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ROLE OF AUTONOMIC NERVOUS SYSTEM IN EMERGENCE OF OBESITY-ASSOCIATED ABNORMALITIES IN ADOLESCENCE

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BACKGROUND : Obesity is a leading cause of the metabolic syndrome (MS), defined by the co-occurrence of intra-abdominal obesity, atherogenic dyslipidemia, raised blood pressure (BP), insulin resistance and/or glucose intolerance, and a pro-inflammatory state (1). In the industrialized world, its prevalence is increasing. Moreover, the syndrome, typically regarded as a middle- to late-adulthood disorder, is now present in childhood and adolescence. It has long been recognized that upper-compared with lower-body obesity is more closely associated with cardiovascular and metabolic abnormalities of the MS (8;9). More recently, this difference has been related to the increased quantity of intra-abdominal fat (IAF) that is frequently found in individuals with upper-body obesity (10). Underlying mechanisms linking intra-abdominal obesity to development of the MS are not well understood. Accumulation of visceral fat, characterized by a relatively high lipid-turnover, may result in higher levels of free fatty acids in the portal circulation (11). This, in turn, may contribute to the development of individual components of the MS via, for example, enhanced lipid synthesis, gluconeogenesis and insulin resistance (10;12;13). Furthermore, IAF correlates positively with activation of the sympathetic nervous system (14) that may further enhance free fatty acid release into portal circulation (15). Sympathoactivation may also contribute to the elevation of BP through its effects on vasculature

and renal handling of sodium and water (16;17). The aim of the present study was to investigate the impacts of IAF, assessed with magnetic resonance imaging (MRI), and gender on individual components of the MS in a population-based cohort of 324 adolescents. We also examined whether the autonomic nervous system, assessed with power spectral analysis of beat-to-beat BP and inter-beat-interval (IBI) (21), contributes to these effects.

METHODS: A population-based sample of 324 adolescents, aged 12–18 years, was recruited as part of the Saguenay Youth Study. Males and females with “high” or “low” intra-abdominal fat (IAF), defined by the median split, were compared. IAF was quantified with magnetic resonance imaging. Primary outcome measures were blood pressure (BP), fasting serum glucose, insulin, lipids and C-reactive protein. Secondary mechanistic measures were cardiovascular variability indices of autonomic nervous system function at rest and in response to physical and mental challenges. Tanner stage of pubertal development and serum levels of cortisol, leptin, and sex hormones were determined. Data were analyzed using mixed model regression analysis with IAF, sex, IAF*sex, Tanner stage and other potential confounding variables included in the model.

RESULTS: Our results indicate that excess IAF is a significant risk factor for the metabolic syndrome in adolescence; the syndrome was completely absent in adolescents with “low” IAF and was present 13.8% of males and 8.3% of females with “high” IAF. Excess IAF was associated with insulin resistance (higher HOMA index: 0.5 [0.3 – 0.8], $p < 0.001$), dyslipidemia (higher triglycerides: 17.7 [9.7 – 25.7] mg/dL, $p < 0.001$, and lower HDL-cholesterol: -3.9 [-6.2 – -1.5] mg/dL, $p = 0.003$), and a pro-inflammatory state (higher C-reactive protein: 0.03 [0.01 – 0.05] mg/L, $p = 0.003$), affecting males and females similarly. In contrast, “high” IAF was associated with elevations of BP and sympathetic activity in males only (higher systolic BP: 6 [1 – 11] mm Hg,

p=0.02 and low-frequency power of DBP: 629 [37 – 1222] mm Hg², p=0.04).

Conclusions: Our results suggest that, already in adolescence, accumulation of IAF promotes development of the metabolic syndrome, affecting the metabolic and inflammatory components similarly in both genders, but impacting on BP adversely only in males. The latter may be attributed, in part, to the augmentation of sympathetic activity also seen only in males.

COMPLEX PARTIAL SEIZURE-LIKE SYMPTOM INVENTORY: PSYCHOMETRIC, STATISTICAL, NON-INTERPRETATIVE ANALYSES

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BACKGROUND: Recently, neuropsychiatrists have called increased attention to a neurobehavioral syndrome characterized by multiple partial seizure-like symptoms in the context of persistent dysphoria and emotional lability. To measure breadth and frequency of these symptoms, Roberts (1992) invented a psychometric tool called CPSI - complex partial seizure-like symptom inventory. The questionnaire encompasses 35 questions describing affective, cognitive and psycho-sensory symptoms associated with partial seizure disorders. The aim of our research was to conduct statistical, non-interpretative analyses of acquired CPSI data in order to find out responses of non-pathological sample. Because we have used slightly modified Czech version of CPSI, psychometric analysis of reliability was also carried out.

METHODS: We administered this questionnaire personally to 184 university students. The group comprises 147 male and 37 female subjects (Mean age = 22.19; Std = 1.77). All subjects have reported themselves to be free of neurological and psychiatric treatment or disorder. To determine the attributes of required data we have used descriptive statistics, Spearman's correlation analysis, factor analysis and we measured the reliability of modified CPSI by way of internal consistency. In CPSI, subjects are asked to rate the frequencies with which symptoms occur on a 6-point scale. "0" means never or not in the last year, up to "5" meaning at least once a day.

RESULTS: The average total symptom score for our sample was 19.07 (Std = 14.10; Median = 16). The histogram reveals unimodal slightly positively skewed distribution. By factor analysis and its scree plot we have found that there is one distinctive factor. Consequently, measure of the reliability of the questionnaire proved good internal consistency (Cronbach's alpha = 0.90). By way of factor analysis and correlation analysis we have found that not all items have "L" distribution as internal consistency suggested. Five items (9,11,27,28,33) are considered as "deviant" items in our sample. Items 9,27,28,33 are scored exceptionally slightly, so these symptoms don't occur in our sample almost at all. Furthermore, item 11 (concerning cephalic pain), is scored with average value but with different trend regarding other items.

CONCLUSION: In non-pathological sample we discovered that thirty items have the particular configuration, but there are five items which don't fit into this configuration. Whether these items are meaningful and significant in the group of neuropsychiatric patients or they are not we have to prove in further investigation.

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THE STRENGTHS OF CHARACTER AND THE SATISFACTION WITH WORK

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Positive psychology focuses largely on strengths. Peterson and Seligman (2004) followed the example of the Diagnostic and Statistical Manual (DSM) of the American Psychiatric Association, and proposed a classification schema of the strengths of character that make the good life possible. The Values In Action (VIA) classification is a descriptive tool and distinguishes between virtues and character strengths. Virtues are the core characteristics that are valued by moral philosophers and religious thinkers: wisdom, courage, humanity, justice, temperance and transcendence. Character strengths are the psychological processes, or mechanisms, that define the virtues. They are a distinguishable way to display one or another of the virtues. They are considered

dimensional traits that exist in degrees with individual differences.

Aim of our research is to explore the relationship between the strengths of character, measured by the VIA Strengths Survey (VSS), and the satisfaction with work measured by an original inventory. The sample includes 165 subjects that have different types of jobs. The main results suggest that the satisfaction with work is only slightly correlated with the character strengths.

DIFFERENT EEG COMPONENTS OF BERGER EFFECT

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BACKGROUND: It's well known (Berger, 1929) that there are visible changes in EEG in transition from eyes opened (REO) state to eyes closed (REC) state. These changes are known as Berger effect. In PET studies (Raichle et al., 2001; Gusnard et al., 2001) no significant changes in blood flow was found for any brain regions, except occipital, in REO-REC comparison. Other investigators (Marx et al., 2003, 2004) in complete darkness demonstrated that not only visual information processing provide the differences in REO-REC comparison. In electrophysiological investigations (Danko, 2006) REC-REO differences have been revealed as changes in system organization of brain functional states. The REC can be considered as an example of "interoceptive" state and REO - of "exteroceptive" state (Marx et al., 2003; Danko, 2006). Changes in patterns of brain activations between REC-REO states can be attributed to at least two components: determined by perception of visual information and by shift of attention from «interoceptive» to «exteroceptive» direction (Danko, 2006).

The goal of this study was to see if mentioned above components can be separated in EEG Berger effect using different light conditions.

METHODS: EEG was recorded from 19 scalp zones with reference electrodes on earlobes during 4 min intervals of REC or REO either. EEG was recorded in complete darkness, or in dim light room illumination with gaze fixation from 30 healthy volunteers. Spectral power and coherence were calculated for seven EEG frequency bands δ (1,5-4Hz), θ (4-7Hz), $\alpha 1$ (7-10Hz), $\alpha 2$ (10-13Hz), $\beta 1$ (13-18Hz), $\beta 2$ (18-30Hz), γ (30-40Hz). Repeated

measures analysis of variance (ANOVA), was applied, a threshold error probability – 0,05.

RESULTS: Changes of EEG power and coherence in REO-REC comparison in darkness should be attributed to attention reorganization. In this comparison the REO state was characterized by reduction of $\alpha 1$ -, $\alpha 2$ -spectral power in all cortex regions, except for frontal lobes, increase of θ -, $\beta 2$ - and γ -power in frontal, temporal regions and reduction of coherence in $\alpha 2$ -, $\beta 1$ -, $\beta 2$ -frequency band. For $\beta 1$ -frequency band the increase of power in REO state in frontal and temporal regions was accompanied by power decreases in posterior regions. EEG changes in REO in dim light-REO in darkness comparison should be attributed to perception of visual information. In this comparison the REO was characterized by reduction of $\alpha 1$ -, $\alpha 2$ - power in all considered regions, by reduction of $\beta 1$ -power in occipital regions, and by reduction of $\alpha 1$ -, $\alpha 2$ -coherence.

Conclusions. It was demonstrated that REO state is strongly different from the REC state even in complete darkness. So here we deal with involuntary changes in brain state most probably in the state of attention system which is automatically shifted to internal from external milieu even in the absence of external stimuli. Illumination changes EEG parameters as well as a consequence of thalamo-cortical activation caused by visual afferent flow.

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COMPLEX PARTIAL SEIZURE-LIKE SYMPTOMS IN PATIENTS WITH ANXIETY DISORDERS: PRELIMINARY CLINICAL STUDY

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BACKGROUND: Complex partial seizure-like symptoms (CPSS) are a relatively stable set of symptoms first described in a population of temporal epilepsy patients, where they are considered as a marker of limbic irritability. Because CPSS highly correlate with traumatic stress and anxiety we decided to study this neurobehavioral phenomenon on a population of anxious patients. In our preliminary clinical study we wanted to

discover the frequency of CPSS among anxious inpatients and detect possible linkage between CPSS and selected psychopathological symptoms.

METHODS: Data were obtained from 30 psychiatric inpatients with anxiety disorder diagnosis (mean age 33 years, number of males = 9). At the time of the assessment all patients were being treated with antidepressant and anxiolytic medication. Control group consisted of 30 healthy subjects (mean age 22 years, number of males = 15). All subjects were administered Complex partial seizure-like symptoms inventory (CPSI), Dissociative Experiences Scale (DES), Trauma Symptom Checklist (TSC-40), Beck Depression Inventory (BDI-II) and Self-rating Anxiety Scale (SAS). Mann-Whitney U-test and Spearman's rank correlation were used for statistical analysis. Means and standard deviations are presented.

RESULTS: Mean CPSI scores were 44.2 ± 29.5 in anxious patients and 18.1 ± 14.5 in healthy controls. The difference is statistically significant at $p < 0.01$. Anxious patients also significantly differ from healthy controls in DES, TSC-40, BDI-II and SAS. All correlations of CPSI mean scores and mean scores of other psychometric measures in a sample of anxious patients (r values from 0.46 to 0.71) are statistically significant at $p < 0.05$. The highest correlation is between CPSI and DES. Similar correlations were also found in a sample of healthy controls (r values from 0.48 to 0.71, $p < 0.01$). To better understand these correlations the sample of anxious patients was divided in subgroups with high (more than 30, $N=19$) and low (less than 30, $N=11$) CPSI score. These two subgroups differ significantly in all psychopathological measures at $p < 0.01$. Both subgroups differ from healthy controls in all variables, with the exception of DES, where subgroup with low CPSI score reached the same value as healthy people, so the deep relation between CPSS and dissociative symptoms was confirmed again.

CONCLUSIONS: Anxious patients report complex partial seizure-like symptoms more often than healthy people. The presence of CPSS is associated with the presence of anxiety symptoms, dissociative symptoms, and psychological traumas in anamnesis and depression symptoms. The most significant connection was found between CPSS and dissociative symptoms. Because CPSS are considered as a marker of limbic irritability, CPSI as a clinical assessment method could be useful for selection of anxious patients possibly responsive to anticonvulsant treatment.

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TYPE A BEHAVIOR PATTERN AS A POSSIBLE CARDIOVASCULAR RISK FACTOR IN SELECTED POPULATION GROUP

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BACKGROUND: Some epidemiological investigations supported the role of psychosocial factors, such as the type A behavior pattern in the etiology of coronary heart disease. Atherogenic components of the coronary-prone or type A behavior pattern, including hostility, as well as stress reactivity are emerging as particularly significant behavioral characteristics, although their pathophysiology is not yet fully understood. The inconsistent results have been reported (positive, negative or no associations among these factors and the coronary risk).

The aim of the present study was to determine the prevalence of cardiovascular risk factors in the sample of young healthy persons according to behavior pattern type. **METHODS:** The sample of 1679 university students (548 men and 1131 women) of mean age 22 ± 1.5 years (men 22.9 ± 1.7 ; women 22.6 ± 1.4 years) was examined to determine the prevalence of the type A behavior pattern and the occurrence of main cardiovascular risk factors. The behavior pattern was detected by Bortner scale. Physical examinations (anthropometric characteristics like body mass index, percentage of body fat, waist circumference; blood pressure); blood examinations (total serum cholesterol level – TC, LDL-C, HDL-C, triglycerides, atherogenic index TC/HDL-C, Framingham risk score and risk score according to SCORE chart after the projection to the age of 60), and some lifestyle pattern (physical activity, smoking, stress load, some nutritional habits) were performed. The total sample was divided into two groups – A type and B type behavior pattern. The comparison of these two groups from the standpoint of cardiovascular risk was made.

RESULTS: The A type behavior pattern was detected more often in the group of women (44.5% vs 40.8% in men; NS). The highly significant A vs B differences were detected in subjectively declared stress load both in men ($p < 0.05$) and in women ($p < 0.01$); predominantly at

school (but no significant differences were in private stress load), and/or in subjectively declared chronic psychogenic stress load – in men A-type 48.2% vs B type 33.1%; $p < 0.01$, and in women A type 4.8% vs B type 35.4%; $p < 0.001$, respectively.

Higher occurrence (NS) of worse values of some objective cardiovascular risk factors (obesity, risky waist circumference, higher levels of BP, higher levels of TC, LDL-C levels and atherogenic indexes TC/HDL-C and log TG/HDL-C) were detected in type-B group of men, even in this group the occurrence of high systolic blood pressure (>140 mmHg) was significantly higher ($p < 0.01$). Similar results were found in women, moreover, in women of type A behavior pattern significantly correlated with oral contraceptive use. On the other hand, in B-type group both in men and women the higher levels of HDL-C were detected (in women $p < 0.001$). The total cardiovascular risk score was slightly worse (NS) in B-type group both in men and in women.

CONCLUSIONS: The results of this study suggest that type-A behavior pattern is not positively associated with physiological (traditional) risk factors for CVD in this young age group, and that Type A behavior pattern is probably a general disease-prone condition rather than merely a specific coronary risk factor.

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PSYCHO-ACOUSTICAL TRANSITIONAL (PAT) SESSIONS AND WELL-BEING. CLINICAL APPLICATIONS AND THEORETICAL HYPOTHESIS CONCERNING THE ROLE OF AUTOPOIETIC PHENOMENA UNFOLDING DURING PAT SESSIONS

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BACKGROUND: The PAT session is a completely defined setting from a mathematical-physical point of view and doesn't need an interaction with other subject to produce an evident modulation of the consciousness' state. The utilization of an "informal" sound-stimulus

bypasses the problems related to the subject's mother tongue and his musical culture (Finsterle, 2006). Therefore PAT Session can be defined as a "primary", scientific intervention's methodology on the mind-body system, of possible universal application (Finsterle, 2007).

METHODS: The effects of increase of intra psychical communication, plasticity and efficiency of the brain-system (Aiello, Finsterle, 2005), have been utilized in conjunction with a psychoanalytical oriented dialogue to improve the quality of life, because of the increased subject's conscious acceptance of the spontaneously emerging new ways to give sense to internal unconscious fantasies and external events.

RESULTS: A relation seems to appear - on one hand - between the kind (coenaesthetic, sonorous, visual) and the unfolding's frequency of autopoietic phenomena and - on the other hand - the subject's level of anxiety and his psychical structure.

CONCLUSIONS: Observing the relation between conscious and unconscious signification process, it seems plausible to hypothesize that the subjective perceived well being and the resilience capability (effective interaction with the "world's" problems) are related with the degree of consonance between conscious and unconscious way to give sense to the events, consonance that tends to reduce the level of anxiety, positively influencing also the domain of external stimuli perception.

DO AERONAUTICAL FACTORS IN THE AIRCRAFT COCKPIT INFLUENCE SOME NEUROBEHAVIORAL, ENDOCRINE-IMMUNE OR ORGAN CHARACTERISTICS IN LURCHER AND WILD-TYPE MICE?

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BACKGROUND: Pilots in the cockpit and other professional group within the aircraft industry, trains as well as in heavy industries are exposed to infrasound (0 – 20 Hz) and low-frequency noise (20 – 500 Hz) (ILFN) (0 – 500 Hz). In dependence on intensity (≥ 90 db) and time of exposure this long-term acting noise can induce a multisystemic whole body pathology named vibroacoustic disease (VAD). Affected are blood vessels, cardiac structure, trachea, lung, kidney, immune and nervous systems.

METHODS: B6CBA Lurcher mutant (Lc/+, suffered from cerebellar degeneration) and healthy wild type mice (+/+) spent 540 flight-hours in the cockpit of CSA aircrafts Boeing 737 in the course of 6 weeks. Immediately after their flights one half of 32 experimental animals of both types as well as controls were examined in open field test and then sacrificed to obtain samples of blood and different organs. The second half of animals was tested in special behavioral procedures: spatial learning using Morris water maze (MWM) and motor functions by means of horizontal wire, ladder and rotarod. After one month these animals as well as controls were sacrificed and their organ and blood samples used for histological, immunological and endocrinological examination in the same way as previous ones.

RESULTS: Open field test and examination of spatial learning in MWM showed no significant differences between experimental and control animals. Mild significant differences were found in swimming velocity, when experimental mice (both Lc/+ and +/+) were slower than controls. Examination of motor functions showed significant differences between experimental +/+ and controls only on the horizontal wire when more successful were experimental animals, while in the rotarod test, control animals achieved better results.

Optical microscopy of various organs showed no differences between experimental and control animals, but electron microscopical examination of lung showed mild enlargement of interalveolar septa in three experimental animals.

Immunological examination of lymphatic organs did not show any significant differences between experimental and control mice while blood samples revealed lower concentration of some interleukins (IL 10, IL 1a) in experimental animals compared to controls.

Experimental animals also showed higher concentration of noradrenaline and dopamine than controls.

CONCLUSIONS: Despite only mild differences between experimental and control animals we found, the effect of ILFN on the living organism and its relationship to VAD should be further studied.

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THE EFFECT OF NITRIC OXIDE SYNTHASE INHIBITORS NITRO-L-ARGININE AND 7-NITROINDAZOLE ON SPATIAL LEARNING AND MOTOR FUNCTIONS IN LURCHER MUTANT AND WILD TYPE MICE

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BACKGROUND: Nitric oxide (NO) is an intercellular messenger that, among other things, plays a role in the nervous system as a gaseous neurotransmitter, modulating LTP induction of synaptic transmission that has been suggested to be the base of memory formation. N-Nitro-L-arginine (NA) is an unselective nitric oxide synthase (NOS) inhibitor which influences, except neuronal, also endothelial NOS with impact on blood pressure. 7-nitroindazole (NI) is a selective neuronal NOS inhibitor without this circulatory effect.

The aim of our work was to observe the effect of acute and chronic administration of both chemicals on behavior, spatial learning and motor functions in Lurcher and wild type mice, derived from B6CBA strain

METHODS: In acute experiments 90 animals were used, 45 wild type and 45 Lurcher mutants. The animals of both types were divided into five groups with application of: 1. NA, 2. diluted 1M HCL (NA-solvent), 3. NI, 4. DMSO (NI-solvent), 5. saline.

In chronic experiments 54 animals were used, 27 wild type and 27 Lurchers. The animals of both types were divided into three groups with application of: 1. NI, 2. DMSO, 3. saline. Both, NA and NI in dose 25 mg/kg as well as control solutions, in relevant volume, were administered i.p. 30 min. before the experiment.

Spatial learning was examined using the Morris water maze (MWM) with a platform hidden under the water surface and four starts daily in 5 days. Motor functions were examined with four different standard tests and

behavioral characteristics we observed using open field method.

RESULTS: In wild type mice acute experiments showed no significant differences in motor functions between influenced and control animals. Also in MWM experiments the latencies of reaching the platform and mean length of swimming trajectories (marker of learning) differed only insignificantly. In Lurcher mutants NI decreased significantly their motor ability, but spatial learning was not affected.

In wild type mice after chronic application of NOS inhibitors (from 2nd postnatal day), we did not find any differences between NI treated animals and controls in both cognitive and motor functions. In Lurcher mutants experimental and control animals differed in cognitive functions also only insignificantly. Though statistically significant decrease of motor ability we found in animals influenced by both NI and DMSO compared to control mice administered with saline.

CONCLUSIONS: Neither Lurcher mutant, nor wild type mice derived from the B6CBA strain were significantly affected by NOS inhibitors NA and NI in above-mentioned doses in spatial learning and memory by acute or chronic application. Nevertheless, administration of NI in acute experiments and long-term effect of both NI and its solvent DMSO in chronic experiments significantly decreased motor ability in Lurcher mutants. The findings will be further studied.

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THE EFFECT OR D1-LIKE RECEPTORS BLOCKADE ON MOTOR FUNCTIONS, SPATIAL LEARNING AND CNS EXCITABILITY IN B6CBA MICE

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BACKGROUND: Dopaminergic neurotransmitter system plays a role in many neural functions, for instance motor system. Dopamine also influences cognitive functions, motivation and behavior.

In this study, the effect of D1-like receptors blocker SCH 23390 on spontaneous motor activity, motor functions, spatial learning and CNS excitability in adult wild type mice derived from the strain B6CBA was investigated.

METHODS: We used 28 adult wild type mice of the strain B6CBA. The animals were divided into two groups. The first group (n=15) was administered with D1-like receptors blocker SCH 23390, 0.5 mg/kg. The other group (n=13) was treated with the saline solution in an equivalent dosage. The experiments started 20 minutes after the application.

Spontaneous motor activity was examined in the open field and trajectory was measured. Motor functions were examined by standard tests for the next three consecutive days. Latencies and criterion meeting were evaluated on the horizontal wire, ladder and rotarod. Two conditions were considered as a criterion meeting: 120 seconds on the apparatus, or active leaving it.

Spatial learning was tested in the Morris water maze. The mice were subjected to find a platform hidden in the southwest quadrant of a pool within an interval of 60 seconds. Four trials a day were performed subsequently from different starting position during 10 days of testing. Latency, criterion meeting, swimming velocity and trajectory length were evaluated.

Audiogenic epilepsy was used for testing CNS excitability. Reaction of mice to the sound stimulus of 90 dB was observed.

RESULTS: D1-like receptors blockade significantly decreased spontaneous motor activity. In the horizontal wire test, the mice treated with SCH 23390 manifested significantly better results in both observed parameters. No significance was found in the ladder test. On the rotarod, the animals with D1-like receptors blockade reached significantly shorter latencies and lower criterion meeting. In the Morris water maze, D1-like receptors blockade led to significant impairment of all tested parameters. Only insignificant differences were found between experimental and control mice in the CNS excitability test.

CONCLUSIONS: Spontaneous motor activity and motor skills were influenced by evoked hypokinesia. Meanwhile in the horizontal wire test it seemed to be advantageous, for the results in the rotarod test it was a definite handicap because this test requires good motor coordination and activity.

The results gained in the Morris water maze indicated that not only hypokinesia played some role but also spatial learning and perhaps motivation were affected.

Despite the CNS excitability in pharmacologically influenced animals were almost twofold lower than in controls, the differences between them were only insignificant. Maybe, if we examined more animals, the

results could be statistically significant and in accordance with the fact that the D1-like family receptors blockade leads to the general inhibition.

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TRANSPLANTATION OF EMBRYONAL GRAFT FROM CEREBELLUM AND ITS INFLUENCE ON THE HIPPOCAMPAL ELECTROGENY IN LURCHER MUTANT MICE: EFFECT OF AGE AND MOTOR TRAINING

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BACKGROUND: The interactions between cerebellar and hippocampal structures in Lurcher mutant mice (LMM, strain C57Bl/7) were studied. LMM represent a model of genetically determined olivocerebellar degeneration which is primarily caused by the mutation of delta-2 glutamate receptor gene and results in excitotoxic apoptosis of Purkinje cell. Loss of granule cells and inferior olivary neurons is secondary.

METHODS: Possible influence of embryonal cerebellar graft transplanted into the adult neurodegenerative brain in LMM on long-term potentiation (LTP) in hippocampus was investigated in the first part of study; sham-operated control animals (where vehiculum was administered by the same procedure) served as controls. LTP was performed under urethane anesthesia, 2g/kg i.p. (stimulation of perforant path and registration in the dentate gyrus, biphasic pulses, basal low frequency 0.1 Hz, duration 0.1 ms, high-frequency stimulation 100Hz, 10 bursts from 16 stimuli each 10 s). A difference in the magnitude of EPSP population spike (amplitude) was evaluated. In the second part of the study, a comparison between hippocampal LTP in trained and untrained group of animals and also possible effect of age were studied. One group of mice (transplantated and control) was exposed to repetitive motor training on the rotarod. Duration of each session was 2 min., sessions were repeated four times in 15 min intervals (5 days weekly, 6 weeks and 2 days in the 7th week), and thus total duration was 32 days. All animals were also divided into two groups according to age – young mice (3 months old) and adult (more than 6 months old).

RESULTS: Main statistical evaluation showed that LMM with transplanted embryonal tissue had significant enhancement of EPSP amplitude in comparison with controls. Trained mice revealed higher LTP ability than untrained animals, with differences between young and adult individuals, but these results had worse statistical significance. Trend of LTP enhancement in transplanted animals correlated with the level of repetitive motor training. The effect of age seemed to be present but it was insignificant.

CONCLUSIONS: The embryonal graft influenced LTP level in host animals. Clear differences between transplanted and control animals suggested possible effect of some trophic factors originated in embryonal tissue which affected the hippocampal electrogeny.

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METHAMPHETAMINE AND TEST OF SOCIAL INTERACTIONS IN ADULT MALE RATS.

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BACKGROUND: Psychostimulants affect human behavior in serious manner; specifically, they induce aggressive behavior and impair social interaction. Experimental data are ambiguous. It was observed increase in aggressive behavior or increase/decrease of social interactions. We used test of social interaction that has been first described by File (1978). This test is known as a test of anxiety. Methamphetamine has anxiogenic effect shown on mice models in other tests of anxiety. Methamphetamine also decreases social interaction. This effect is due to high doses or long duration of application. The aim of the present study was to assess the effect of single low dose of methamphetamine (MA) on social interaction in adult male rats.

METHODS: Adult male rat were tested in 3 different stress or anxiety conditions: low stress (familiar arena and low light), middle stress (unfamiliar arena, low light) and high stress (unfamiliar arena and high light). We had 5 groups in each stress condition. Control group without any treatment, group with saline administration a groups with methamphetamine application in 3 different doses:

0.5, 1.0 or 1.5 mg/kg. The social interactions were tested in adult male rats 30 minutes after subcutaneous drug injection. Test was performed on pairs of animals with the same treatment and weight (n = 8 pairs). Their interaction behavior was tested in the open field and video recorded during 5 minutes. The video-recording then was evaluated with use of computer program ODLog (Macropod Software). Observation units were both animals and their interaction. Assessed parameters were: (A) active social interaction (sniffing, crowding, following, grooming) and (B) non-social activity: locomotion and rearing.

RESULTS: Our data demonstrate that acute treatment of low dose MA (0.5, 1.0 and 1.5 mg/kg) decreases social interaction in all stress conditions. We confirmed that increase in stress condition significantly decreases time of social interaction in all groups without changes in frequency of it. However, MA increases time of locomotor and rearing behavior. Acute MA treatment increases locomotion in dose dependent pattern under low stress condition. Increased stress condition causes locomotion raise in all groups, in addition disappears MA dose dependent effect. Rearing behavior is more pronounced in MA groups under higher stress conditions. Increase in non-social activities partially is due to MA treatment, however, increased stress condition (unfamiliar arena and light intensity) causes raise also, due to exploratory activity. Applied low doses of MA do not cause occurrence of stereotypical behavior.

CONCLUSIONS: Methamphetamine acute treatment does not change frequency of social interaction; however, even in low dose it significantly changes character of interaction and decreases time of it. Because intensity of social interaction is often associated with anxiety in rats, our results also suggest that MA may have anxiogenic effect.

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CORRELATION BETWEEN FREE SALIVA TESTOSTERONE LEVELS? POLYMORPHISMS OF TESTOSTERONE METABOLISM GENES AND COGNITIVE ABILITIES IN DIFFERENT GROUP OF PATIENTS.

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BACKGROUND: Aim of the study was to observe correlations between free saliva testosterone levels, polymorphisms of testosterone metabolism genes and cognitive abilities in different groups of individuals. Various groups of patients were used in this project: gifted children, elderly hypogonadic patients, patients with prostate cancer and individuals with autistic phenotype features. Effects of testosterone could be influenced by several types of polymorphisms in genes, whose products participate on metabolism of steroid hormones, e.g.: androgen receptor gene (AR), aromatase gene (CYP19), 5 α -reductase gene (SRD5A2), estrogen receptor gene (ESR1) and gene for sexual hormone binding protein.

METHODS: DNA samples were isolated from buccal cells in saliva and subsequently DNA was amplified by PCR. The CYP19 C1558-T and SRD5A2 A49T polymorphisms were determined by RFLP analysis and the AR (CAG)_n polymorphism was determined by fragment analysis with fluorescently labeled primer. Salivary testosterone levels were measured with radioimmunoassay. Cognitive abilities were assessed via standard psychological tests – coefficient of mental rotation (CMR) and coefficient of spatial abilities (CSA).

RESULTS: We found significant correlation between polymorphism A49T of SRD5A2 gene and CMR, as well as CSA in the group of gifted children. Polymorphisms of AR and CYP19 genes did not correlate with cognitive abilities. Gifted children of both sexes had lower levels of testosterone in comparison with their peers in common population.

CONCLUSIONS: Based on the hypothesis that intelligence and spatial abilities are influenced by genetic as well as epigenetic factors, it is not surprising that certain correlation between previously mentioned polymorphisms and cognitive abilities exist.

TESTOSTERONE INFLUENCE ON REELIN EXPRESSION ASSOCIATED WITH AUTISM PATHOGENESIS

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BACKGROUND: Testosterone as a sex steroid hormone plays a crucial role in neurodevelopment. Autism is the most genetically based neurodevelopmental disorder, although the genetic basis of its manifestation is not understood. Different gene defects have been observed in different autistic cases, including the gene encoding reelin protein. It has a major role in neuronal migration and during prenatal development of neuronal connections. Autistic brain has been described as a hyper-masculine, because of high systemization and spatial cognitive abilities. High prenatal testosterone levels seem to result in masculinized brain anatomy and behavioral patterns. It was found that testosterone influences the expression of reelin in brains of male starlings. Thus it is possible that the linkage between testosterone levels and reelin mediated neuronal development exists also in mammals, including humans. Our purpose was to reveal the possible relationship between testosterone levels and reelin expression and to explain one of the possible mechanisms of Autism pathogenesis.

METHODS: Adult rats were exposed to high testosterone doses. Reelin expression was measured in hypothalamus, cerebellum, frontal and parietal cortices using Real Time PCR. Reelin expression was measured in newborn rats. Testosterone levels in blood of newborns were measured using ELISA analysis. Genetic polymorphism in RELN gene was assessed in autistic patients.

RESULTS: Adult male rats were treated with testosterone and cyproterone acetate, androgen receptor inhibitor. We found no effects of testosterone, neither cyproterone acetate on reelin expression in hypothalamus and frontal cortices. Reelin expression in cerebellum and in frontal cortex is higher in male newborn rats. Reelin expression in hypothalamus and in parietal cortex is higher in female newborns, however with relatively high variability.

CONCLUSIONS: Acute treatment with high doses of testosterone does not seem to affect brain reelin expression in male adult rats. Newborn rats seems to express reelin in a gender- and brain area-specific quantity, however, the differences are rather minor. Our preliminary data on a small cohort of autistic patients show that a slightly increased number of CGG repeats in the 5'UTR of reelin is associated with a risk of autism. Experiments assessing reelin expression in brain regions of newborn rats whose mothers were pretreated with high testosterone doses

during pregnancy are in progress. Further studies on larger cohort of autistic patients are necessary to elucidate reelin polymorphism association with autism spectrum.

SALIVA COMPOSITION AND EXERCISE

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BACKGROUND: In athletic training an anaerobic threshold is defined as the critical intensity of exercise without lactate accumulation in blood. Despite widespread use of blood lactate assessment, several authors have described the possibility of evaluating changes produced in the composition of saliva in response to exercise [1,2]. However the outcomes have been contradictory. It has been documented that sympathetic-adrenal activity does increase during submaximal incremental exercise [3]. The purpose of this study was to determine the anaerobic threshold from analyze of ionic (Na⁺, Cl⁻, K⁺) and protein concentration in saliva and compare to anaerobic threshold from that of lactate acid concentration in blood.

METHODS: 16 top level biathlons performed incremental lactate threshold test on rolling skies to exhaustion on rolling track. Lactate threshold test consisted of four stages (one stage corresponds to one circuit on rolling track). Each stage has been performed with relative constant intensity as based on heart rate. Every following stage was performed with higher intensity. After every completed stage the capillary blood samples (25 µl sample) were taken via ear lobe and subsequently analyzed (Biosen C_line, Germany). Simultaneously with blood sampling each subject chewed a cotton tampon in duration of 1 min. Saliva samples were immediately frozen (-78,5 °C) and subsequently analyzed in laboratory (Hitachi 917, Japan). Intensity of anaerobic threshold was calculated from the average speed of the representative stages and concentration of lactate acid known as lactate curve [4]. This model was used as well with ionic and protein content in saliva.

RESULTS: The results showed no significant differences (6.06 ± 0.74 vs. 6.03 ± 0.82 m.s⁻¹) when expressed as mean velocity that correspond to anaerobic threshold but strong correlation (r= 0.98, p<0.01) between lactate acid and total salivary protein content method. From ionic

analyzes only Na⁺ showed a correlation ($r=0.97$, $p<0.01$) with lactate.

CONCLUSION: The findings of this investigation suggest validity of the analysis of changes in total salivary protein content and Na⁺ as an additional noninvasive method for determining anaerobic threshold in an incremental test. Salivary composition during exercise may warrant further research of the physiological bases of the anaerobic threshold and its relationship to sympathetic nerve activity.

APPLICATION OF SALUTOGENETIC MODEL TO DIABETIC CARE

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BACKGROUND: The salutogenetic model enables in practice to identify and develop the so-called health factors which help a human being to maintain and strengthen health (Antonovsky, 1986, 1993; Krivohlavy, 1990).

Diabetes mellitus is a chronic disease which has one thing in common for all patients: from the time the disease is discovered, the patient has to bear in mind his or her metabolic state which is associated with certain limitations, distressful situations, serious and unpleasant health complications etc. An individual's vulnerability and ability to cope with stressful situations is in direct relationship to an individual's subjective well-being. Health factors enable consideration of individual capacity of a patient to cope with a disease.

METHODS: Monitoring was carried out at the Diabetological Centre in Hradec Králové (2000 – 2006), 162 type 2 diabetic patients (75 men and 87 women, 57.7 ± 14.4 years, 82.6 ± 9.4 kg), 94 patients with diet, 52 with PAD, and 16 with IIR. The whole period of therapy was 11 ± 5.9 years.

For the quantitative and qualitative evaluation we have chosen methods enabling us to objectify: individual predisposition to manage stress and a perceived life sense (S.O.C. type resistance) and the quality of subjective perception during a one year period (SUPOS 7).

RESULTS: In comparison with other groups in the population, the S.O.C. type resistance values show an increased vulnerability in diabetic patients. Higher

vulnerability can influence the course of disease and the success of treatment in a negative way and can be one of the predisposing health complication factors in diabetes mellitus. A lower mean value of resistance is reflected in lower individual S.O.C. dimension values.

A different predisposition to managing life's difficult situations is reflected in percentage representation of usual psychological state components, the component values of the so-called disintegration block "INUDS", mainly N (noncomfortable disturbance, ill-feeling), U (anxious expectations, worries), D (depressive mood, feelings of exhaustion) and S (dejection) prevail. The negative polarity of the usual psychological state is besides the common situational influences also a reflection of the chronicity of the disease which negatively influences the subjectively perceived quality of a female patient's life.

CONCLUSIONS: These results found confirm the existing relations between salutoprotective factors and predisposition to manage chronic disease. In practice it is, however, necessary to include these variables functionally in the complex diagnostics and treatment of each individual patient. The assessment of individual predisposition to coping with a severe life situation on the scale of vulnerability – resistance (coherence) extends the scope of the therapeutic choice in the modern medicine (education, counseling, individual and group psychotherapy).

PRENATAL METHAMPHETAMINE EXPOSURE AND FLUROTHYL SEIZURES IN ADULT MALE AND FEMALE RATS

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BACKGROUND: There are studies demonstrating that repeated administration of psychostimulants such as methamphetamine (MA) enhances locomotor activities in response to later administration of the same or related drugs in rodents. This phenomenon is defined as behavioral sensitization or reverse tolerance. Once behavioral sensitization is established, it persists for several months. On the other hand, there are many studies showing tolerance after chronic MA administration. However, there are, no studies investigating possible sensitization or tolerance in prenatally MA-exposed adult

animals. Stimulants, such as cocaine, amphetamine and MA, are often associated with increased seizure susceptibility or induction of seizures. Gamma-aminobutyric acid (GABA) receptors are considered to play a mediatory role in the effect of stimulant drugs on seizure susceptibility. Flurothyl is a convulsant ether that is suggested to interfere with GABAA receptor-mediated neurotransmission. The purpose of the present study is to examine the hypothesis that prenatal MA exposure alters susceptibility to flurothyl seizures in adult rats.

METHODS: Adult male and female rats exposed prenatally to MA (5mg/kg), saline or neither (controls) were divided into groups; one group received acute MA (1 mg/kg s.c.) injection and the other group received saline. Rats were then challenged with flurothyl at a constant flow rate to induce seizures. The threshold of the first clonus, clonic seizures and tonic-clonic seizures were analyzed.

RESULTS: Effects of prenatal drug exposure: In animals without acute MA administration prior to seizure testing, prenatal MA exposure decreased threshold of the first clonus relative to control animals. This decrease in threshold was not apparent in groups pretreated with acute MA injection. Effects of acute MA administration: There was an increased threshold to both, first clonus and clonic seizures in animals with acute MA injection than in animals without it. The increase induced by acute MA pretreatment was higher in prenatally MA-exposed animals relative to controls. Further, clonic seizures were shorter and developed faster into tonic-clonic seizures in these acutely injected animals compared to animals without acute MA injection. Effects of hormones: The threshold of all measured attributes was decreased in males. Hormonal influences did not lead to changes between groups of prenatal exposure or acute MA administration. Threshold of tonic-clonic seizures was increased in females in proestrus/estrus stage of the estrous cycle relative to diestrus females.

CONCLUSIONS: The present study demonstrates that: (1) prenatal MA exposure decreases seizure threshold in adult male and female rats; (2) prenatal MA exposure makes the animals more sensitive to the effect of an acute MA pretreatment prior to flurothyl seizures; (3) acute MA administration in a dose of 1 mg/kg has “protective” effect on flurothyl-induced seizures regardless of prenatal drug exposure, and (4) there are gonadal hormone-induced differences in sensitivity to seizures in adult male and female rats.

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PRENATAL AND ACUTE METHAMPHETAMINE TREATMENT - THE TEST OF LEARNING AND MEMORY IN ADULT MALE RATS

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BACKGROUND: Studies showed that stimulant drugs that affect the monoaminergic system, such as amphetamine and cocaine, alter both behavioral and cognitive processes. Little is, however, known about the effect of methamphetamine (MA) on cognition. Some clinical studies reported that MA administered to drug-naive subjects produced improvements in cognitive processing. However, in contrast to acute MA administration chronic MA use is associated with impaired performance on a number of cognitive tasks. In addition, other studies demonstrated that repeated administration of MA enhances locomotor activities in response to later administration of the same or related drugs in rodents. This phenomenon is defined as behavioral sensitization and may last for months. The aim of the present study was to examine the effect of prenatal MA exposure on learning and memory in adult male rats and to determine whether the prenatal MA exposure changes sensitivity to acute MA injection in adulthood.

METHODS: Adult male rats prenatally exposed to MA (5 mg/kg), saline or no injection were tested for learning in Morris water maze. Half of the animals were injected daily with MA (1 mg/kg) after finishing the trials. Four points on the rim of the pool were marked north (N), south (S), east (E), and west (W), thus dividing the pool into four quadrants. In each day animals were exposed to 8 consecutive trials with 4 different start positions. Camera recording and software Ethovision (Noldus) was used in the experiment. The latency to reach the hidden platform, the length of trajectory, the frequency of presence in quadrant with hidden platform and the search error was measured in each trial. Three types of tests were used: (1) test of learning was performed for 5 consecutive days (“Place navigation test”), (2) “Probe test” in 6th day of experiment without hidden platform, and (3) test of memory in day 12 of the experiment (“Retention memory test”).

RESULTS: Our results demonstrate that prenatal MA exposure did not affect the test of learning and the "Probe test". In the test of memory prenatally MA-exposed rats showed better results when compared to controls. Further, acute MA administration increased the speed in swimming in all rats regardless of prenatal drug exposure. Prenatal MA exposure did not affect the sensitivity to acute drug injection in any of the tests used in the present study.

CONCLUSION: The present study demonstrated that: (1) Prenatal MA exposure does not affect learning in Place navigation test and Probe test. (2) Rats prenatally exposed to MA have better memory than rats prenatally exposed to stress. (3) Prenatal MA exposure does not affect the sensitivity to acute drug injection in any of the tests used in the present study.

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POSTNATAL RAT PUP DEVELOPMENT – EFFECT OF DRUGS AND MATERNAL CARE

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BACKGROUND: Our previous studies demonstrated that methamphetamine (MA) administered during gestation and lactation periods impairs maternal behavior as well as the postnatal development of rat pups. The present study tested the hypothesis that the postnatal care of adoptive mother influences the development of rat pups. The aim of our study was to distinguish the extent of the drug-induced effect and the extent of the effect induced by impaired maternal care.

METHODS: Mothers were daily exposed to injection of MA (5 mg/kg) or saline (S) approximately for 9 weeks: about three weeks prior to impregnation, throughout the entire gestation period and during lactation until the weaning period. As an absolute control (C) females with no injections were used. On postnatal day (PD 1), pups were cross-fostered so that each mother received some of her own and some of the pups of mother with the other two treatments. Based on the prenatal and postnatal treatments 9 experimental groups (CC, CS, CM, SC, SS, SM, MC, MS, MM) were tested. Pup's development and sensorimotor coordination was examined between PD 1

and PD 23. Following behavioral tests were used: negative geotaxis (PD 9 and 11), tail pull on cellulose cotton wool and on grid (PD 10, 12 and 14), righting reflex on surface (PD 12), righting reflex on mid-air (PD 17), rotarod (PD 23) and bar-holding (PD 23). Further, the pups were examined for physiological maturation (weight gain during lactation, startle response, tooth eruption and ear and eye opening).

RESULTS: Our results showed that the birth weight in prenatally MA-exposed pups was lower than controls or saline-exposed pups regardless of sex. Prenatally MA-exposed pups gained less weight than controls or saline-exposed pups regardless of postnatal treatment and sex. On the other hand, prenatally MA-exposed pups fostered by control or saline-exposed dams gained more weight during lactation. MA-exposed pups regardless of postnatal drug exposure and sex had displayed startle response, ear and eye opening later than control or saline-exposed pups. Further, our data demonstrated that pre- and postnatal MA exposure impairs sensorimotor functions in these tests: negative geotaxis, tail pull, righting reflex on surface, righting reflex in mid-air and rotarod. On the other hand, postnatal care of control mothers at least partially suppressed the negative effect of prenatal MA exposure.

CONCLUSIONS: The present study demonstrated that prenatal MA exposure impairs development of pups and performance of sensorimotor tests. Moreover, the effect of MA as well as the effect of prenatal stress was affected by postnatal breeding. Our results support the hypothesis that variation in rat maternal care could serve as a mechanism for a nongenomic behavioral mode of transmission of traits.

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COMPARISON OF CREATIVE AND NONCREATIVE TASK'S PERFORMANCE OF VARIOUS COMPLEXITY LEVEL

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BACKGROUND: Our main hypothesis was that as the brain mechanism, processes of creative thinking and noncreative thinking of the comparable level of complexity may differ. This problem seems to be really new for neurophysiology of creativity, as we didn't find any direct data.

METHODS: Four tasks with well-known Russian proverbs and sayings, written without their endings were presented to subjects: CR – creative task (subjective complexity level of the task defined as 5-6 on 10th level scale). Subjects were 1st - to recall ending of it, 2nd –to produce their own and original ending, changing the well-known meaning of the text; M, AN, AS – noncreative, memory retrieval tasks (1-2; 5-6; 9-10 subjective complexity level correspondingly). In noncreative tasks subjects were to recall well-known ending of the text and name it, but in M - task words were presented in normal manner, in An task - as anagrams, in An task - as anagrams with additional fortuitousness syllables 12 right-handed (5 male:7 female) volunteers without neurological or psychiatric disease and current medication took part. We registered EEG monopolarly from 19 derivations (10-20). EEG spectral power was quantitatively processed (WinEEG software package - Ponomarev V.A., St. Petersburg) and statistically analyzed (2-way ANOVASTATExZONE with Greenhouse-Geisser correction). For the following analysis we used LSD – Fisher test. As the results in high frequency bands (B1 - 13-18 Hz, B2 - 18.5-30 Hz, G – 31-40 Hz) are more valid in condition of analysing short EEG intervals, we considered preferably them.

RESULTS: We obtained significant differences for STATExZONE interaction with Greenhouse-Geisser correction in B1 ($F=2.84$, $e=0.04$, $p<0.01$), B2 ($F=4.29$, $e=0.04$, $p<0.001$) and G ($F=2.84$, $e=0.04$, $p<0.01$) frequency bands and did consider them as the preliminary ones. We found out, that creative and noncreative tasks of the same subjective complexity level differ in their EEG spectral power. Creative task was characterized by generalized increase of it in beta1, Bbeta2, gamma bands. Observed increase of EEG spectral power seems to be distinguishing feature for creative task fulfillment, thus in comparison: creative task versus M task, it was also observed. Increase of spectral power in beta, gamma bands, obtained for comparison creative versus noncreative tasks on new subject's group of presented study confirms our previous published results (Bechtereva et al., 2004, 2006, 2007). We also found out, that two noncreative tasks of different subjective complexity levels (An, As) in comparison with easiest one (M) revealed isolated and not well pronounced increase and decrease of EEG spectral power.

CONCLUSIONS: It seems that those memory retrieval processes don't differ too much because of the different subjective complexity levels of the tasks. So, obtained preliminary data don't contradict our hypothesis that

correlates of creative and noncreative tasks of various subjective complexity levels may reflect different states and perhaps - neurophysiologic mechanisms, underling solving of creative and noncreative tasks.
