg + Ang II 50 μg) microinjected into the left CA1 area improved learning and memory. These findings suggest that Ang II infused on the background of the inhibited CA1 hippocampal AT1 receptors ameliorated the cognitive processes. CCK-8 (0.01 μg) exerted a favorable effect on learning and memory when injected into the left but not into the right hippocampal CA1 area. VIP (50 ng) microinjected into the left hippocampal CA1 area impaired learning and memory but there is no effect when applied into the right CA area.
In conclusion, the hippocampal lateralized learning and memory effect of AT II, CCK-8 and VIP depends on the hemisphere of injection. These findings suggest a differential hemispheric distribution of AT II, CCK-8 and VIP receptors mediating learning and memory proceses or an interaction between brain neurotransmitters (serotonin, CCK, GABA, Ach), or a differential distribution of their receptors in the brain hemispheres.

PP3. ESTERASE STATUS FOR DIAGNOSTICS AND PROGNOSIS OF OPC INTOXICATIONS

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Organophosphorus compounds (OPCs) with anticholinesterase properties are widely used as insecticides; to a less extent they are used as therapeutic agents. Some highly toxic OPCs were produced and used in several countries as chemical warfare agents. The growing threat of international terrorism brings new scenarios for disaster in which known organophosphorus agents can be used or OPCs of an unknown structure may arise as a result of attacks on chemical plants or stockpiles of pesticides and other chemicals.

Defending against such agents requires rapid, sensitive and specific detection of them and their biological effects. Thus, the development of biomarkers of human exposures to OPCs and their quantification is a vital component of a system of prediction and early diagnosis of induced diseases. Real-time, sensitive and specific exposure assessment would be a vital component of consequence management of such exposures by national authorities, and would lead to minimizing effects of terrorist acts on civilian populations.

In 2012, a new NATO SfP Project "Esterase status for diagnostics and prognosis of OPC intoxications" started. **The aim** of the project is to develop a system for rapid assessment of exposure to OPCs, for the accurate diagnosis and effective prognosis of progressing of the OPC-caused intoxications based on esterase status as a complex biomarker. New electrochemical biosensors are under development for routine on site "point-of-care" monitoring of esterases. The study is focused on investigation of esterase status as a complex biomarker of exposure to OPCs and an aid in accurate diagnosis; development of a nanofilm-based biosensor system for blood esterases analysis and routine on site monitoring of esterase activity; creation of a laboratory prototype of a portable biosensor system for analysis of several blood esterases (acetyl- and butyrylcholinesterases, carboxylesterase, neuropathy target esterase, and paraoxonase) and assessment of esterase status; using the developed biosensor system for investigation of the esterase status of reference groups and groups of individuals contacted with OPCs; genotyping esterases in the same groups of individuals. Interpretation of the results of esterase status determination along with esterases molecular polymorphism data and search for relationships between these parameters allow improving prognosis of intoxications development as well as for working out of individual treatment strategy. The developed technologies can be used for consequence management in chemical accidents and chemical terrorist acts as well as for biomonitoring of individuals involved in occupational contacts with OPCs (pesticides, CWA, etc).

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PP4. VISUAL FEEDBACK POSTUROGRAPHY AS AN EFFECTIVE METHOD OF VESTIBULAR REHABILITATION

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The maintenance of upright stance during different environmental and support conditions is a complex task, which critically depends on an adequate sensory integration and reweighting of the information from the visual, vestibular and somatosensory inputs, especially in the cases of sensory conflict when this information may be absent and/or distorted.

The postural instability and dizziness are frequently complaints in patients with most neurological and psychiatric disorder.

Vestibular rehabilitation therapy have a helpful place to restore the postural control mechanism in CNS disturbed by vestibular diseases.

The vestibular rehabilitation includes exercise and movement for self usage, repositioning maneuvers, and computerized static and dynamic posturography. Visual feedback represents a promising method of vestibular rehabilitation, but in our country is little used in clinical practice.

The aim of this study was to create a vestibular rehabilitation program that include visual feedback and balance training for improve the postural stability after peripheral vestibular lesion.

A static posturography system was used to measure the balance ability. The two software modules for vestibular training were applied. The first one include quiet stance on stable support and on foam pad: open eyes with and without visual feedback, and closed eyes. Duration of each trial was between 30 to 60 seconds repeated in 10 to 20 series. The second include bipedal stance with fixed feet position on stable platform and moving the body weight to place the cursor into targets, which were displayed on a computer screen in front of the subject in indicated directions (left –right or anterior-posterior). Several parameters are measured: sway velocity, sway amplitude, mean displacement of center of foot pressure (sway path), time to reach target, time to go back from target, sway path to reach target and sway path to go back to begining position.

The system is designed to train skills of balance, concentration, attention, coordination, sensibility and proprioception. Exercises on balance stimulate the vestibular system and lead to improve postural stability after vestibular lesion or create new models of motor skills for keep the equilibrium.

PP5. VERP AMPLITUDE ATTENTIONAL MODULATION IN RESPONSE TO SELECTIVE S-CONE AND LUMINANCE STIMULI

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Human daylight vision is subserved by three types of cones, short wavelength (S-cones), middle wavelength (M-cones) and long wavelength (L-cones). The information from the M and L cones along ON and OFF pathways is segregated at level of cone-bipolar cell synapse. However, the existence of separate ON and OFF pathways in human of S-cones is a matter of debate. Moreover, previous studies showed difference in attentional modulation between S-cone and luminance stimuli.

The aim of the present study was to evaluate the effect of attention on luminance in blue-yellow stimulation.

Visual Event Related Potentials (VERP`s) were recorded from occipital and parietal regions in two task conditions – passive and mental. To selectively stimulate the S-cones we applied a modified two-color threshold method of Stiles and blue test stimuli were presented on bright yellow background. Control experiments involved presentation of blue test stimuli on a blue background when all three types of photoreceptors are involved in stimulus detection. The stimulus duration was 500 msec. Increments and decrements were presented in separated blocks.

The results showed an increase in P3 wave amplitude in response to the stimulus onset and offset in all conditions except offset of luminance increment as well as the offsets of selective S-cone increment and decrement.

The result for N1amplitude showed increase in response to the stimulus onset of luminance increment and decrease in response to the offset of luminance increment.

Wave present results showed certain differences in attentional modulation of cortical responses to selective S-cone and luminance stimuli.

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PP.6. AGE-RELATED CHANGES IN BRAIN ACTIVATION DURING AUDITORY DISCRIMINATION TASK: EVENT-RELATED POTENTIAL STUDY

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The brain as a system with gradually decreasing resources maximizes its chances by reorganizing neural networks to ensure efficient performance. Auditory event-related potentials were recorded in 28 healthy volunteers comprising 14 young and 14 elderly subjects in auditory discrimination motor task (low frequency tone – right hand movement and high frequency tone – left hand movement). The amplitudes of the sensory event-related potential components (N1, P2) were more pronounced with increasing age for either tone and this effect for P2 amplitude was more pronounced in the frontal region. The latency relationship of N1 between the groups was tone-dependent, while that of P2 was tone-independent with a prominent delay in the elderly group over all brain regions. The amplitudes of the cognitive components (N2, P3) diminished with increasing age and the hemispheric asymmetry of N2 (but not for P3) reduced with increasing age. Prolonged N2 latency with increasing age was widespread for either tone while between-group difference in P3 latency was tone-dependent. High frequency tone stimulation and movement requirements lead to P3 delay in the elderly group. The amplitude difference of the sensory components between the age groups could be due to a general greater alertness, less expressed habituation, or decline in the ability to retreat attentional resources from the stimuli in the elderly group. With aging, a neural circuit reorganization of the brain activity affects the cognitive processes. The approach used in this study is useful for an early discrimination between normal and pathological brain aging for early treatment of cognitive alterations and dementia.

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PP.7. COMPUTERIZED SYSTEM FOR PHYSIOLOGICAL AND PHARMACOLOGICAL RESEARCH

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The system consists of electrostimulator, four channel dynamometer and software.
Characteristics of electrostimulator:
* Ability to stimulation with constant current or constant voltage;
* Maximum output current: 100 mA
* Maximum output voltage: 100V
* Ability to change the amplitude of the stimulation during operation of the pacemaker;
* Independent adjustment of temporal parameters of stimulation
* Digital tuning of packages period
* Digital adjustment of pulse period
* Digital adjustment of packages length
* Digital tuning of pulse width.
Characteristics of four channel dynamometer:
* Number of input channels: 4
* Input Sensitivity: 2mV / V, 5mV / V, 10mV / V, 20mV / V
* Resolution data: 16 bit
* Frequency: 50 samples / second
* Communication with PC, via USB port
* Ability to manage through a specially developed software package
* Ability to manage through MATLAB, LabView or other specialized scientific software package
* Available drivers for Windows XP, Windows 7, Windows 8, WIndows CE, Linux, Mac OS, Android (Java)
Software "Dynamometer"
Capabilities of software "Dynamometer - RECORD"
* Independent calibration of each of the four channels
* Real-time preview of forces introduced by shooting dynamometers on PC screen
* Drawing in real-time graph of signal dynamometers, with the possibility of varying the speed of the sweep
* Ability to set the program in "PAUSE"
* Mode "PAUSE" does not affect the measured time
* Possibility of "brand" to mark various events during the experiment
* Automatically storing measurement data in a file
* Data Format - ASCII, allow easy entry into specialized programs for processing and analysis of signals

Capabilities of software "Dynamometer - MEASUREMENT"
* Preview of the recorded data channels
* Different colors for different signal channels
* Changing the time scale signal
* Visualization of time from the beginning of the experiment
* Easy measurement of the signal amplitude
* Easy measurement of time parameters of the signal

PP.8. BRAINBOW – AN AMAZING TECHNIQUE IN NEUROSCIENCE

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One of the greatest problems of modern neuroscience is developing a connection between the structure and function of the synaptic network. Scientists need to have good visualization methods in order to make conclusions about the neurological function of a given synaptic contact and to establish the exact meaning of a particular part of the brain. Most staining techniques give little information as they dye only some structures of the neuron randomly and their one color nature doesn't allow distinguishing between different neurons and their connections.

Brainbow is a new technique, based on stochastic expression of different fluorescent proteins in the neural tissue. The result is different coloring of the neural network such as every neuron dyes in its own cue which makes it clearly differentiated from its neighboring neurons. Brainbow uses the tools of genetic engineering to create a gene construct that carries genes for more than one fluorescent proteins and a recombination system, consisting of a recombinase enzyme and marking sequences, which mark the exact spot where the recombination will occur. Injection of several constructs in the studied organism via virus vectors results in stochastic expression of different constructs in different cells that give expression to different fluorescent proteins. Brainbow is able to dye a particular part of the brain with more than 160 colors at once. Thus we can see trough the messy neuron network and separate one neuron from another. We can visualize very well what kind of contacts a neural cell makes and via many other tests we can make conclusions about its role in the network. This kind of information could be essential when it comes to brain pathology especially neurodegenerative diseases such as Parkinson, Alzheimer and many others.

Brainbow draws a line between observing the structure of a given brain part and establishing its functions.

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