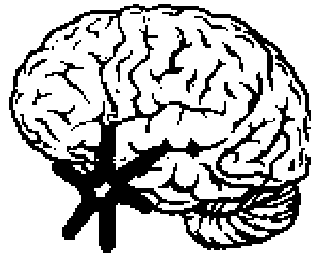


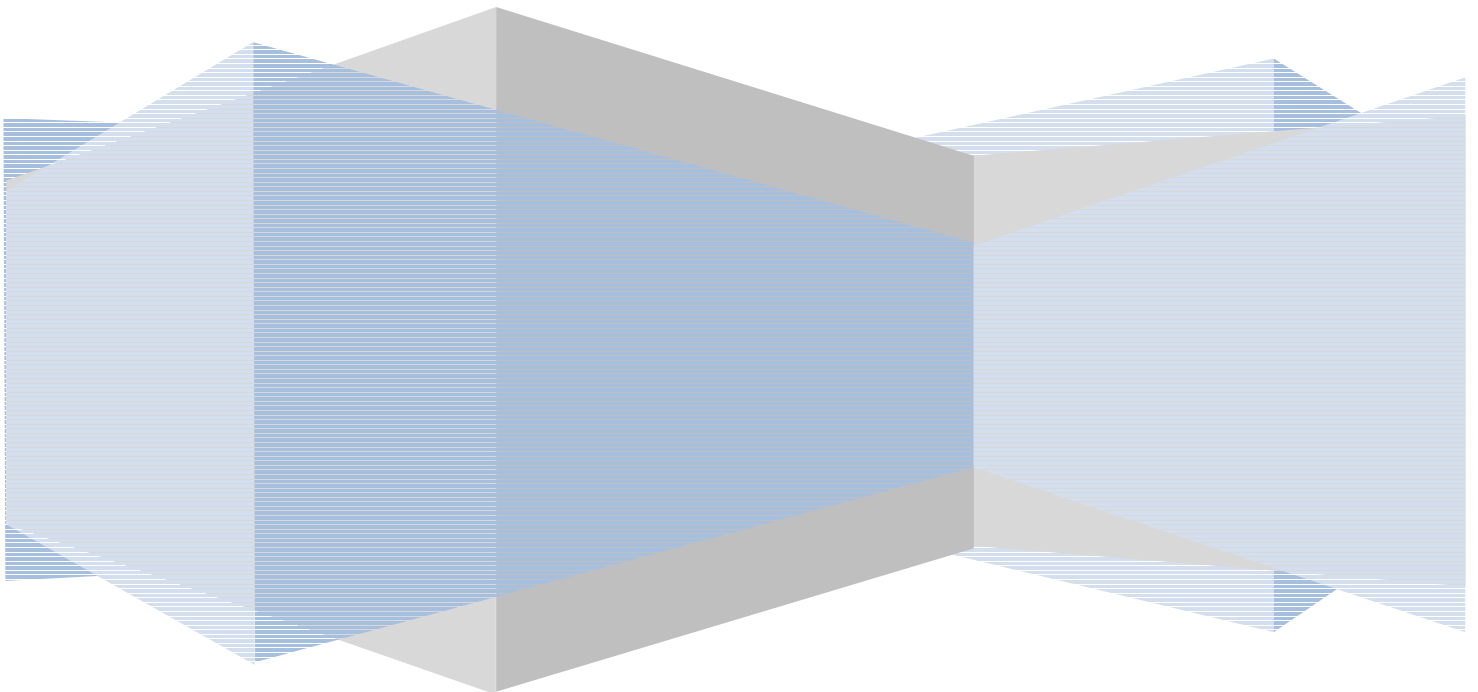
10-th Jubilee Multidisciplinary International Conference
of Biological Psychiatry

"Stress and Behavior"

St. Petersburg, Russia
May 16-20, 2007



CONFERENCE PROCEEDINGS



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Conference Proceedings
10-th Jubilee Multidisciplinary International Conference of Biological Psychiatry
"Stress and Behavior", St-Petersburg, Russia, May 16-20, 2007

Conference at glance

Day 1. May 16, 2007

Time	Blue hall	Fireplace hall
8.00-18.00	Conference Registration (lobby, 5 th floor)	
9.00-9.40	Opening ceremony	Opening ceremony
9.40-11.00	Plenary lectures	Plenary lectures
11.00-11.20	Coffee Break	
11.20-13.00	Symposium 1. Experimental models of stress - I	Symposium 2. Clinical Psychiatry and Psychology - I
13.00-14.00	Lunch time	
14.00-16.00	Plenary lectures	Plenary lectures
16.00-16.20	Coffee Break	
16.20-18.00	Symposium 3. Clinical Psychiatry and Psychology - II	Symposium 4. Experimental models of stress - II
18.00-19.00	Welcoming Reception	

Day 2. May 17, 2007

Time	Blue hall	Fireplace hall
9.00-18.00	Conference Registration (lobby, 5 th floor)	
9.00-9.40	RSBP and USBP Annual meetings	
9.40-11.00	Plenary lectures	Plenary lectures
11.00-11.20	Coffee Break	
11.20-13.00	Symposium 5. Clinical Psychiatry and Psychology - III	Symposium 6. Biofeedback treatment of stress
13.00-14.00	Lunch time	
14.00-15.00	Plenary lectures	Plenary lectures
15.00-15.20	Coffee Break	
15.20-18.00	Symposium 7. Psychopharmacology	Symposium 8. S.A. Chepurinov's Memorial Symposium

Day 3. May 18, 2007

Time	Blue hall	Fireplace hall
8.00-18.00	Conference Registration (lobby, 5 th floor)	
9.00-10.20	Plenary lectures	
10.20-10.40	Coffee Break	
10.40-13.00	Symposium 9. Translational research in stress neuroscience	Symposium 10. Experimental models of stress - III
13.00-14.00	Lunch time	
14.00-15.00	Plenary lectures	
15.00-15.20	Coffee Break	
15.20-17.00	Symposium 11. Why do we need models of stress?	Symposium 12. Behavioral and biological markers of stress

Day 4. May 19, 2007

Time	IEM Conference Hall
9.00-14.00	Conference Registration (lobby)
9.00-10.30	Plenary lectures
10.30-11.00	Coffee Break
11.00-13.00	Special Plenary Symposium: Psychoneuroimmunology
13.00-16.00	Joint Poster Session and Coffee
16.00-17.00	Closing Ceremony

Welcoming Address from the Conference Chair

Dear colleagues and friends,

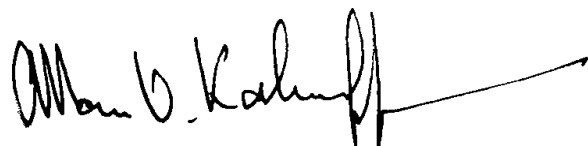
It is my great pleasure to welcome the delegates of 10th Jubilee International "Stress and Behavior" Conference - outstanding experts in clinical and biological psychiatry from more than 35 countries worldwide. Now that St. Petersburg is preparing to inspire our scientific creativity this May, there are several issues that I would like to discuss – formally or informally – during the meeting.

While stress has always been the main focus of our conferences, this year marks the 100th anniversary of H. Selye's birth. Not a neuroscientist himself, Selye (1907-1982) has made a major contribution to the theory of stress, that has a lasting actuality for behavioral neuroscience and psychiatry. It is therefore now timely to acknowledge this great scientist, and his seminal works that continue to influence generations of researchers working in our field. I believe that many of his ideas will be addressed during our meeting.

An important goal of our conference is to bring together "biological" and "psychical" in animal and human behaviors. We all know that cognitive dysfunctions – reflecting "psychical" mechanisms that went wrong - are commonly seen in many stress-related disorders. How crucial is the contribution of cognitions in stress-related disorders? Mounting clinical and animal evidence strongly supports the notion that disturbed cognitions represent an important pathogenetic factor per se, and may play a key role in integrating different mental illnesses within a common stress-precipitated developmental pathway. I hope the role of cognitive mechanisms in brain and behavioral disorders will also be comprehensively and critically evaluated during our meeting.

Finally, I am pleased to note that our ten successful international conferences have another important outcome. They have generated a growing and active network of specialists dealing with human and animal behavioral responses to stress. As promoting translational collaborative and multidisciplinary research has always been our main goal, it is now time to make the next logical step in this direction. This year we plan to establish the new professional organization - the International Stress and Behavior Society (ISBS). Integrated into the world's neuroscientific community, this new society will foster further research in behavioral neuroscience of stress. Our Secretariat works hard to complete all necessary formalities, and I invite all interested colleagues to contact me with your suggestions and ideas.

With such an exciting agenda for this year's meeting, we look very much forward to welcome you all in St. Petersburg.



Allan V. Kalueff, PhD Hon

Welcoming Address
from the Program Committee Chair

Dear colleagues!

Welcome to St. Petersburg and to the 10th Conference on Neuroscience and BioPsychiatry "Stress and Behavior". As this year we celebrate its 10th anniversary, it is a special pleasure for me to see this conferences again held in our beautiful city.

As we all know, Neuroscience is developing extremely fast today, with new information gained, methods implemented and approaches used – all calling for a regular revision of accepted concepts, terms and definitions. Unfortunately, there is still a big gap between the large amount of scientific knowledge about the brain, and our understanding of fundamental mechanisms of normal and deviant behaviors.

For 10 years, annual "Stress and Behavior" Conferences provide an excellent possibility for neuro- and psychophysicologists, psychologists, neurochemists and psychiatrists to enrich each other with new information, and to establish fruitful and long-term contacts. We also appreciate the fact that geography of the participants is widening each year, and the Program covers more and more topics and problems. This year we will have many exciting lectures and symposia, as well as educational tours to Pavlov's memorial office and his Department of Physiology in the Institute for Experimental Medicine, where the author of conditioned reflexes theory has worked for more than fifty years.

The second half of May in St. Petersburg is particularly good for a scientific conference. Between sessions, there will be opportunities to explore and enjoy the rivers and channels of our city, its magnificent palaces and cathedrals. Importantly, St. Petersburg is also recognized as a cultural capital of Russia. A number of outstanding neurophysiologists and psychiatrists who have lived and worked in our city – Sechenov, Pavlov, Bekhterev, Vvedensky, Uhtomsky, Orbely, and many others - have become a part of the world inheritance.

We are confident that international "Stress and Behavior" conference will continue to contribute to cultural and scientific life of our city, which we all love and admire. I wish you a successful conference, fruitful discussions, new scientific contacts and many bright impressions from the Russia's North capital.



Professor Viktor M. Klimenko, PhD, MD

PLENARY LECTURES

Day 1. May 16, 2007. Venue: Oktyabrskaya Hotel, Ligovsky Prospect, 10

- **MISMATCH NEGATIVITY IN SCHIZOPHRENIA.** R Naatanen, Cognitive Brain Research Unit, Department of Psychology, University of Helsinki. Helsinki, Finland
- **NEUROKYNURENINES AND SOME DISTANT AFTER-EFFECTS OF STRESS.** IP Lapin, Bekhterev Psychoneurological Research Institute, St. Petersburg, Russia
- **MITOCHONDRIAL ULTRASTRUCTURAL ABNORMALITIES AND DEFECTIVE NEUROTRANSMITTER-STORAGE BODIES IN PARKINSON'S DISEASE.** MR Issidorides, Dept. of Psychiatry, University of Athens, Medical School, Athens, Greece
- **INTEGRATIVE EXPERIMENTAL MODELLING OF ANXIETY, DEPRESSION AND RELATED BRAIN DISORDERS IN THE ERA OF PARADIGM SHIFTS IN CONTEMPORARY PSYCHIATRY.** AV Kalueff, Center for Physiology and Biochemical Research, Moscow, Russia, Bethesda, MD, USA
- **STRESS, NITRIC OXIDE AND RAPID TESTOSTERONE SUPPRESSION.** BA Weissman, MP Hardy, Department of Pharmacology, Israel Institute for Biological Research, Ness Ziona, Israel, Center for Biomedical Research, Population Council, Rockefeller University, New York, USA
- **HYDROCEPHALY AT MEDICI COURT OF 16TH CENTURY'S FLORENCE.** G Fornaciari, M Castagna, University of Pisa, Pisa, Italy
- **SPECIAL LECTURE OF THE RUSSIAN SOCIETY FOR BIOPSYCHIATRY (RSBP): SEROTONIN SYSTEM GENES: WIDESPREAD DEVELOPMENTAL INFLUENCES ON ANXIETY, STRESS-RESPONSIVITY AND PSYCHOPATHOLOGY**
- **NEURODEGENERATION AND THE POSSIBLE WAYS OF ITS PREVENTION.** MI Aghajanov, Department of Biochemistry, Yerevan M. Heratsi State Medical University, Yerevan, Armenia
- **ADAPTIVE SELF-REGULATION STRATEGY FOR CORRECTION OF ADOLESCENT DEVIANT BEHAVIOR.** VM Klimenko, Institute for Experimental Medicine RAMS, St. Petersburg, Russia
- **STRESS AND THE CEREBROPROTECTIVE EFFECTS OF CORTEXIN AND SELANK ON BRAIN DYSFUNCTIONS IN THE ASCENDING ROW OF MAMMALS.** TN Sollertinskaja, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia

MISMATCH NEGATIVITY IN SCHIZOPHRENIA. R Naatanen. Cognitive Brain Research Unit, Department of Psychology, University of Helsinki. Helsinki, Finland

Research on schizophrenia using the mismatch negativity (MMN), an automatic brain response to sound change indexing sound-discrimination accuracy, will be reviewed. One of the most robust abnormalities in the brain function of patients with schizophrenia is the considerable attenuation of the MMN amplitude found in most studies in response to change in sound frequency or duration. As this abnormality is similarly found both with long and short interstimulus intervals (ISI), it can be regarded as reflecting inaccurate sensory memory trace formation (and thus sound perception) rather than abnormally short trace maintenance. The results of several psychopharmacological studies suggest that the deficient MMN generation, as well as the central auditory functions affected in schizophrenia, can be explained by the inadequate functioning of the NMDA-receptor system. One of the central lines of current MMN research on schizophrenia consists of studies trying to determine the effects of the disease on the two main processes generating the scalp-recorded MMN, viz., those occurring in the auditory and those occurring in the frontal cortex. According to the results obtained so far, it appears that the frontal generators are, in general, much more affected than the auditory cortex ones. In view of the results suggesting a critical role of these frontal generators in conscious perception and attention switching, the dampened functioning of these generators might, in addition to the inferior performance of these patients in certain auditory tasks, in part explain their negative symptomatology. Consistent with this, the magnitude of the MMN deficit correlates with the severity of these negative symptoms. Moreover, very recent data show that MMN indexes the gradual cognitive decline

occurring during the course of the illness, suggesting that the impaired MMN generation might index a core feature of the disorder. Furthermore, some recent results suggest that the MMN might be used as indices of both the genetic predisposition to schizophrenia and illness progression.

NEUROKYNURENINES AND SOME DISTANT AFTER-EFFECTS OF STRESS. IP Lapin. Bekhterev Psychoneurological Research Institute, St. Petersburg, Russia

The neuroactivities of neurokynurenines (NEKY), including effects on behavior and stress, are overviewed in I.P. Lapin's "Stress-Anxiety-Depression-Alcoholism-Epilepsy (Neurokynurenine mechanisms and new approaches to treatment)", Dean, St. Petersburg, 2004, 220 p. The problems reviewed less often are the following: 1. Various forms of Posttraumatic Stress Disorders [The slow developing neurochemical abnormalities, e.g. intensified metabolism of NEKY and slowed turnover of GABA, determine the increased vulnerability of children and adolescent and high risk of psychiatric and neurological symptoms after traumatic events. For this reason the early psychiatric and psychological examination is highly desirable]. 2. The decrease of coping, a psychological universal mechanism of adaptation. [Deterioration of coping is associated with the increase of anxiety (NEKY have a marked anxiogenic action)]. 3. Insomnia during stress is based on the antagonism of NEKY and melatonin, the major neuro-hormone of sleep. 4. Activation of the immune system via increase of production of cytokines in macrophages, which resulted in activation of synthesis of anxiogenic NEKY. 5. Arterial hypertension due to activation of dopamine-B-hydroxylase, increase of concentration of noradrenaline and adrenergic sensitization. Among all studied neuroactivities of NEKY the most important for stress seem to be the antagonism to GABA as well as to inhibitory amino acids taurine and glycine.

MITOCHONDRIAL ULTRASTRUCTURAL ABNORMALITIES AND DEFECTIVE NEUROTRANSMITTER-STORAGE BODIES IN PARKINSON'S DISEASE. MR Issidorides, V Kriho, I Kloukina, S Havaki. Dept. of Psychiatry, University of Athens, Medical School, Eginition Hospital, Greece, Dept. of Anatomy and Cell Biology, College of Medicine, University of Illinois at Chicago, USA, Neurobiology Research Institute, Theodor Theohari Cozzika Foundation, Athens, Greece

The presence of Lewy bodies (LB) is an absolute requirement for a definitive diagnosis of Parkinson's disease (PD). Our previous histochemical studies have shown that LB emanate from cytoplasmic spherical acidophilic inclusions, which in the human brain are normal components of all monoamine neurons (Issidorides et al 1978). These inclusions, termed protein bodies (pb), were found to be drastically reduced or missing from catecholamine (CA) neurons in PD, but their basic-protein reaction was localized in the LB (Issidorides et al 1978). Moreover, when reacted with fluorochromes, their lipid components were found disrupted, coalesced or aggregated, or forming the core of the LB (Issidorides et al 1991). Our ultrastructural studies have established that pb in control brains originate as "dense bodies" in the matrix of mitochondria, which gradually lose their cristae, as these spherical inclusions grow and reach their mature form, filling the entire matrix with an electron-dense homogeneous body, surrounded by the mitochondrial double membrane (Issidorides et al 1996). Furthermore, we have recently demonstrated with immunogold that pb are storage sites of neurotransmitters (Issidorides et al 2004). First hints pointing to a contribution of mitochondria to PD pathogenesis were obtained on the basis of a study showing that the neurotoxin MPTP causes PD in humans; this toxin acts via inhibition of complex I of the mitochondrial respiratory chain (Langston et al 1983). Actually, a biochemical defect of complex I has been described in a relative large group of confirmed PD cases (Schapira et al 1990). Since, several investigators have subsequently confirmed in PD the involvement of mitochondrial dysfunction and abnormal morphology (Lach et al 1992; Trimmer et al 2000), we designed to study with electron microscopy, mitochondrial ultrastructure in the CA neurons from 9 PD patients and 5 matched control subjects, in order to elucidate mitochondrial involvement. Fresh frozen post-mortem tissue of locus coeruleus (LC) and substantia nigra (SN) was processed with the potassium permanganate (KMnO₄) method, which is recommended for the preservation of membranes and the formation of KMnO₄ / CA precipitates (Hököfelt and Jonsson, 1968). In control neurons, the results showed the usual complement of mitochondria and groups of pb with electron-dense cores of KMnO₄ / CA precipitate, surrounded by the double membranes of the mitochondrion of origin. In PD neurons, very few mature pb were evident. We noticed defective pb with interrupted outer membranes and variable electron-density of the core, presumably implying, according to the KMnO₄ method, deficiency of the neurotransmitter. Many of these pb were attached to a mitochondrion with abnormal structure. Several mitochondria were swollen with missing or disrupted cristae, inner membranes forming stacks of split cristae or

concentric structures. Small pb were found sequestered at one end of elongated mitochondria without cristae. The most striking findings, revealed by the electron microscope, were patterns of mitochondrial abnormalities, such as budding of the outer membrane, occasionally enlargement of the buds resulting in separation of outer and inner membrane and further expansions of the intermembrane space. In some cases, whorls of concentric cristae were observed and contained central densities. In other mitochondria, inner membranes had a fuzzy appearance. The present results from our ultrastructural observations of mitochondrial abnormalities and related defective protein bodies in SN of Parkinson's disease revealed that the involvement of mitochondria in this disorder is a consequence of their role in giving rise to neurotransmitter-storage bodies in the monoamine neurons (Issidorides et al 1996; 2004). This role was found to be interrupted in the material that we studied, resulting in a lack of mature functional storage bodies in PD. In conclusion, our data support the widely held concept that "defective sequestration of dopamine into vesicles, leading to the generation of reactive oxygen species in the cytoplasm, is a key event in the demise of dopaminergic neurons in Parkinson's disease, and might represent a common pathway that underlies both genetic and sporadic forms of the disorder" (Lotharius and Brundin, 2002).

INTEGRATIVE EXPERIMENTAL MODELLING OF ANXIETY, DEPRESSION AND RELATED BRAIN DISORDERS IN THE ERA OF PARADIGM SHIFTS IN CONTEMPORARY PSYCHIATRY. AV

Kalueff, Center for Physiology and Biochemical Research, Moscow, Russia, Bethesda, MD, USA
Stress plays a key role in pathogenesis of anxiety and depression. Animal models of these disorders are widely used in behavioral neuroscience to explore stress-evoked brain abnormalities, screen anxiolytic/antidepressant drugs and establish behavioral phenotypes of gene-targeted or transgenic animals. Here we discuss the current situation with these experimental models, and critically evaluate the state of the art in this field. Noting a deficit of fresh ideas and especially new paradigms for animal anxiety and depression models, we review existing challenges and outline important directions for further research in this field. Potential strategies for the development of new animal paradigms include 1) modeling different subtypes of anxiety and depression, 2) their common pathogenesis, 3) the use of a wider spectrum of parameters, techniques and model objects. With psychiatric nomenclature and diagnostic criteria subject to constant modifications and reconsiderations, we may also benefit from 4) targeting a wider cluster of related behavioral phenomena (e.g., obsessive-compulsive disorders, Tourette's syndrome, addiction), 5) expanding models beyond traditional "anxiety" and "depression" domains, and 6) using "hybrid" models and tests. Together, these approaches will allow a better focus on the neurobiology of stress, enabling further integrative modeling of mood, behavioral and personality disorders consistent with recent trends and paradigmatic shifts in modern psychiatry. One of the main reasons to invest time and efforts into new "integrative" models of anxiety and depression is the possibility to discover new agents or even principally new classes of psychotropic drugs, the need for which has long been recognized. In addition, this approach will increase our understanding of pathogenesis of anxiety and depression, and the link between these disorders and other brain illnesses.

STRESS, NITRIC OXIDE AND RAPID TESTOSTERONE SUPPRESSION. BA Weissman, MP Hardy. Department of Pharmacology, Israel Institute for Biological Research, Ness Ziona, Israel, Center for Biomedical Research, Population Council, Rockefeller University, New York, USA

Various forms of isolation such as immobilization stress (IMO) induce a rapid increase in glucocorticoid secretion (in rodents, corticosterone, CORT) and a parallel decrease in circulating testosterone (T) levels. In the same time, nitric oxide (NO), a reactive free radical and a fast acting neurotransmitter that has been reported to be produced at higher rates in some tissues during stress, is known to dramatically suppress the biosynthesis of T by Leydig cells. Several studies were directed towards the goal of assessing the roles of CORT and/or NO in stress-mediated reduction of T production. For that purpose, the pharmacokinetics and pharmacodynamics of CORT have been studied in IMO-stressed wild type (WT) and inducible nitric oxide synthase knockout (iNOS^{-/-}) mice. Notably, similar basal plasma and testicular T levels are present in both genotypes and their exposure to 3 h of IMO resulted in a marked elevation in plasma CORT and a dramatic reduction in T concentrations. In addition, testicular T levels exhibited the same pattern while the concentrations of nitrite and nitrate, the stable metabolites of NO in testicular extracts did not show any difference. Studies performed using WT mice have shown that the changes in CORT and T levels are very rapid. Together, these findings raise the issue of the role of NO-pathway in testicular T regulation and the question the presence of the NOS enzyme family in Leydig cells. In tissues such as brain or adrenal

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glands, NOS isoforms may act as mediators of enzymatic activity and hormone release, thereby modulating the response to stress.

HYDROCEPHALY AT MEDICI COURT OF 16TH CENTURY'S FLORENCE. M Castagna, S Fattori, A Vitello, D Caramella, N Villari, G Fornaciari. Pathological Anatomy III, Department of Surgery, Department of Oncology, Transplants and Advanced Technologies in Medicine, Division of Diagnostic and Interventional Radiology, University of Pisa, Pisa; Department of Clinical Physiopathology, Section of Clinical Radiology, University of Florence, Florence, Italy

Hydrocephalus is a congenital or acquired pathology of CNS caused by a misbalance between the production of cerebrospinal fluid and its absorption. Within the framework of the "Medici" Project (studying the rulers of Renaissance Florence), a paleopathological team of experts from the University of Pisa, the University of Florence and the Superintendence for Florentine Museums, is carrying out a study on 49 tombs of some of the Medici family members (16th-18th centuries) housed in the so-called Medici Chapels of the Basilica of San Lorenzo in Florence. The most recent biomedical technologies have been employed to obtain as much information as possible about the genetic make-up, eating habits, life styles and diseases of these important rulers of Renaissance Florence. The skeletal remains of a child, recovered inside a small crypt of the Basilica of S. Lorenzo revealed a little boy of about 5 years, with a stature of 1.15 m. This individual has been identified with Don Filippino (1577-1582), young son of the Grand Duke Francesco I (1541-1587). The abnormally enlarged skull of this subject was submitted to macroscopic and radiological study (standard X-ray and CAT). The paleopathological study, cranial dimensions and calculation of cranial capacity show evident hydrocephaly. The curvature of the left tibia and fibula demonstrates light rickets. A portrait of don Filippino, painted in the same year of death (1582), shows a picture of non-severe hydrocephaly, with low implant of the orbits and auricles and evident expansion of the cranial vault. This case of hydrocephaly is important not only from paleopathological point of view, but also because it is the first time that a diagnosis of this disease is supported also by an artistic representation.

NEURODEGENERATION AND THE POSSIBLE WAYS OF ITS PREVENTION. MI Aghajyanov, KB Yenkovyan, VA Chavushyan, JS Sargissyan. Department of Biochemistry, Yerevan "Heratsi" State Medical University, Laboratory of Compensation of CNS Function, Orbeli Institute of Physiology, Yerevan, Armenia

The beta-amyloid peptide (Abeta) is centrally related to the pathogenesis of Alzheimer's disease (AD) and is potently neurotoxic to central nervous system neurons. The neurotoxicity of Abeta has been partially related to the over activation of glutamatergic transmission and excitotoxicity. Taurine, a non-protein sulfur containing amino acid, is the most abundant free amino acid and has been shown to play several essential roles in the human body and affects the major causes of cellular toxicity, namely, Ca²⁺ overload, oxidative stress and osmoregulation. It is widely distributed in high concentrations in brain. It is also observed that activation of GABA(A) receptors protects neurons against Abeta toxicity in AD-affected regions of the mammalian brain. To assess aminoacids, particularly glutamate, GABA and taurine changes in cerebral cortex and hippocampus after intracerebroventricular (i.c.v.) injection of neurotoxic domain of amyloid peptide – aβ 25-35. The experimental model of AD was created in rats by intracerebroventricular (i.c.v.) injection of 3.0μl aggregated Aβ (25–35) solution (1mg/ml) into each cerebral lateral ventricle at a rate of 1μl/min. Fifty young adult male rats, weighing 230–290 were divided into 2 groups: the control group consisted of vehicle treated animals; the experimental group was i.c.v. injected aggregated Aβ. Rats were killed by decapitation after anesthetizing with Nembutal 40mg/kg ip. The selected brain regions, i.e, cerebral cortex and hippocampus were dissected according to the stereotaxic atlas of Paxinos and Watson. Brain regions after freezing in liquid nitrogen were weighed and homogenized in a glass-glass homogenizer with 20 fold excess of .1M perchloric acid. The homogenate were centrifuged for 15 minutes at 12000g at 4°C and the supernatants were filtrated through a .45 μm filter (MultiChrom). Isocratic separation of Glutamate, Taurine and GABA derivates were obtained using a reverse-phase HPLC- system with electrochemical detection, which comprised 150x4.6mm "Nucleosil" 100-5 C18 column. The concentration of aminoacids expressed as ng/g wet tissue. It was shown a great decrease of Taurine both in cerebral cortex (about 3.6 times) and hippocampus (about 3 times). The concentration of Glutamate was higher in cerebral cortex in comparison with control level about 1.8 times and decreased about 1.5 times in hippocampus, whereas the level of GABA practically did not change. At mentioned changes the Glu/GABA coefficient increased in cerebral cortex about 1.3 times and decreased in hippocampus about 1.2 times. These results suggest that Taurine is a target

aminoacid in AD related neurodegeneration and its great decrease may be a result of involvement of Taurine in the mechanisms of neuronal protection. Increase of Glutamate concentration in cerebral cortex may be linked with disturbance of Glutamate reuptake and may induce glutamatergic excitotoxicity. The decrease of glutamate in hippocampus is possibly resulted the death of glutamatergic neurons, but at the same time this effect does not except the phenomena of glutamatergic excitotoxicity, which can occur in some neuronal population or can be the main inductor of hippocampal neuronal death. There was no change observed in total GABA concentration. In our opinion GABA is involved in neurodegeneration in different biochemical mechanism and serves as a buffer aminoacid in Glutamate/GABA interrelation. Our findings revealed new aspects of the role of some aminoacids in the process of neuronal damage and survival via correlation of neurotransmission and metabolism.

ADAPTIVE SELF-REGULATION STRATEGY FOR CORRECTION OF ADOLESCENT DEVIANT BEHAVIOR. VM Klimenko, KV Konstantinov, NM Yakovlev. Institute for Experimental Medicine RAMS, St. Petersburg, Russia.

Disturbances in the brain reward systems play a key role in the etiology and pathogenesis of addictive disorders and other forms of deviant behavior in adolescents. The leading factor is a deficit of the positive reinforcement of mesocorticolimbic structures of the brain, which disintegrates the mechanisms of autonomic, emotional, and mental functions and disturbs adaptive behavior. A common drawback of pharmacotherapy, especially the use of neuroleptics, is that the consequences of long-term medication are unpredictable; these may be addiction, neuroleptic syndrome, blockage of natural compensatory resources, etc. Two methods of functional feedback correction of behavior have become popular in recent years. These methods differ in the mode of the patient's involvement in adaptive self-regulation. In the first, more traditional method, the patient is given explicit instructions regarding the conditions necessary for achieving the desired clinical effect and receives positive reinforcement of some form in the process. The other method uses the patient's involuntary self-regulation of a feedback signal from a parameter of a physiological process, e.g., the EEG. The data transformation algorithm in the feedback loop is developed to impart aversive properties to the signal if the parameter deviates beyond the set (normal) limits. The purpose of this study was to compare and substantiate the methods of voluntary and involuntary adaptive self-regulation of the functional state and find the optimal combination of these methods as part of integrated treatment of adolescents with behavioral disorders. The sample comprised 15 male adolescents aged 14-16 years with residual organic lesions of the brain and behavioral disorders that were inpatients of Skvortsov-Stepanov Psychiatric Hospital no. 3 (St. Petersburg) at the moment of the study. All patients had attention deficit hyperactivity disorder and behavioral disorders resulting from postnatal minimal cerebral dysfunction and encephalopathy. All patients receiving rational pharmacotherapy were divided into two groups. The first group comprised seven patients with intact intellect, minor attention deficit and behavioral disorders, and moderate impulsiveness. The second group comprised eight patients with depressed emotionality and volition, mental-autonomic disorders, attention deficit, memory disorders, a destructive component of aggression, and a history of suicidal behavior against the background of depression. Our earlier data on healthy adolescents served as a control. The course of treatment consisted of 10-12 sessions with a duration of 20 min each. In the first group, we performed cognitive (voluntary) correction of the pathological state with the use of EEG-controlled biofeedback (EEG-BFB) aimed at increasing the alpha-rhythm intensity. The sound of music was used as a feedback signal. The music was switched on if the amplitude of the current alpha-wave exceeded a set threshold and switched off if the amplitude of the wave decreased below the threshold. The patients had to feel the mental state in which they heard the music continuously and learn to reproduce this state in the future. The second group of patients underwent sessions of involuntary (unconscious) self-regulation of the mental state. EEG bioacoustic correction (EEG-BAC) procedures consisted of patients hearing the acoustic image of their own EEGs. The acoustic image was created by computer transposition of the current EEG waves into audio range and was presented to the patient in the real-time mode. During the procedure, the patients merely had to listen to the "sounds" of their own brains. The patients modified the acoustic images according to their preference for specific sound patterns and thereby rearranged the structures of their EEGs. In the course of EEG-BAC procedures, the cerebral BEA was reorganized; proportion of slow-wave components of the EEG and interhemispheric asymmetry were decreased. Positive changes in the EEG pattern rearrangement were confirmed by the analysis of cognition in sensorimotor response tests. The results of estimations in both groups of patients showed that the latent period of the

sensorimotor response to verbal stimuli decreased. After the course of treatment, emotional tension and fatigue were decreased in both groups of patients. The autonomic reactivity coefficient decreased from 1.8 to 1.3, which indicated a transition from the predominance of sympathetic to the predominance of parasympathetic control. The general trend of the emotional state of patients in the course of EEG-BAC training was observed in improved self-feeling, mood, and activity (according to the results of the SAM test and Luscher's test) and increased motivation and willingness to continue the training. Improvement was observed after each procedure and remained stable during a month after the course of functional therapy. Apparently, the disturbance of the maintenance of the frontal cortical tone and the deficit of active attention and action sequence control are related to the deficiency of the left-hemispheric dopaminergic system [Malone et al 1997]. Our tests of sensorimotor responses confirmed this hypothesis. It has been shown that performing a double acoustic signal and discerning verbal stimuli are the most difficult tests for adolescents with attention deficit syndrome. Poor results of the "attention maintenance" test are a typical manifestation of cognitive dysfunction and learning difficulties in children and adolescents with these disorders. Analysis of the obtained results allows us to draw the preliminary conclusion that it would be reasonable to include both methods of functional modification described here in an integrated treatment, where they should be used sequentially. We may expect that EEG-BAC will be more adequate at the initial stages of functional treatment because this method does not require strict selection of patients according to intelligence level and severity of mental disorders, including attention and memory impairment. In adolescents with deviant behavior with associated pathology (somatic or mental disease or head injury), combination of the EEG-BAC and EEG-BFB techniques is indicated, with the strategy of involuntary adaptive self-regulation of the functional state of the CNS preceding the strategy of voluntary neurobiological control. Apparently, the EEG-BFB method is more adequate and reliable for the formation of a stable skill of maintaining a comfortable mental state.

STRESS AND THE CEREBROPROTECTIVE EFFECTS OF CORTEXIN AND SELANK BRAIN FUNCTION DISTURBANCES IN THE ASCENDING ROW OF MAMMALS.

TN Sollertinskaja, MV Shorochov, NF Miasoedov. IM Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Institute of Molecular Genetics RAS, Moscow, Russia

Brain neurotic disturbances are the most spread after-effects of different extreme factors as well as many neurological and psychosomatic diseases. For this reason, the search for new drugs with the effective neuroprotective properties increasing the organism's resistance to different stresses, without accessory effects, is one of the key problems in modern neurophysiology and medicine. The great role for the correction of brain functions disturbances belongs to biologically active peptides. They are very effective in small doses, have a high degree selectivity and no accessory effects. Cortexin and Selank are peptide-bioregulators of new generation. Cortexin (Cor) was developed at the Military Medical Academy (St.-Petersburg) in 1986, and Selank (Sel) – is an anxiolytic drug derived from the biologically active peptide group, a synthetic derivative of endogenous peptide taftsin [developed at the Institute of Molecular Genetics (Moscow)]. The application Cor in clinical practice over the last five years has proved its broad therapeutic potential for many diseases of CNS including vascular, vegetative, metabolic traumatic, and stress-related disorders (Skoromets 2005, Golovkin 2005). Currently, there are no experimental data on the compensatory influence of above-mentioned drugs on the Higher Nervous Function disturbances in the available literature. Experimental data have shown, that Sel processes a prolonged neurotropic activity and improving the elaboration of conditional reflexes in mice (Kozlovskaja, Kozlovsky 2005). Here we assess the role of Sel and Cor in terms of the possibility to compensate the Higher Nervous and Homeostatic Function distortions in the ascending row of mammals (insectivores, rodents and primates). The experiments have been carried out using food model and multiparametrical registration of objective (electroencephalographic – EEG, vegetative and motor) components of Higher Nervous Activity. The experiments were performed in two series. The first series was made with freely moving animals, while the second one used monkeys placed into primatological chair. Besides the positive conditional reflexes the following types of memory have been investigated: conditional (the delayed conditional reflexes – DCR), short-term, long-term, working memory and operative memory ones. Sel and Cort were induced intranasally or intramuscularly as 30-100 mkg/kg and .1-1,0 mg/kg, accordingly. Emotional stress was provoked by overloading the analytico-synthetic brain activity (hedgehogs), the prolonged (1-1,5 hour) immobilisation (rats) or by extremal conditions (monkeys). We showed that the role of Cor and Sel is wholly uniform in hedgehogs with neuroses. Such effects are more expressed with the inherent forms of behavior being increased. It has been shown that the drug effects on the simple forms of Higher

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Nervous Activity have nonspecific facilitatory character. The differentiation of Sel and Cor compensatory effects on the disturbed brain functions are indistinctly expressed. It is manifested as the tendency in more expressed, short-term (up to 5 days) of Sel effects on the brain function disturbances. In contrast to hedgehogs, Cor and Sel effect in rats have different character of regulatory and compensatory influence on brain function disturbances. The Cor influence in the formation and restoration of DCR in rats is more significant, showing a tendency to memory intensification and longer action (4-5 days). The correct responses were recorded mainly at the delay phase ($p < .05$, $n = 10$). After Cor, the formation DCR with the delay time of 20-25 s is possible (intact – 10 s). Sel possesses the expressed compensatory influence upon the brain function disturbances. The effects are more expressed at small (30 mkg/kg) doses and are mainly seen on simple forms of Higher Nervous Activity, and vegetative indices. The respiratory frequency was normalized, and the amplitude of respiratory waves increased. The compensatory effects of Sel on DCR is short-term (3 days) and incomplete, the restoration of DCR is up to 40-50% only. It has been shown, that in contrast to hedgehogs and rats Cor and Sel in neurotic monkeys exerted distinct effects on disturbed brain functions. The compensatory effects are dependent on the types of neurotic disturbances (excitatory or inhibitory). Sel intranasal administration induces the long-term changes of the disturbed neurotic monkeys behavior, such as removal of aggression, orientation activity increase, the facilitation of handling reactions. After Sel, the long-term (up to 6 months) compensation of the brain function disturbances (memory and homeostatic parameters) in neurotic monkeys takes place. The antistress Sel effects do not depend on the type of neurotic disturbances. They are observed at the both types of neurosis. The cerebroprotective effects of Sel are especially significant at the administration of the drug small (30 mkg/kg) doses. The phone EEG and reactions of desynchronization of the new cortex become normalized. After the Sel introduction EEG indicators of DCR were recorded mainly at the delay phase, the latter indicate their intensification. They are strongly pronounced in the frontal associative newcortex. The delay time was increased till 90 s (in neurotic monkeys it is about 10 s). The vegetative parameters of conditioned reflexes were restored by their patterns and become more pronounced. The characteristic feature for the phone ECG after Sel administration was the decrease of the heart rate to 176-186 heart beat/min (at the neurotic monkeys it amount to 280-290 heart beat/min). The disturbances of heart rhythms and smooth down of P-Q-R-S complex by the form and duration disappere. The Cor administration to neurotic monkeys increases the attention concentration and visual memory. The compensatory effect of drug is manifested mainly at the inhibitory type of neurosis. After Cor, the motor activity and emotional state increases. Cor produced considerable (1-1,5 months) intensification of DCR and the extention of delay time. Thus, cerebroprotective and antiamnestic influence of biologically active drugs such as Sel and Cor at the disturbed Higher Nervous Functions is increased in the process of evolution. In insectivores, the effects of Sel and Cor are totally uniform, have a nonspecific character (more expressed with the simple forms of Higher Nervous Activity). The compensatory drug effects on the disturbed Higher Nervous Functions are similar. The clear tendency for more significantl Cor influence on conditioned memory is seen in rats, while Sel exertes the stronger influence on the Higher Nervous Function disturbances. In summary, Sel and Cor effects on brain disturbances in primates have differential specific features depending on the type of neurotic disturbances of Higher Nervous Activity. These data may serve as a neurophysiological backround for more differentiated clinical aplication of Cor and Sel in neurological clinics to treat different forms of post-stress disturbances.

Day 2. May 17, 2007. Venue: Oktyabrskaya Hotel, Ligovsky Prospect, 10

- CHILD HYPERACTIVITY AND ATTENTION DEFICIENCY: MODERN APPROACH TO CORRECTIONAL DIAGNOSTICS. N Tolmacha, Center of Psychoneurophysiological and Bioregulation Research, Riga, Latvia
- STRESS IS NOT JUST IN YOUR MIND: THE ROLE OF A SYMPATHETIC NEUROTRANSMITTER, NEUROPEPTIDE Y. Z Zukowska, Department of Physiology and Biophysics, Georgetown University, Washington DC, USA
- PHENOMENOLOGY OF ADDICTIONS. AY Egorov. IM Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg State University, St. Petersburg, Russia
- ANTI-STRESS ACTIVITY OF GINSENOSE RB1. Jun-Tian Zhang, Institute of Materia Medica, Chinese Academy of Medical Sciences & Peking Union Medical University, Beijing, China

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- COGNITIVE IMPAIRMENTS IN PTSD PATIENTS: A POSSIBLE VARIANT OF ADULT ADHD COMORBIDITY. M Segal, Flugelman's Mental Health Medical Center, Acre, Israel
- DIFFERENT INVOLVEMENT OF AMYGDALOID AND HYPOTHALAMIC CRF RECEPTORS IN THE REINFORCING EFFECTS OF HYPNOSEDATIVE AND PSYCHOSTIMULANT NARCOGENS IN RATS. PD Shabanov, Department of Pharmacology, Military Medical Academy, St. Petersburg, Russia
- PROTECTIVE PROPERTIES OF HEAT SHOCK PROTEINS: NEW IMPLICATIONS FOR SLEEP-WAKE BEHAVIOR, STRESS AND EPILEPSY. YuF Pastukhov. Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia

CHILD HYPERACTIVITY AND ATTENTION DEFICIENCY: MODERN APPROACH TO CORRECTIONAL DIAGNOSTICS. N Tolmacha, I Solomenikova, J Vandans. Centre of Psychoneurophysiological and Bioregulation Research, Riga, Latvia

In order for the child to perform well at school it is required to have an optimal state of the cognitive functions: attention, memory, and thinking. Based on the data by diverse researchers, 6% to 24% of schoolchildren are unable to coordinate their own actions with common norms. For such kids characteristic are deficiency of focus and concentration, unstable memory, increased distractibility and low study efficiency both home and at school. In medicine such behavioristic deviation are classified under Attention Deficiency Syndrome with/without Hyperactivity (ADSH). On a chronic basis, such behavioristic deviations cause children's discomfort up to disgust to studies even though if their intellect level is high. Social importance of the problem is marked by the fact that the behavioristic deviations might substantially increase by the teenage. Teenagers with hyperactivity fall into risk group in committing anti-social acts and crimes, and have a trend of alcoholic or narcotic dependence. Taking this into consideration, efforts should be made as to the early warning as well as timely correction of cognitive functions and behavior on the whole. Earlier research on ADSH-classified children's cognitive functions and EEG data (Tolmacha, Vandans, 2005, 2006) there were revealed uneven presence of brainwave frequency characteristics in cortex of areas large cerebral hemispheres often with low amplitude in some areas, brain biological current dysfunction in frontal areas with increased theta and beta rhythms, increased slow wave activity compared to the age norm, etc. Research on ADSH children cognitive functions have revealed decrease in short-term as well as long-term memory, focus and attention deficiency, impulsivity disorder, low logical capabilities, low study productivity, high distractibility, etc. The mentioned research assumed specific and general mechanisms of deviations in forming electric brain activity, specifically blood circulation. The aim of the present research is comparative study of the central and peripheral blood circulation of SDVG-classified children of pre-school and early school age. The research is based on 40 children of 5-6 years of age and 50 school first-graders 7-8 years of age (78-82% - boys). The research of the central blood circulation was performed in A. Vertebralis basin based on the common methodology of revealing implicit dysfunction (Zenkov, Ronkin, 1991). Peripheral blood circulation was estimated based on pletismogram data on index finger of the left hand. Uninterrupted monitoring of pletismogram -PG over time span of 20 minutes allowed researching indicator dynamics in background, reaction for verbal and visual irritants. The latter in the background there were accompanied by sonic irritants with the help of the stress-test software "Reacor" Medicom MTD (Russia). The software allows estimation of stress intensity for diverse types of irritants as well as children's adaptivity using the 20 minutes time limit. It was determined that ADSH-classified children of the both age groups for 85% and 78% of cases respectively showed changes in peripheral blood circulation compared to the corresponding age norm. Children of 5-6 years of age perceived stress factors, background research, verbal irritants, and visual combined with sonic irritants. The amplitude magnitude of the PG indicated the general level of activity and anxiety. However, children were absolutely calm and showed interest in the research whereas the there was indicated anxiety unconscious to the child. For this age group clear characteristic is inertness of stimulation with increased peripheral influences. Children of 7-8 years of age showed the highest level of activation during background research, whereas for verbal and sonic stress factors PG indicators gradually stabilized, which speaks of given age arbitrariness in regulation of the general functional state. The PG-index, value of the background activation, can be considered individual value of the "stress ability" of each child in the age group. In addition, we observed clear individual differences in character of reaction for verbal and visual combined with sonic irritants. Consequently, the age features of the PG reflected peculiarities of vegetative nervous system regulation of the respective age groups. Analysis of pulse blood flow in spinal artery vessels showed that 81% and 73% of children of both age groups

had lower amplitude values of 26% to 38% compared to the age norm. For some children, head turning left to right the value of rheographic wave dropped further 14% to 19% which indicates implicit disfunction of the brain blood flow. Disfunction in blood circulation of spinal artery vessels, as well as deviations in vegetative regulation of peripheral blood circulation for many children is largely undetected and is implicitly affecting development of brain functions. Neurological tests revealed low muscle tone and diverse spine damages. Thus, obtained data on spinal arteries and peripheral blood circulation disfunction for hyperactive children indicates the need for early diagnostics of ADHD children for timely functional correction.

STRESS IS NOT JUST IN YOUR MIND: THE ROLE OF A SYMPATHETIC NEUROTRANSMITTER, NEUROPEPTIDE Y. Z Zukowska, Department of Physiology and Biophysics, Georgetown University, Washington DC, USA

Stress has many faces, and it also has different meanings in various fields of science. It is considered a matter of the mind, the place where perception of 'disturbance of homeostasis' is born, leading to activation of hypothalamic-pituitary-adrenocortical axis and sympathetic nerves. However, the patterns of stress-induced responses are highly variable, and depend also on factors outside the brain. Cardiovascular and metabolic changes during stress vary with duration and intensity of stress, and this is reflected in a differential pattern of the release of sympathetic neurotransmitters, norepinephrine (NE), purines and neuropeptide Y (NPY) at the peripheral tissues. Mild and acute stress releases NE, whereas more intense and/or prolonged one is required for NPY. In addition to elevating plasma NPY levels, prolonged stress-induced sympathetic activation also raises platelet NPY levels; hence platelet NPY may be a good index of chronic stress. NPY's actions are both similar and dissimilar to those of NE. Like NE, NPY is a vasoconstrictor acting directly via its Y1 receptor (R), and indirectly, by potentiating NE-induced constriction. However, unlike NE, NPY is a potent growth factor, stimulating vascular smooth muscle cell growth via Y1R and angiogenesis via Y2/Y5R. An endothelial dipeptidyl peptidase IV (DPP-IV) serves as a molecular switch, inhibiting Y1R- and promoting Y2/Y5R-mediated activities – by forming a non-Y1, Y2/Y5R-preferring agonist, NPY3-36. Activation of the NPY-Y1R system by stress results in formation of occlusive atherosclerotic-like lesions in vessels injured by angioplasty. Conversely, tissue ischemia activates NPY-Y2-DPP-IV system and leads to angiogenesis, but stress appears to inhibit those actions. While NPY-induced angiogenesis plays a physiological role in revascularization of ischemic tissues, it is also pathological in retinopathy, obesity and tumors. Thus, genetically or stress-induced high NPY levels are indicators and risk factors for cardiovascular and metabolic disorders and cancer, and can be stress-related disorders can be treated with specific NPY-R antagonists.

PHENOMENOLOGY OF ADDICTIONS. AY Egorov. IM Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg State University, St. Petersburg, Russia

Nowadays it is obvious that the spectrum of addictive disorders consists of at least two groups: chemical and nonchemical (or behavior) addictions. R. Brown [1993] and M. Griffiths [1996] introduced six common features of addictive behaviors: salience, mood changes, tolerance, withdrawal symptoms, conflict and relapse. H. Shaffer [1997] intentionally called the field of addictology a "conceptual chaos". Recent studies in the US have shown that some specialists (mostly of an older generation) understand addiction as a physical dependence from psychoactive drugs while the other part of professionals (mostly of a younger generation) understand it as a compulsive-habitual behavior [Walters, Gilbert, 2000]. The addiction nature consists of a compulsive drug search and intake besides negative medical and social consequences, but not of a withdrawal syndrome [Leshner [1997] . This point of view (addiction as an obsessive-compulsive phenomenon) was supported by some Russian psychiatrists [Piatnitskaya, 2003; Portnov, 2004]. Nevertheless, it is in Russian tradition to consider pathological drug craving as a psychotic disorder [Altshuler, 1994], which includes ideational, affective and behavioral components [Vinnikova, 2003], or is similar to paranoid delusion [Chirko, Demina, 2002]. Earlier we have noted the phenomenological similarity of pathological craving in chemical and nonchemical addictions and *idée fixe* [Egorov, 2004]. Mendeleevich [2003] considered the presence of change in conscious states as the main diagnostic criteria in all types of addictions. These states are comparable as a phenomenon both to exceptional conscious states and twilight disorder of conscious. Sivolap [2006] has introduced a compromising opinion that addictive disorders represent a separate addictive psychopathological register, which belongs to the motivation disorder sphere and forms a particular nosologic group including chemical and behavioral types of addiction. Long-term experience shows that treatment and rehabilitation

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success of chemical addiction may be achieved in the cases when a patient can be "switched" to any other activity which occupies him completely and provides a positive emotional effect. Nonchemical addictions cover all spectrum of human behavioral activity such as love, sex, work, money and shopping, religion, sport etc. It seems that each human behavioral act may be potentially addictive. In other words, normally any human being has specific polyaddictiveness when in one person several potential addictions peacefully coexist, one of them being preponderant. Usually it is potential workaholism in a socially active man; in a housewife it may be communicational addiction; in a priest it is religion addiction; in a sportsman it is exercise addiction etc. Potential addiction, which plays the most important role in the present period of life, which does not suppress, does not force out the others we propose to call prevalent addiction. Prevalent addiction is transient, can fall under some external action and can coexist with other potential addictions. One gets a problem when one of potential addictions begins to dominate and force out the others. It may be either a prevalent addiction or any other, even a new one (for example, chemical addiction). In this case we talk about the dominant (fixed) addiction origin. A human being becomes an addict. The dominant addiction fills up the consciousness totally, forces out other potential addictions and resists external influence. Essentially dominant or fixed addiction has features close to psychopathological characteristics of *idée fixe*, which is highly resistible to any therapeutic influence, is inclined to relapse and transform to other *idée fixe*. If one considers addiction as a separate phenomenon with ideational (fixed) and obsessive-compulsive components, we can find the same psychopathological patterns. Obsessive-compulsive behavior is sufficiently resistant to therapy, often relapses; some obsessions and compulsions can easily transform into the others different in the content. The reasons why the dominant addiction is formed are all macro- and microsocial, psychological and biological factors of addictive behavior, which are described in lot of manuals in detail. Clinical experience shows that one addiction can easily transform into the other. It happens both in chemical (drug addiction transforms into alcoholism) and nonchemical addictions (sportive addict becomes a problem gambler). Besides chemical addiction can transform into nonchemical and vice versa. Essentially the treatment of a socially unacceptable addiction (drug addiction, alcoholism) comes to addict shift into a socially acceptable form of the addiction. This state is called stable remission. Thus the basic idea of prophylactics brings to maximum versatile personality education (i.e. polyaddictive personality). In this case the basic idea of rehabilitation of a chemical addict should be realized in strictly individual search and following strengthening of socially acceptable nonchemical addiction. If it is impossible, unfortunately the next step should be methadone maintenance treatment.

ANTI-STRESS ACTIVITY OF GINSENOSE RB1. Jun-tian Zhang, Xiao-yun Lian, Xiao-ying Wang, Zhi-wei Qu. Institute of Materia Medica, Chinese Academy of Medical Sciences & Peking Union Medical University, Beijing, China

Throughout the life, animal and human beings are challenged with various physiological and pathological stressors. Although certain type of mild stress show some beneficial effect on the organism, the chronic stress causes premature aging and pathogenesis of many age-related disorders such as Alzheimer's disease, depression, etc. To develop a new drug with anti-stress effect, ginsenoside Rb1 was used here for studying its anti-stress activity. Four stressors (tail hanging, forced swim in cold water, fasting and restraint) were used in the present experiments. Our results showed that chronic or repeated stress induced impairments of memory and sexual function as well as brain degeneration. Ginsenoside Rb1 blocked stress-induced impairment of sexual function and brain damage. The protective mechanisms of Rb1 against stress have been elucidated. Firstly, the nootropic mechanism of Rb1 was characterized by increasing neural plasticity including enhancement of acetylcholine content and M-cholinergic receptors density in CNS, up regulation of synaptic plasticity in both efficacy and structure, increase of expression of neurotrophine-NT-3 and BDNF and early immediate gene *c-fos*, increase of hippocampal neurogenesis, activation of PLC-PKC-CREB phosphorylation pathway. Secondly, Rb1 increased sexual function may attribute to increase of testosterone level in plasma and activation of NO/cGMP pathway in corpus cavernosum leading to penile erection. Thirdly, maintenance of homeostasis of the HPA axis is important for protection of brain against stress; Rb1 decreased noradrenaline level in hypothalamus and inhibited excitatory amino acid and corticosterone secretion as well as increased BDNF expression suggesting that Rb1 block stress response at early stage and consequently prevent many damages induced by stress.

COGNITIVE IMPAIRMENTS IN PTSD PATIENTS: A POSSIBLE VARIANT OF ADULT ADHD COMORBIDITY. M Segal, A Avital, V Mironov, M Pavlov, S Sandbank, S Kertzman, A Weizman.

Flügelman's (Mazra) Mental Health Medical Center, Acre, Rappaport Faculty of Medicine, Technion Israel Institute of Technology, Haifa; Department of Neurobiology, Weizmann Institute of Science, Rehovot; Department of Behavioral Sciences, The Max Stern Academic College of Yezreel Valley, Beer Yaakov Mental Health Center, Beer Yaakov; Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv; Anima Scan Ltd, Ashdod, Research Unit, Gehah Psychiatric Hospital, Petach Tiqva, Israel

Posttraumatic Stress Disorder (PTSD) is a syndrome characterized by involuntary and disturbing cognitive phenomena. Attentional resources are invested towards the recognition of threatening stimuli. Chronic PTSD has been associated with cognitive impairment involving memory and attention. The data on the neuropsychological impairment is sparse. In the present study we aimed to assess possible differences in cognitive functioning between 40 chronic PTSD patients and 38 matched healthy volunteers. Most of the PTSD patients were treated by SSRI or SNRI antidepressants. Exclusion criteria were physical illness including any cerebral or endocrine pathology, alcohol or drug abuse. Was used a 60-75 minute computerized Cognitive Scanning Battery (CogScan) for neuro-cognitive tests that evaluated sorts of attention: focused (Simple Reaction Time), selective (Stroop) and sustained (Continuous Performance Test), memory: immediate and delayed (Picture, Verbal and Face Recognition), working memory (WCST, Digit Span, Digit Running and Digit Symbol) impulsivity (MFFT, Tower of London); information processing (Choice Reaction Time); motor performance (Finger Tapping Test); perseveration (Alternation Test) and planning (Tower of London). The results showed significant lower performances of the PTSD group in most of the parameters that were examined: longer reaction time and more errors. The only item with no significant difference from the control group was of focused attention (Simple Reaction Time) that appears to confirm the enhanced arousal and hypervigilance of the patients. The results seem to indicate clear and profound neurocognitive impairment in chronic PTSD and a symptomatic cluster of inattention-impulsivity that suggests a form of acquired Adult ADHD.

DIFFERENT INVOLVEMENT OF AMYGDALOID AND HYPOTHALAMIC CRF RECEPTORS IN THE REINFORCING EFFECTS OF HYPNOSEDATIVE AND PSYCHOSTIMULANT NARCOGENS IN RATS. PD Shabanov, AA Lebedev, VF Streltsov. Department of Pharmacology, Military Medical Academy, Research Institute for Experimental Medicine RAMS, St. Petersburg, Russia

Drug addiction, also known as substance dependence, is a chronically relapsing disorder that is characterized by (1) compulsion to seek and take the drug, (2) loss of control in limiting intake and (3) emergence of a negative emotional state (e.g. dysphoria, anxiety, irritability) when access to the drug is prevented. Drug administration and withdrawal have been associated with the production and release of corticotropin-releasing factor (CRF) in extrahypothalamic brain sites and anxiogenic responses. The repeated administration of psychomotor stimulants (cocaine or amphetamine) or morphine has been shown to sensitize the stimulant (or morphine)-induced release of CRF in the central nucleus of the amygdala. A neuroanatomical entity termed the extended amygdala (Heimer and Alheid, 1991) may represent a common anatomical substrate for acute drug reward and the negative effects of compulsive drug administration on reward function. The extended amygdala is comprised of the bed nucleus of the stria terminalis, the central nucleus of the amygdala and a transition zone in the medial subregion of the nucleus accumbens (shell). The extended amygdala receives numerous afferents from limbic structures such as the basolateral amygdala and hippocampus and sends efferents not only to the medial part of the ventral pallidum but also a large projection to the lateral hypothalamus, thus further defining the specific brain areas that interface classical limbic (emotional) structures with the extrapyramidal motor system. The hypothalamic self-stimulation in a Skinner box was used to assess the reinforcing properties of some narcogens of hypnosedative (morphine 1 mg/kg, ethaminal-natrium 5 mg/kg and leu-enkephalin 1 mg/kg i.p.) and stimulant (amphetamine 1 mg/kg i.p.), action after the blockade of the brain CRF receptors by astressin (1 µg/µl, administered into the central nucleus of amygdala or the paraventricular region of hypothalamus) in Wistar rats. Amphetamine (1 mg/kg), morphine (1 mg/kg) and ethaminal-natrium (5 mg/kg) activated self-stimulation of the lateral hypothalamus of rats in different degree (+18-37%). Astressin (1 µg/µl), a nonselective antagonist of CRF receptors, administered into the central nucleus of amygdala or paraventricular region of hypothalamus, depressed self-stimulation reaction of lateral hypothalamus by 55% and 17%, respectively. The blockade of extrahypothalamic (in the central nucleus of amygdala) CRF receptors by means of astressin changed the effects of different narcogens on self-stimulation reaction. On that background, ethaminal-natrium and amphetamine supported the significant psychoactivative effect, but morphine changed its stimulating effect on depressant one. Leu-enkephalin possessed the stable depressant effect, strengthening the action of

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astressin. The blockade of hypothalamic (in the paraventricular area) CRF receptors by means of astressin changed the effects of narcogens on self-stimulation reaction in less degree. The psychostimulant effect was registered for amphetamine, morphine, and ethaminal-natrium, but leu-enkephalin did not change the depressant effect of astressin. It is suggested that CRF system of amygdala activates hypothalamic reinforcing systems. Perhaps, the strengthening of depressant action of leu-enkephalin on self-stimulation by means of astressin is associated with temporary excluding of activative influence of the central nucleus of amygdala on hypothalamus.

Day 3. May 18, 2007. Venue: Oktyabrskaya Hotel, Ligovsky Prospect, 10

- CENTRAL NERVOUS SYSTEM DISORDERS AND DAMAGE: IMPLICATIONS FOR STRESS, ANXIETY, AND DEPRESSION. PS Seibert, St. Alphonsus Regional Medical Center, Boise State University, Boise, ID, USA
- EARLY EXPOSURE TO STRESS MODULATES THE RESPONSE TO STRESS IN THE ADULT RAT. A Avital. Weizmann Institute of Science, Rehovot; The Max Stern Academic College of Yezreel Valley, Israel
- EVALUATION OF THE EFFECT OF AMITRIPTYLINE AND FLUOXETINE ON ANXIETY USING GROOMING ANALYSIS ALGORITHM IN RATS. N Enginar, Istanbul University, Istanbul Faculty of Medicine, Department of Pharmacology and Clinical Pharmacology, Istanbul, Turkey
- POST-TRAUMATIC STRESS DISORDER, DEPRESSIVE AND ANXIETY DISORDERS AMONG ADULT VICTIMS AFTER THE MARCH 11TH TERRORIST ATTACKS IN MADRID. O Medina, Department of Psychiatry, Gregorio Maranon General Hospital, Madrid, Spain

CENTRAL NERVOUS SYSTEM DISORDERS AND DAMAGE: IMPLICATIONS FOR STRESS, ANXIETY, AND DEPRESSION. PS Seibert, PD Parker, CM Patterson, N Whitener, J O'Donnell, CG Zimmerman. St. Alphonsus Regional Medical Center, Boise State University, Boise, ID, USA

Experiences of anxiety and depression, at both clinical and non-clinical levels, are found across many disorders and/or damages of the CNS. In addition, stress is frequently reported as a precursor to CNS injury and/or illness as well as a resultant. Though rates of stress can be more difficult to measure than anxiety and depression due to less specific diagnostic criteria and symptoms, high levels of stress are believed to complicate and hinder treatment, as well as exacerbate symptoms of disorders and/or damages to the CNS. Samples of those with Parkinson's disease (PD) and traumatic brain injury (TBI) have been known to experience increases in rates of stress, anxiety, and depression. Obviously these increases could be attributed to both biological and psychiatric causes. Furthermore, those with diagnosed sleep disorders (SDs) report similar symptoms prior to receiving treatment for SDs. In addition, many medications used to treat physical symptoms of CNS disorders may have an effect on stress, anxiety, and depression. We investigated the incidences of stress, anxiety, and depression in a sample of disorders and/or damages to the CNS across a total of 961 participants. Our sample included 658 people who were referred to our institution for evaluation and treatment of SDs, 176 people who sustained a TBI and are participating in a 20-year long longitudinal study, 28 people who underwent deep brain stimulation (DBS) treatment for a movement disorder (MD), and 99 people who responded to a state-wide questionnaire regarding PD. Of those evaluated for SDs, 83% reported experiencing stress, 56% reported anxiety, and 59% reported feeling depressed. Additionally, 54% had been diagnosed with a psychological disorder (most prevalent were depression and anxiety disorder) prior to being diagnosed and treated for sleep problems. Of 176 people who sustained a TBI, 78% reported experiencing stress, 42% reported anxiety, and 35% reported feeling depressed following their injury. Of the 99 people who answered our questionnaire on PD, 89% reported experiencing anxiety, 82% reported feeling depressed, and 92% reported experiencing stress. Despite the high rates of anxiety and depression, only 22% were diagnosed with an anxiety disorder and 33% with depression. In the sample of people who underwent DBS, 71% reported feelings of depression, 82% reported anxiety, and 82% reported stress. Interestingly, our study indicates that many variables influence symptoms, and/or treatment for them. For instance, the population of people in the sleep study tends to be younger and have higher rates of a variety of diagnoses than people who had movement disorders. The age and generational differences may influence behavior related to seeking treatment. Untreated psychological problems may hinder recovery and or treatment of CNS disorders and/or damage. This study also indicates that certain

treatment of the primary disorder may reduce feelings of stress, anxiety, and depression. For example, people who underwent DBS reported decreased rates of stress, anxiety, and depression 6-months post surgery. On the contrary, though, for those who answered our PD questionnaire, stress, anxiety, and depression were actually negatively correlated with motor symptoms of PD; bradykinesia, speech impediments, and rigidity, for example. Anxiety and depression were both negatively correlated with having experienced hallucinations, a side effect of the PD medications. Depression was also, negatively correlated with a decreased appetite. Despite the fact TBI, MDs, and SDs effects on the CNS vary greatly, all demonstrate widespread relationships associated with stress, anxiety, and depression. Given the nature of compromises to the CNS, resultant connections to stress, anxiety and depression are not surprising. The implementation of these findings, though, suggests treatments related to the CNS should encompass more than those traditionally related to the disorder and/or damage. Addressing the roles of stress, anxiety, and depression contributes to better understanding of disease and recovery process, which in turn may facilitate improved physical treatment modalities. The unexpected negative correlations within our PD sample illustrate the challenges in researching areas so prone to individual differences in experience and perception. Moreover, these findings demonstrate the need for further research into stress, anxiety, and depression to better understand their potential roles in treatment and recovery.

EARLY EXPOSURE TO STRESS MODULATES THE RESPONSE TO STRESS IN THE ADULT RAT. A Avital. Department of Neurobiology, Weizmann Institute of Science, Rehovot; Department of Behavioral Sciences, The Max Stern Academic College of Yezreel Valley, Israel

It has been proposed that exposure to stress during early childhood may disturb emotional and cognitive functioning in adulthood. We examined the behavioral consequences of early exposure to stress, and in particular, on the ability to cope with stress in adulthood. Post-weaning and Pre-puberty, at the age of 4 weeks, rats were placed on a platform in the middle of a water pool, for 30 minutes (Platform stress). In the 1st experiment, we used as late stress the Host-intruder interaction at the age of 8 weeks. All rats were then tested in an open-field, the Morris water-maze and the startle-reflex test. In the 2nd experiment adult rats were trained under stress condition (two-way avoidance task) in a shuttle box, followed by affective examination. We report here that an early exposure to stress led to elevated levels of anxiety, as measured in the open-field and startle response tests. However, the rats that were exposed to the combination of early and late stress exhibited the highest level of anxiety. In addition, and as was previously reported, the early + late stress group acquired a stressful spatial learning task faster. Furthermore, rats that were exposed to stress early in life did not learn the two-way avoidance task in adulthood. These findings suggest that an early exposure to stress may have lasting effects on both emotional and cognitive abilities in adulthood, as is indicated by its effects on anxiety levels and on the performance in a spatial learning and two-way-avoidance tasks.

EVALUATION OF THE EFFECT OF AMITRIPTYLINE AND FLUOXETINE ON ANXIETY USING GROOMING ANALYSIS ALGORITHM IN RATS. N Enginar, I Hatipoglu, M Firtina. Istanbul University, Istanbul Faculty of Medicine, Department of Pharmacology and Clinical Pharmacology, Istanbul, Turkey

The antidepressant drugs amitriptyline and fluoxetine both have distinct actions in animal models of anxiety. Acute and/or chronic administrations of these drugs mostly produced anxiolytic effect, but also resulted in ineffectiveness or even in anxiogenic activity. It has been suggested that grooming behavioral sequencing, rather than its general "activity" measures, can effectively measure pharmacologically induced anxiolytic and anxiogenic-like effects. Thus, the effect of amitriptyline and fluoxetine on grooming in rats was evaluated using grooming analysis algorithm to clarify their anxiolytic efficacy. Male Wistar albino rats were randomly divided into 5 groups and were injected i.p. with saline (control), amitriptyline (5 or 10 mg/kg) or fluoxetine (5 or 10 mg/kg). Twenty-five minutes following treatments, animals were individually placed into a glass cylinder (19X19 cm) with a wire mesh cover. Novelty-induced grooming activity was evaluated for 5 min, as described by Kalueff and Tuohimaa (J Neurosci Methods, 2005). Then, exploratory activity was recorded in an hole board for 5 min by counting the number of squares crossed, head dippings and rearings. Data were analysed by Kruskal-Wallis followed by a post hoc Mann-Whitney tests for comparisons between control and drug groups. Amitriptyline (5 and 10 mg/kg) and fluoxetine (5 and 10 mg/kg) decreased the duration of grooming bouts and the total number of patterns and transitions. Amitriptyline (5 and 10 mg/kg) decreased skipped and increased aborted transitions and reduced the average duration of a single

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bout and the average number of patterns and transitions per bout. Fluoxetine increased aborted transitions at 5 mg/kg, reduced the average number of patterns and transitions per bout at 10 mg/kg and decreased the number of incomplete bouts at both doses. Amitriptyline (5 mg/kg) increased forepaw grooming patterns and fluoxetine (5 and 10 mg/kg) increased genital grooming. Amitriptyline (10 mg/kg) and fluoxetine (5 and 10 mg/kg) decreased rostral grooming interruptions. In the hole board, fluoxetine (10 mg/kg) reduced the number of head dippings and rearings. Present findings showed that amitriptyline and fluoxetine not only affect the traditional gross measures, but also alter the behavioral microstructure of grooming activity in rats. Decrease in time spent grooming indicates that the drugs exert anxiolytic effect. However, changes in incorrect transitions and regional distribution of grooming behavior are somewhat contradictory findings. On the other hand, high dose of fluoxetine produces an anxiogenic profile with reduced head dippings and rearings in the hole board. The effects of amitriptyline and fluoxetine on the general "activity" in the grooming behavior in rats suggest that both drugs possess anxiolytic activity. However, grooming analysis algorithm and hole board measures do not fully support this suggestion.

POST-TRAUMATIC STRESS DISORDER (PTSD), DEPRESSIVE AND ANXIETY DISORDERS AMONG ADULT VICTIMS AFTER THE MARCH 11TH TERRORIST ATTACKS IN MADRID. O Medina, J Conejo-Galindo, D Fraguas, S Teran, E Sainz-Corton, C Arango. Department of Psychiatry, Gregorio Maranon General Hospital, Madrid, Spain

On March 11, 2004, Madrid experienced the worst terrorist attack in its history. Ten bombs exploded on four different commuter trains headed for the central station in Madrid. The death toll rose to 192. Approximately 2000 people were injured. This terrorist attack was unprecedented in scope, both in Spain and in the European Union. The social repercussions of this tragedy and its long-term economic effects are still unknown. Our study aimed to describe the prevalence and correlates of post-traumatic stress disorder (PTSD), depressive and anxiety disorders, or any other mental disorder among adult victims treated in a hospital at different points in time after the March 11th terrorist attacks in Madrid. Representative random samples of 56 individuals injured in the attacks were interviewed in person at one, six, and twelve months after the attacks. Current DSM-IV mental disorders: depressive disorders and anxiety disorders (PTSD, generalised anxiety, agoraphobia, social phobia, and panic disorder) were assessed with the Spanish version of the MINI (Mini International Neuropsychiatric Interview), a structured, lay-administered psychiatric interview. PTSD was the most prevalent psychiatric disorder (35.7% at month 1, 34.1% at month 6, and 28.6% at month 12), followed by major depression (28.6%, 22.7% and 28.6%, respectively). Others relevant conditions were suicide risk, generalised anxiety disorder, agoraphobia, and panic disorder. No significant differences in the prevalence of the disorders were found between the different assessment times. The only predictive factor for PTSD at month 12 was PTSD at month 6 (OR=14.007). The only predictive factor for major depression at month 12 was major depression at month 6 (OR=15.847). In the present study, there was a high prevalence of PTSD and major depression one year after the terrorist attacks. The prevalence of the disorders decreased in the follow-up, but they were not statistically significant.

Day 4. May 19, 2007. Venue: IEM RAMS - Institute of Experimental Medicine RAMS, 69/71 Kamennostrovsky Prospect

- DOMAIN INTERPLAY CONCEPT IN BIOLOGICAL PSYCHIATRY. AV Kalueff, Center for Physiology and Biochemical Research, Moscow, Russia, Bethesda, MD, USA
- NEURODEGENERATION AND ITS CORRECTION IN DEMYELINATING AUTOIMMUNE DISEASES. VM Klimenko, IA Abdurasulova, Institute of Experimental Medicine RAMS, St. Petersburg, Russia.
- SPECIAL LECTURE OF THE UKRAINIAN SOCIETY FOR BIOLOGICAL PSYCHIATRY (USBP): RECENT ADVANCES IN SEROTONIN NEUROTOXIC SYNDROMES

NEURODEGENERATION AND ITS CORRECTION IN DEMYELINATING AUTOIMMUNE DISEASES

VM Klimenko, IN Abdurasulova. Institute of Experimental Medicine RAMS, St. Petersburg, Russia
Demyelinating diseases, and multiple sclerosis (MS) in particular, originate in impairment of systems' interaction. As the result, "aggressive" immune cells percept tissues of the brain as their target.

Autoimmune nature of demyelinating diseases has become the reason for intensive study of immune factors role in the process, first of all, of cytokines (mediators of inflammation). Experimental allergic encephalomyelitis (EAE) – the model used in numerous researches on animals - has proved that proinflammatory cytokines (tumor necrosis factor α , interleukin-1 β (IL-1 β)) play significant role in pathogenesis of MS. At the same time, anti-inflammatory cytokines - interleukin-10 and receptor antagonist IL-1 (IL-1r.a.) provide protective action. Understanding of reciprocal effects of pro- and anti-inflammatory cytokines and of necessity of their balance for normal immune response allowed to develop approaches to medical treatment based on β -interferon drugs. Broad application of this treatment is hampered by its significant duration and expensiveness. Besides, this approach sometimes is not effective. It means that there is a necessity of development of therapy aimed at other elements of pathogenesis. Recently, the role of glutamate excitotoxicity and oxidative stress in MS pathogenesis has become the topics of hot discussions. Specific impairments caused by oxidative stress accompany the death neurons under many neurodegenerative diseases. This fact points to certain identity of mechanisms involved into destruction. Oxidative stress causes cell damage due to modification of different principal molecules, inducing apoptotic cascade. Thereby the oxidation of nucleonic acids can cause mutations, peroxidation of membrane lipids and proteins including receptors of neurotransmitters and of trophic factors. The oxidation can cause impairments of cell membrane and ionic homeostasis, and a lot of ferments, particularly ATPase or dehydrogenase, may be the reason of destroyed metabolism of energy and of excitatory amino acids. All these disorders are incompatible with normal cell's activity due to apoptosis program automatically getting started. Active forms of oxygen are being created in cells as a result of both normal metabolic reactions and oxygen supply disorders of cells. Under physiological conditions oxygen radicals are not accumulated in cells but their concentration might be increased (1) by growing of free radicals creation and (2) inhibiting of cell's ability to the neutralization. Tissue protection of oxidative stress is maintained by special antioxidative system. Nitrogen monoxide (NO) is one of the principal oxygen radicals. NO production rate is controlled by NO-synthase of phagocytes, neurons, smooth vessel cells etc. NO freely penetrates cell membrane and participates in transmission of cytokine's signal to glial and endothelial cells of circumventricular organ. Enhanced production of NO is tightly linked with hyperactivation of NMDA glutamate receptors. NO is involved into antimicrobial protection, blood flow regulation, blood-brain barrier permeability, neuronal activity modulation, hypophysial stress hormones release rate, neurotransmitters secretion control. NO is synthesized by three forms of the ferment coded by different gene sequences. The pathologic processes are linked mainly with inducible NO-synthase (iNOS). Under normal conditions its concentration in CNS is very low but it is significantly increased during pathology development. The iNOS synthesis is then activated by proinflammatory cytokines (IL-1, IL-2, TNF, INF) and endotoxin (LPS). The iNOS activation leads to NO increased production, which in turn stimulates the neurotoxic cascade: increasing of peroxide ions \rightarrow peroxy-nitrites synthesis \rightarrow generation of free OH radicals and NO₂. This results in development of neuro-destruction. Hence signal transduction, which is activated by proinflammatory cytokines, active forms of oxygen, and excitatory neurotransmitters, is characterized by the crossing of intracellular transduction ways. The latter makes evident the probability of their mutual modulation. Other hand glutamate, proinflammatory cytokines, and NO participates actively in regulation of neurogenesis. Some of them inhibit and others stimulate the process. Finally the result of cell's surviving depends on the quotation of both intracellular pro- and anti-apoptotic signals, and extracellular microenvironment. MS patients and animals with EAE have increased level of glutamate in liquor and decreased activity of ferments, which are responsible for glutamate degradation, in astrocytes. Pro-inflammatory cytokines produced by glial cells stimulate glutamate production. Increased activity of glutamatergic system and oxidative stress may cause neurodegeneration, which is present in MS as proved by modern medical technologies - magneto-resonance tomography and spectroscopy. It means that there is a necessity of neuroprotective therapy for MS. Glutamate receptors activity regulation with the help of low affinitive blockers of ionic channels, especially blockers with complex NMDA/AMPA activity, may be used. Favorable prospects of this pharmacologic approach have been endorsed by published data as well as by our own research with EAE model. It has been revealed that such treatment is able to produce protective effect at several levels: at the periphery (to decrease immune cells activity and, as a consequence, levels of circulating TNF); at the BBB level (to decrease BBB permeability as the result of NMDA-receptors activity regulation); and directly in CNS (to block AMPA receptors of oligodendrocytes, NMDA- and AMPA- receptors of neurons, and reduce overall excitotoxicity). Given that neurodegenerative processes may be based on similar mechanisms, this type of treatment is applicable for cure of other neurodegenerative diseases besides MS. Another

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approach to neurodegenerative diseases treatment is natural neurogenesis stimulation. It has been found that proliferation of stem nervous cells and new neurons formation in two parts of the front brain (subventricular zone and gyrus dentatus of hippocampus) of mammals and humans take place during entire life of a being. Presently there is scarce information on endogenic factors regulating this process. As neurogenesis consists of several stages (stem neurocellular proliferation, neuroblasts migration and new neurons survival), factors regulating each of them may be chosen as a target for pharmacologic treatment. Neurogenesis activity slows down with aging, by some diseases and by stresses and by other harmful factors.

CONFERENCE SYMPOSIA

Day 1. May 16, 2007. Venue: Oktyabrskaya Hotel, Ligovsky Prospect, 10

Symposium 1. Experimental models of stress – I. Chairs: VM Klimenko, YuF Pastuhov

- **STUDY OF EFFECTS OF THERMAL PRECONDITIONING AND QUERCETIN ON SEIZURE ACTIVITY AND CONTENT OF HEAT SHOCK PROTEIN 70 KDA IN BLOOD PLASMA IN WISTAR RATS.** IV Ekimova, LE Nitsinskaya, luF Pastukhov, IV Guzhova. Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, Institute of Cytology, RAS, St. Petersburg, Russia
- **UPBRINGING BY THE FOSTER MOTHERS AS A RISK FACTOR OF DEVELOPMENT OF PSYCHOEMOTIONAL DISORDERS.** TV Avaliani, NK Apraksina, OR Fedotova. Institute for experimental medicine RAMS, St. Petersburg, Russia
- **ANTICONVULSANT EFFECTS OF PROTEIN 70kDa AND THERMAL PRECONDITIONING IN KRUSHINSKII-MOLODKINA RATS.** KA Hudik, YuF Pastukhov. Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia
- **EFFECT OF HEAT SHOCK PROTEIN 70 KDA ON THERMOREGULATORY CHARACTERISTICS DURING THE INTOXICATIONAL STRESS IN RATS AND PIGEONS.** KV Lapshina, IV Ekimova. Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St.-Petersburg, Russia

STUDY OF EFFECTS OF THERMAL PRECONDITIONING AND QUERCETIN ON SEIZURE ACTIVITY AND CONTENT OF HEAT SHOCK PROTEIN 70 KDA IN BLOOD PLASMA IN WISTAR RATS. IV Ekimova, LE Nitsinskaya, luF Pastukhov, IV Guzhova. Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, Institute of Cytology, RAS, St. Petersburg, Russia

INTRODUCTION: Over the last years, molecular and cell mechanisms of epileptogenesis attract great attention. The great interest is associated with issues related to participation of endogenous regulators, particularly protein-chaperones of the family Heat Shock Proteins 70 kDa (HSP70), especially cytoplasmic member of this family, heat shock protein with molecular mass 70 kDa (Hsp70), in the regulation of seizures. It has been recently demonstrated that elevated brain Hsp70 in warm-blooded animals induced a hypnosedative effect in the form of an increase in time of slow wave sleep and a decrease of muscle tone and vegetative parameters [Pastukhov et al 2005; Pastukhov and Ekimova, 2005]. These data suggest the involvement of Hsp70 in mechanisms of regulation of integrative brain function. Investigations carried out in rats with hereditary forms of epilepsy and in Wistar rats showed that thermal preconditioning is capable to attenuate audiogenic convulsions and the severity of seizures and movement disorders induced by hyperactivation of NMDA-type glutamate receptors [Ekimova et al Nitsinskaya et al 2006]. All this implies further participation of Hsp70 in the regulation of seizure activity and a search for the point of application of anticonvulsive properties of Hsp70 in a model of corasol (pentylentetrazole, PTZ)-induced seizures. A model of PTZ seizures is especially attractive for the elucidation of therapeutic potential of Hsp70, given the mechanisms of pathogenesis are close to generalized absence and generalized tonic-clonic epilepsy in humans. The objective of the investigation was to study effects of thermal preconditioning and quercetin, inhibiting Hsp70 expression, on PTZ-induced seizures and content of Hsp70 in plasma in Wistar rats.

METHODS: The investigations are carried out in male Wistar rats (mass 150-220 g). Seizures were induced by intraperitoneal injections of convulsant doses (75-80 mg/kg) of PTZ (Sigma). Bioflavanoid quercetin (ICN) was used to inhibit Hsp70 expression. Quercetin (5 mg/kg) was injected intraperitoneally 3.5-4 h before PTZ. To enhance endogenous expression of HSP thermal preconditioning was used 24 h prior to PTZ-induced seizures. For this purpose, anesthetized with nembutal (50 mg/kg) animals were subjected to a short-term superheating inside heat-chamber up to 41°C of rectal temperature. The period of observation over seizure activity and movement disorders lasted 30 min following PTZ injections. The intensity of seizures was registered using a modified Racine's scoring system. To measure the levels of Hsp70, blood samples were subjected to the analysis with the aid of a novel diagnostic developed by the authors (BAM, IG), Russian Patent N 2242764. It is based on the high affinity of Hsp70 to immobilized ATP. ATP was conjugated with the ovalbumin and the latter was immobilized on the surface of a 96-well enzyme immunoassay plate (Greiner, Microlon, Germany). **RESULTS AND DISCUSSION:** PTZ induced convulsive seizure with a latent period of 43 s in all rats. The onset of clonic-tonic seizures was identified in 90% of animals,

with the duration being 22 s. The lethality of animals with PTZ-induced seizure was 80%. The neurotoxic effects of PTZ lasted after seizures, manifested in the form of ataxia. Thermal preconditioning, as compared to control (anesthetized animals), in 24 h resulted in a greater increase (80%) in a latent period of convulsive seizure, totally prevented development of tonic seizures in 50% of rats, decreased the lethality and the manifestation of ataxia symptoms in 60% of rats. The concentration of endogenous Hsp70 in the blood of rats under control conditions is very low and reaches only 7.0 ng/mL. 15 min following treatment with thermal preconditioning, the concentration of Hsp70 increased up to 22.5 ng/mL ($p < .05$). However, 30 and 60 min following thermal preconditioning, the blood level of Hsp70 reached only 9.1 and 3.4 ng/mL, accordingly (showing that within 30 min Hsp70 is eliminated from the circulation). Quercetin considerably increased total time of generalized clonic (2.7-fold) and tonic (27%) PTZ seizures. These results show a pro-convulsing effect of selective inhibitor of Hsp70 expression. No marked effect of quercetin on ataxia symptoms was found. No endogenous Hsp70 in plasma was found 4 h following injection of quercetin, which indicates suppression of Hsp70 synthesis by quercetin. Collectively, this shows Hsp70 involvement in regulation of a variety of motor components of PTZ-induced seizures and behavior. Molecular mechanisms underlying anticonvulsive effect of endogenous Hsp70 remain unclear, and requires further studies.

UPBRINGING BY THE FOSTER MOTHERS AS A RISK FACTOR OF DEVELOPMENT PSYCHOEMOTIONAL DISORDERS. TV Avaliani, NK Apraksina, OR Fedotova. Institute for Experimental Medicine RAMS, St. Petersburg, Russia

INTRODUCTION: Upbringing of reception children is actual problem of present day. The conflicts arising between the foster mother and the child can result in tragic consequences. The reasons for these conflicts have both social and biological bases. It is possible to analyze the biological reasons of occurrence of the conflicts and, as a consequence it, development of psychoemotional disorders at the reception posterity using the cross upbringing rates. The purpose of this research was to reveal psychoemotional frustration in control rats and rats with deviations of development caused by change of parent environment in early ontogeny. **METHODS:** Wistar rats tested according to Peterson (1951) to reveal lateral motor preference. In a group of rats, we also modeled acute psychogenic trauma by putting them inside the terrarium to the tiger python one month before the conceptions or for the first 14 days of pregnancy. **RESULTS AND DISCUSSION:** The upbringing of the normal females by the right-handed animal of reception normal posterity caused at the rats hyperactive behavior in the open field (OF) test, and upbringing by the left-handed females decreased locomotor of activity in comparison with behavior of normal rats, brought up by the native mother. In both groups the orientation-investigative and emotional behavior was distorted. The change of amount and duration of the separate acts did not result to the disturbances of integrity of behavior. In the test PM at reception children of these groups the increased of the uneasiness and decrease of research activity - long stay in the closed sleeve, reduction of the drooping and stay at the centre of a labyrinth was registered. In the greater degree, the uneasiness was increased at the offspring, which brought up by the left-handed mothers. Earlier we investigated psychomotor emotional frustration and infringement of structure of behavior at posterity of the rats with a trauma sensomotor cortex and psychogenic trauma. The pronounced character of these frustration depend from lateralization of a brain's trauma, terms of influence stressing of the factors and interhemisphere of functional asymmetry of the mothers. The upbringing by the normal left-handed of a posterities, born by the females with lateralised of a brain's trauma, resulted in normalization locomotor and research behavior. But at the rats the emotional deviations were not corrected, the increased uneasiness was kept, and the structure of behavior was destroyed even in the greater degree, than at upbringing by the own mothers with a brain's trauma. The upbringing by the healthy right-handed foster animal of a posterity from female with a trauma of a brain promoted normalization research behavior, but only partially reduced displays hyperactivity. Complete restoration of structure of the behavior at the rates was not observed. Besides at the rats these groups the uneasiness in the test PM grew. The upbringing of the offspring by normal female from rates stressed during pregnancy, resulted in normalization locomotor behavior, but caused disorder of the grooming behavior, suggesting high emotional intensity. The structure of behavior of the majority rats of this group essentially did not differ from structure of behavior normal rats. At upbringing by the normal mothers of the offspring, born from stressed before the pregnancy of the rats, also it was marked restoration locomotor and research behavior. However structure of behavior was broken and consisted from several patterns, one of which demonstrated authentic interrelation of the acts in a dyad «moving on the spot» and «grooming», suggestive of

increased emotionality and depression-like component of behavior. Disrupted integrity of behavior in this group was more expressed, than in stressed rats born and brought up by the own mothers. Despite of normalization of some behaviors in rats, born by the female with psychogenic or physical trauma of a brain, the upbringing by normal female did not restore behavior. At the normal rats the upbringing by the foster- mother resulted in disorder of behavior. Pronounced behavioral deviations in 1 m.o. offspring by each of groups carried individual character and depend on specificity prenatal influence, interhemisphere functional asymmetry of the mothers and relation of mother to reception posterity. Last thesis proves to be true by results of the analysis of parent behavior at the collecting own and another's rats in a jack and survival of the reception posterity in comparison with native rats. The females the right-handed animals both own, and normal receptions rats, collect in a jack in 2-3 times faster, than female left-handed. Time of the collection of the offspring from female with motor deficiency or psychogenic trauma was increased more strongly in normal females than in the right-handed group. To offspring born from females with motor deficiency, per the first day of the postnatal period foster-mother concerned worse, than to the posterity from the stressed mothers. But the index lactation and index of viability at such posterity was higher, than at the stressed posterity. **CONCLUSIONS:** Thus, psychoemotional disorders can arise or be aggravated under action of the biological factors. Pronounced character and the specificity of these disorders depends on features of parent behavior and identification by the females of abnormal behavior of posterity on different terms of the ontogeny.

ANTICONVULSANT EFFECTS OF PROTEIN 70kDa AND THERMAL PRECONDITIONING IN KRUSHINSKII-MOLODKINA RATS. KA Hudik, YuF Pastukhov. Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia

INTRODUCTION: Currently, epilepsy is one of the most extensive brain disorder. Basic mechanism of epilepsy is a disturbance of balance between mechanisms of activation and inhibition in brain. One of the key problem in this field is development of different methods for recovery this disbalance and reduction of the severity of epileptic seizures. We know that increased concentration of chaperones (Heat Shock Proteins, HSP), under thermal preconditioning and central injections of exogenous Hsp70, considerably reduce severity of epileptic seizures caused by injection of NMDA (agonist of glutamate receptors) (Ekimova et al 2005). The aim of the present investigation is to study anticonvulsant effects of exogenous Hsp70 and thermal preconditioning in a model of genetic audiogenic epilepsy in Krushinskii-Molodkina rats. **MATERIALS AND METHODS:** The investigation was carried out in Krushinskii-Molodkina male rats with genetic audiogenic epilepsy. Convulsive activity caused by sound (intensity 50 dB, frequency 8 kHz) from a generator. The following parameters were registered: the latent period of the beginning of epileptic seizures, the duration of the "wild" running phase and clonic-tonic seizures. The severity of seizures was assessed in balls according to modified scale created on the basis of Krushinskii classifications (Krushinskii, 1967). Two methods of an increase in concentration of HSP70 were used in this investigation: intracerebroventricular microinjections of exogenous Hsp70 and thermal preconditioning, inducing endogenous stimulation of HSP70. Exogenous Hsp70 obtained in the Institute of Cytology RAS (Guzhova et al 1998) was used in our experiments. To precondition anesthetized animals (nembutal/oxibutirat) were exposed to heat at rectal temperature 41°C during 5-7 min. Convulsive activity after thermal preconditioning was tested following 1 or several days. Records and analyses of convulsive activity were carried out with system of video surveillance and computer registration (Logitech). **RESULTS AND DISCUSSION:** Audiogenic stimulation induced intensive "single-wave" seizures consisting of the "wild" running phase and clonic-tonic seizures. Latent period of the "wild" running phase was 2.1 ± 1 s, the duration of this phase was 4.2 ± 2 s and the duration of clonic-tonic seizures was 14.7 ± 3 s. Symptoms of catalepsy were observed for a long period (10-20 min) after tonic seizures. It is found that a decrease in the duration of clonic-tonic seizures was occurred (by 34%, $p < .01$) in 3 h after microinjections of Hsp70 (5 mkg/.5 mkl) into 3-rd brain ventricle. Statistically significant changes in duration of the latent period and the "wild" running phase were not observed. Microinjections of Hsp70 (10 mkg/1 mkl) caused a decrease in the duration of clonic-tonic seizures in 2 h (by 23%, $p < .01$) and in 5 h (by 49.6%, $p < .001$). A tendency for an increase in the duration of the latent period (by 68%, $p > .05$) was observed in 2 h after microinjections of Hsp70 (10 mkg/1 mkl), whereas a significant increase in the duration of the latent period (by 68%, $p < .05$) was observed in 5 h after microinjections of Hsp70. Hsp70 reduced total time of audiogenic seizures: by 25% ($p < .05$) in 3 h after injection Hsp70 at a dose of 5 mkg, by 20% ($p < .001$) in 2 h and by 35% ($p < .001$) in 5 h after injection Hsp70 at a dose of 10 mkg. A decrease in the severity of epileptic seizures in comparison

with the control (audiogenic stimulation) was found. Thermal preconditioning caused a significant increase in the duration of the latent period of seizures in 2.4 times during the 2-7 days, with maximum of effects observed at 4-th day (in 4.8 times, $p < .01$) after heat. Significant changes in the duration of the "wild" running phase and a clonic-tonic seizure were not found. Second session of thermal preconditioning was performed in 10 days after first session. Significant increase in the latent period was observed earlier, in 24 and 48 h after thermal preconditioning. Thermal preconditioning did not reduce total time of audiogenic seizures and the severity of epileptic seizures. Short-term thermal preconditioning (5-7 min) was used in this investigation. It is likely that this method is not sufficiently intensive stimulus to increase expression of chaperones. Long-term thermal preconditioning (10 min) resulted in lethality 75% of all animals. It is possible that Krushinskii-Molodkina rats with genetic audiogenic epilepsy have breed points in expression of HSP during thermal preconditioning. **COLCLUSIONS:** Comparative analysis of antiepileptic effects of exogenous Hsp70 injections and thermal preconditioning showed that intracerebroventricular microinjections of Hsp70 were more effective (especially for reducing the duration of clonic-tonic seizures and the severity of epileptic seizures) in comparison with thermal preconditioning. The study was supported by RFRF.

EFFECT OF HEAT SHOCK PROTEIN 70 KDA ON THERMOREGULATORY CHARACTERISTICS DURING THE INTOXICATIONAL STRESS IN RATS AND PIGEONS. KV Lapshina, IV Ekimova.

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INTRODUCTION: The development of endotoxaemia and sepsis in warm-blooded animals is accompanied by complex changes in thermoregulatory, immune, nervous, endocrine systems etc [Gurin, 1993; Bruemmer-Smith et al 2001]. This pathological state is one of the main causes of death (36-46%) in the intensive care units. Thus, one of the most important problems in the modern biology and medicine is the search of the endotoxin antagonists. Heat shock proteins 70 kDa (Hsp70) may be very perspective in this respect. It was revealed that thermal preconditioning stimulates the synthesis of Hsp70 and may protect cells against the cytotoxic proinflammatory factors such as TNF- α и IL-1- β [Jaattela, Wissing, 1993; Muller et al 1993]. In vitro studies showed that thermal preconditioning attenuates the synthesis of the proinflammatory cytokines and declines mortality rates in rats, which were injected with a fatal dose of bacterial endotoxin lipopolysaccharide (LPS) [Hotchkiss et al, 1993; Paidas et al 2002]. Inasmuch as one of the main features of endotoxaemia is a febrile reaction, the goal of our study is to investigate the influence of exogenous Hsp70 on thermoregulatory characteristics during the intoxicational stress. **METHODS:** Experiments were carried out in freely moving male Wistar rats and pigeons (*Columba livia*) of both sexes. All animals were adapted to the temperature-controlled experimental chamber, where the temperature was maintained at $25 \pm 1^\circ\text{C}$ and light-darkness period 12:12 was in effect. Food and water were given ad libitum. The toxic stress was evoked by the intravenous LPS injection (*Escherichia Coli* 0111:B4 (Sigma); 100 mkg/kg). Exogenous Hsp70 was obtained and purified from contamination at the Institute of Cytology RAS. Hsp70 was injected intravenously 15 min before LPS (75 mkg/kg). In the control, saline in the same volume as the Hsp70 was injected. Thermoregulatory characteristics (brain temperature, tail temperature (rats) and temperature of unfledged part of the leg (pigeon), contractile muscular activity, heart rate) were registered by the computer system SASR (USA). **RESULTS AND DISCUSSION:** LPS injection evoked the fever in rats and pigeons. It was characterized by an increase in the brain temperature, contractile muscular activity and heart rates. Also biphasic vasomotor reaction was observed. At the beginning there was vasoconstriction and later it was replaced by the vasodilatation. The fever in pigeons in comparison with the rats had more prolonged latent period of the rise of brain temperature. The intravenous injection of Hsp70 induced only a decrease in heart rates during the non-active phase in pigeons. We did not find any difference from the baseline in all the rest parameters. Hsp70 injection 15 min before the intoxicational stress prevented the rise of the brain temperature, but vasoconstriction was remained. The combined effect of Hsp70 and LPS resulted in a decrease in contractile muscular activity and heart rates below the baseline in pigeons. In contrast to pigeons, rats revealed Hsp70-induced attenuation of fever, but vasomotor reactions did not differ from the baseline. Our experiments showed that Hsp70 can attenuate the fever. The mechanisms of this effect remain unknown. It was suggested that protective effects of Hsp70 are due to its ability to modulate the immune responses. An increase in Hsp70 concentration due to thermal preconditioning suppressed the synthesis of key mediators of fever, such as IL-1 β and TNF- α [Ding et al 2001]. It is likely that the attenuation of febrile reaction in our investigation could be the result of the capability of Hsp70 to suppress the proinflammatory signal. Furthermore, other studies demonstrated that extracellular Hsp70 could stimulate the innate immunity. It caused the NO production by

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macrophages and facilitated the recovery after the subsequent LPS challenge [Campisi et al 2003]. Finally, several investigators reported the LPS-binding property of Hsp70 [Gao, Tsan, 2003; Kustanova et al 2006]. As there is evidence that Hsp60 has specific LPS-binding site [Habich et al 2005], Hsp70 may have the similar site as well. Thus, the suppression of febrile response could be a result from LPS-binding properties of Hsp70. **CONCLUSIONS:** Our data suggest that Hsp70 can have protective effect against the intoxicational stress and probably can be used as a component of the complex therapy of sepsis. This study was supported by St. Petersburg Scientific Centre of RAS.

Symposium 2. Clinical Psychiatry and Psychology – I. Chairs: M Issidorides, IP Lapin, AV Kalueff

- AN ASSOCIATION ANALYSIS OF SOME CANDIDATE GENES OF SEROTONERGIC BRAIN SYSTEM IN MAJOR DEPRESSIVE DISORDER. TG Noskova, DA Gaysina, AR Asadullin, EK Khusnutdinova. Institute of Biochemistry and Genetics, Bashkir State Medical University, Ufa, Russia
- ASSOCIATION BETWEEN THE C939T POLYMORPHISM OF THE DOPAMINE RECEPTOR D2 GENE AND SCHIZOPHRENIA IN RUSSIAN POPULATION. MV Monakhov, VE Golimbet, KV Chubabria, VL Karpov. Engelhardt Institute of Molecular Biology RAS, Mental Health Research Center RAMS, Moscow, Russia
- INTELLIGENCE STRUCTURE DURING ADAPTATION TO INFORMATION STRESS IN UNIVERSITY STUDENTS. NA Kulakova, OM Razumnikova. Novosibirsk State Technical University, Novosibirsk, Russia
- DEMONSTRATION OF THE FORMATION OF LEWY BODIES FROM DISRUPTED NEUROTRANSMITTER- STORAGE ORGANELLES IN PARKINSONISM. M Chrysanthou-Piterou, P Spiliopoulos, I. Kloukina, MR Issidorides. Dept. of Psychiatry, University of Athens, Medical School, Eginition Hospital, Neurobiology Research Institute, Theodor Theohari Cozzika Foundation, Athens, Greece

AN ASSOCIATION ANALYSIS OF SOME CANDIDATE GENES OF SEROTONERGIC BRAIN SYSTEM IN MAJOR DEPRESSIVE DISORDER. TG Noskova, DA Gaysina, AR Asadullin, EK Khusnutdinova. Institute of Biochemistry and Genetics, Department of Psychiatry, Bashkir State Medical University, Ufa, Russia

INTRODUCTION: Major depressive disorder (MDD) is a serious disorder with increased mortality, particularly due to a high suicide rate (15%). MDD is the leading cause of worldwide disability among individuals between 15 and 44 years old. The World Health Organization estimated that MDD will take the second place among the leading causes of mortality worldwide by 2020. Depression is a heterogeneous disorder of thinking which appears as a result of multiple interactions between genes themselves and environment. Heritability based on twin studies is 40% to 50%. Abnormalities in functioning of the serotonergic brain system such as low level of serotonin are believed to be involved in the pathogenesis of depressive illness. The aim of our study was to test a contribution of 5 polymorphisms of some candidate genes of serotonergic brain system in major depressive disorder, namely – Stin2VNTR and 5-HTTLPR in the serotonin transporter (SLC6A4), A1438G in the serotonin 2A receptor (HTR2A) (Msp1 - RFLP), G861C in the serotonin 1B receptor (HTR1B) (HincII – RFLP) and A6526G in the tryptophan hydroxylase 1 (TPH1) (BstMB I - RELP) genes. **MATERIALS AND METHODS:** 108 individuals (age range 19–72 years) with MDD (they were diagnosed according to DSM-IV diagnostic criteria) and 244 healthy controls (age range 19–72 years) who are volunteers from the Republic Bashkortostan (Russia) were included in the study. In our investigation we used the following methods: 1) extraction of genomic DNA from whole blood according standard procedures; 2) polymerase chain reaction (PCR) for genotyping all genes; 3) gel electrophoresis of PCR products; 4) digestion of PCR products with specific restriction enzymes (only for RFLP). Each group was tested for conformity to Hardy-Weinberg equilibrium. The distribution of genotype and allele frequencies of the polymorphisms of group of MDD patients was compared with that of control group by using a chi-square test. $P < .05$ was considered statistically significant. We also calculated odds ratios (ORs) for MDD. **RESULTS AND DISCUSSION:** We found significant differences in Stin2VNTR genotype frequencies ($\chi^2=7.42$, $P=.01$) between patients and controls. An increase of the Stin2*10/*12 genotype ($\chi^2=14.47$, $P=.001$, $OR=2.65$) frequency and decrease of the Stin2*10/*10 genotype ($\chi^2=5.69$, $P=.02$, $OR=.34$) frequency were registered in the depressive group compared to those in

the control group. No significant differences in the 5-HTTLPR genotype or allele frequencies distribution were found between MDD patients and control groups. There were observed significant differences in SLC6A4 genotype frequencies ($\chi^2=7.42$, $P=.01$) between patients and controls. HTR2A*G/*G genotype ($\chi^2=6.52$, $P=.01$, $OR=1.88$) and HTR2A*G allele ($\chi^2=5.82$, $P=.02$, $OR=1.55$) are associated with an increased risk of MDD. There were no statistical differences registered between MDD patients and healthy controls in the genotypic and allelic distribution of the HTR1B and TPH1 polymorphism investigated. **CONCLUSIONS:** Our study suggests that the Stin2*10/*12 genotype ($OR=2.1$, $95\% CI=1.1-3.98$) may be involved in development of major depressive disorder among Russian population. Also the results are consistent with an association between the HTR2A*G/*G genotype ($\chi^2=6.52$, $P=.01$, $OR=1.88$) and *G allele ($\chi^2=5.82$, $P=.02$, $OR=1.55$) and cases of MDD. We conclude that the 5-HTTLPR polymorphism of the SLC6A4 gene, the polymorphisms of the HTR1B and TPH1 genes are unlikely to have a major role in the pathogenesis of MDD. But due to the limitations of our samples and the fact that we had no statistical significance of some genes, further research of these genes on case-control phenotypic groups is of high importance. The research was supported by the Russian Humanitarian Research Fund (grant 06-06-00163a).

ASSOCIATION BETWEEN THE C939T POLYMORPHISM OF THE DOPAMINE RECEPTOR D2 GENE AND SCHIZOPHRENIA IN RUSSIAN POPULATION. MV Monakhov, VE Golimbet, KV Chubabria, VL Karpov. Engelhardt Institute of Molecular Biology RAS, Mental Health Research Center RAMS, Moscow, Russia

INTRODUCTION: Schizophrenia is a common mental disorder with lifetime prevalence of approximately .5-1%. Despite of intensive genetic and biochemical studies, the molecular mechanisms of disease remain elusive. Linkage studies and physiological evidence suggest a number of candidate genes for schizophrenia susceptibility locus, including DRD2, COMT, NRG1, DTNBP1, DISC1 and others. However, the mode of inheritance is thought to be complex with many loci involved. We examined the allele/genotype frequencies of the DRD2 C939T (rs6275) single nucleotide polymorphism (SNP) in samples from Russian population. **METHODS:** 323 schizophrenic patients (288 men and 41 women; mean age 40.7, standard deviation (SD) 13.1) and 350 healthy controls (223 men and 128 women; mean age 33.1, SD 13.7) were recruited in Mental Health Research Center of RAMS (Moscow) and Clinical Psychiatric Hospital (Kirov). Mean age at disease onset was 24.7 (8.1) years. A diagnosis of schizophrenia was made according to ICD-10 criteria. DNA was isolated from venous blood, and genotyping was carried out using RT-PCR with TaqMan assay. **RESULTS AND DISCUSSION:** We have genotyped the DRD2 C939T SNP in samples of schizophrenic patients and healthy controls. Genotype and allele frequencies in both samples were in Hardy-Weinberg equilibrium. Frequencies of the CC genotype ($\chi^2=3.87$; $P=.0493$; $OR=1.36$, $95\% CI=1-1.84$) and alleles ($\chi^2=3.88$; $P=.0489$; $OR=1.26$, $95\% CI=1-1.58$) significantly differ between case and control samples. DRD2 C939T (rs6275) is a synonymous SNP, and its impact in aetiology of schizophrenia is presumably due to altering mRNA stability, or linkage with unknown functional polymorphisms. **CONCLUSIONS:** We have found an association between DRD2 C939T gene variants and schizophrenia in the sample from Russian population.

INTELLIGENCE STRUCTURE DURING ADAPTATION TO INFORMATION STRESS IN UNIVERSITY STUDENTS. NA Kulakova, OM Razumnikova. Novosibirsk State Technical University, Novosibirsk, Russia

INTRODUCTION: Research of human intelligence has progressed at different levels of analysis including neurobiology, behavior, and health [Gray, Thompson, 2004; Grigorenko, Sternberg, 2001; Haier et al 2004]. Higher intelligence appears to buffer people against various forms of mental and psychosomatic diseases perhaps because they can better compensate for cognitive difficulties. Education-related stress in first-year students has been associated with modification of the psychosocial environment and new volume information acquisition. At this time special hierarchical structure of intelligence, including analytical, practical, emotional, and creative aspects of intelligence may be at a premium to prevented informational stress-induced health degeneration. Neurobiological base of the association between an intelligence and adaptation is the interactions of cortical-subcortical regions and plasticity of brain structure in response to training that related to emotional states and cognitive abilities [Davidson, 1993; Razoumnikova, 2003; Svyatogor et al 2005]. Another important psychosocial factor that may underpin the stress experience and behavioral disorders concerns the system of dominant life goals [e.g. Piko, Keresztes, 2006]. Although this association

might not hold under all circumstances, it has proven to be fairly consistent in educational activities. Thus, the general strategy for the study was to assess the relationships between student's structures of intelligence, profile of dominant life goals and self-reported adaptive functioning in terms of adaptive physical health and stress items. **METHODS:** The sample included 278 university students from technical and humanitarian departments. Adaptive functioning was estimated during a period of first half-year education by self-report measures and external rating of progress in studies for each person. A physical-health-status score was calculated on the basis of participants' answers to questions about their subjective perception of well-being and stressful incidents. Anxiety and frustration were assessed using the Eyzenk's Mental States Test. The Amthauer's analytical and Gilford-Sullivan's social intelligence scores were measured by traditional tests adapted in Russia. To measure the components of emotional and creative intelligence we used, respectively, the IPIP items and original method based upon standardized creativity tests [Mednick, 1962; Torrance, 1984; Razumnikova, 2002]. The measure of practical intelligence was designed as self-report instrument, assessing practical skills of students in the social domain and knowledge acquisition. The modified version of Schwartz's test [Schwartz, 1990] was used to determine the profile of human values. The t-test, cluster and factor analysis were used to analyze the data. **RESULTS AND DISCUSSION:** Factor analysis of different intellectual abilities revealed two principal components. The first factor (I) combined analytical, practical, and social intelligence. The second (II) was presented by emotional intelligence (IQe) and the ratings in first half-year negatively correlated with IQe scores. We used self-reported IQe scoring that presented mostly a feeling and exhibition of emotions. Thus, emotional reactivity has dominant influence on progress in studies during initial stage of education. The higher rating group of students had lower stress score ($p=.01$) and self-reported training difficulties ($p=.0007$) but higher analytical intelligence (IQa) than did those lower in rating. Although the working hours according to a curriculum were similar for students from technical and humanitarian departments, the formers estimated their training difficulties greater than the latter (correspondingly, 2.47 and 1.84, $p=.00008$). This index together with stress score was increased in a group of newly arrived vs. native persons, who tended to be more subjective healthy and scoring higher for IQa. Anxiety and frustration scores did not differenced between examined groups. Complex cluster and factor analysis of all IQ testing data and the human values yielded four principal components. The three varimax-rotated principal components can be labeled IQa, IQe, and creative (IQcr) abilities, respectively I,II,III factors. The practical intelligence (IQpr) had loadings both in the factor II and IV. The letter was formed by some items of structure of human values, in particular by 'sense of life', 'pleasure', and 'choice of personal goals'. At the same time, IQa had significant positive correlations with IQcr, IQpr, and social intelligence scores, but negative correlation with IQe. So, IQa is the integral unit of IQ structure related the adaptation to informational stress. This fact indicates primary importance of analytical thinking in hierarchical structure of mental abilities in university students. In general, it is consistent with positive relationship between both IQa, and IQpr and adaptive functioning [Jensen, 1998; Sternberg et al 2000; Grigorenko, Sternberg, 2001]. The related sets of IQ components were differenced in the students from technical and humanitarian departments. Specifically, technical students were characterized by high profile of IQcr in the factor structure, but humanitarian students – IQpr. So, these results show that different aspects of intelligence can be used to predict a quality of adaptation to the stressful environment. The association of intelligence components and successful adaptation could be explained by efficiency of biological determined central nervous system. **CONCLUSIONS:** It is shown that the measures of relationships between analytical, emotional, creative, and emotional components of intelligence are distinctive and useful in understanding abilities to protect the adverse effects of informational stress. The risk of poor progress in the first examinations is raised in the higher scoring emotional intelligence group of university students. This study was supported by the Russian Humanities Research Fund (05-06-06179a).

DEMONSTRATION OF THE FORMATION OF LEWY BODIES FROM DISRUPTED NEUROTRANSMITTER- STORAGE ORGANELLES IN PARKINSONISM. M Chrysanthou-Piterou, P Spiliopoulos, I. Kloukina, MR Issidorides. Dept. of Psychiatry, University of Athens, Medical School, Eginition Hospital, Neurobiology Research Institute, Theodor Theohari Cozzika Foundation, Athens, Greece

Our histochemical and ultrastructural studies, have identified, in all human catecholamine neurons of controls, abundant and large, spherical inclusions - termed protein bodies (pb) - which contain neurotransmitter-synthesizing enzymes (for review, Issidorides et al 2004) and are, evidently, an evolutionary species-specific adaptation of monoamine-storing organelles in man. In Parkinsonism,

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Lewy bodies (LB) share a similar distribution in the aminergic systems of the brain, as that of pb, and, also, display common macromolecular components, among others sphingomyelin, arginine-rich proteins, and glutathione-S- transferase (Issidorides et al 1991). The question, thus, arises to what extent LB originate from altered protein bodies. Since LB, as a rule, immunostain for α -synuclein and ubiquitin (UBQ) (Trojanowski and Lee, 1998; Gai et al 2000) we applied polyclonal antibodies against these two proteins, in order to study their possible presence in pb. We also applied the Mallory's trichrome conformation stain, which, in previous studies, had shown that the pb in Parkinsonism gradually aggregate, coalesce and give rise to elongated structures, which eventually develop into LB (Issidorides et al 1991). We used paraffin sections of formalin fixed, postmortem substantia nigra (SN) from 20 Parkinsonian patients and 10 control subjects. With the application of UBQ antibody no immunoreactivity (UBQ-IR) was evident into control tissues. In contrast, in Parkinsonian tissue, UBQ-IR localized not only in spherical, mature LB, but, also, in irregular compact formations, as well as in linear formations, surrounding irregular "clear areas" in the cytoplasm, probably, enclosing disrupted, coalesced or aggregated pb. The presence of the stress protein UBQ in these specific patterns, could be interpreted as the induced response for the removal of damaged, misfolded, oxidized proteins (Ciechanover et al 1984), which are presumably derived from the proteins of the disrupted pb. Although α -synuclein antibody, similarly, did not bind to pb of control tissue, in Parkinsonian tissue it localized in the LB, as well as in the irregular "clear areas" which lie inside the ubiquitin "enclosures", thus confirming the presence of disrupted, coalesced and aggregated pb in these areas. Histochemically, the acidic stain aniline blue, one of the three conformational stains of the Mallory's trichrome procedure, qualifies as a common denominator - marker at all of the above stages of pb transformation, as it binds to the pb through all stages. The link of the coexistence of α -synuclein with ubiquitin in the same areas of the Parkinsonian neurons, is the disrupted pb, i.e. the disrupted neurotransmitter storage bodies. We conclude that in Parkinsonian's SN, altered, modified pb components are segregated in LB. This lack of storage sites leads to "defective sequestration of dopamine into vesicles, leading to the generation of reactive oxygen species in the cytoplasm, is a key event in the demise of dopaminergic neurons in Parkinson's disease, and might represent a common pathway that underlies both genetic and sporadic forms of the disorder" (Lotharius and Brundin, 2002).

Symposium 3. Clinical Psychiatry and Psychology – II. Chairs: IV Ekimova, AV Kalueff

- ANOMALIES OF AUDITORY ODDBALL N100 AND P300 AS THE MARKERS CLOSELY RELATED TO THE PATHOGENESIS OF SCHIZOPHRENIA. I Lebedeva, V Kaleda, A Barkhatova, M Streltsova. National Mental Health Research Center, Moscow, Russia
- INVOLUNTARY SELF-REGULATION BASED ON EEG-ACOUSTIC BIOFEEDBACK FOR CORRECTION OF BEHAVIOR AND IMPAIRMENTS ATTENTION FUNCTION OF CHILDREN WITH ADHS. VN Trushina, KV Konstantinov, VM Klimenko. Institute for Experimental Medicine RAMS, St. Petersburg, Russia
- MICROELEMENTOSIS OF SCHOOL CHILDREN CAUSED BY CHRONICAL INFLUENCE OF CHEMICAL FACTORS OF ENVIRONMENT AND THEIR INFLUENCE ON PSYCHOSOMATIC HEALTH AND BEHAVIOR. LI Gubareva, GV Ermolenko, SP Popova, VV Potapenko. Department of Psychophysiology, State University, Stavropol, Russia
- CONTROL OF THE ROSTRAL ANTERIOR CINGULATE OVER ACTIVITY IN THE AMYGDALA: A NEUROBIOLOGICAL MODEL OF PANIC DISORDER TESTED BY LONGITUDINAL FMRI. N Chechko, M Czisch, A Erhardt, D Hohn, R Wehrle, PG Samann. Max Planck Institute of Psychiatry, Munich, Germany
- NEW PSYCHOTECHNIQUE FOR CORRECTING PERSONALITY, FEAR AND ANXIETY DISORDERS, AND DEVIATIONS. SR Sokolovsky, Department of Practical Psychology, Pyatigorsk Linguistic State University, Pyatigorsk, Russia

ANOMALIES OF AUDITORY ODDBALL N100 AND P300 AS THE MARKERS CLOSELY RELATED TO THE PATHOGENESIS OF SCHIZOPHRENIA. I Lebedeva, V Kaleda, A Barkhatova, M Streltsova. National Mental Health Research Center, Moscow, Russia

INTRODUCTION: The anomalies of event-related potentials waves in auditory oddball paradigm are the most robust finding in neurophysiology of schizophrenia. However the most pronounced attention was paid to reduction and prolongation of the so-called late cognitive waves (particularly P300). At the

same time, the characteristics of the other components were studied insufficiently in respect to different stages of the disease development. The aims of the present study were to determine the whole profile of neurophysiological anomalies of the auditory event-related potentials as the possible markers of liability to schizophrenia, the magnitude of anomalies during the first episode of the disease and in the clinically stabilized patients with schizophrenia who were ill for more than 5 years. **METHODS:** The sample comprised 44 patients with endogenous psychosis during the first episode (who were later diagnosed as patients with schizophrenia), 50 clinically stabilized patients with schizophrenia with illness duration more than 5 years. Also, examination was done in 40 unaffected parents of patients with schizophrenia (from 22 families with so-called sporadic cases and from 22 families where the other spouse was either diagnosed with mental disease or have a first degree relative with schizophrenia). The control group comprised 70 subjects. All subjects gave the written consent for examination. The study was approved by the ethical committee of NMHC. Auditory ERPs were recorded with on the Brain Atlas mapping system (Bio-logic, USA). The standard auditory oddball paradigm was used (tones, 60 dB, 80% non-targets (1000 Hz) and 20% targets (2000 Hz)). Total number of targets comprised 30, the tones were presented with interstimuli interval 1.5 s (with 20% variation). The subjects were informed that they had to react to the higher pitched ones by pressing button by thumb of the dominant hand (the correctness of the responses was controlled). EEG was sampled with 60 ms pre-stimulus baseline and 512 ms of epoch analysis. An automatic artifact rejection system excluded the EEG fragments exceeding 100 mV. EEG was recorded on Era-14-21 (Italy) in 16 leads with referent separate ipsilateral earlobe electrodes (10-20 system). Electrode impedance was below 10 kΩ . Electrical activity was amplified and filtering with bandpass of .3-35 Hz. The analysis of the ERP data was done by one of investigators (Dr. Lebedeva) who was blind to familial characteristics. The peak amplitudes and peak latencies of N100 and P200 to non-target stimuli, N100, N200, P300 to target stimuli were determined in F3, F4, T3, C3, CZ, C4, T4, P3, PZ, P4 leads. The intergroup comparison was done in the sex and age matched groups. **RESULTS AND DISCUSSION:** The family studies showed that only reduction of non-target N100 and target P300 were found in the unaffected parents of patients with schizophrenia-possible carrier of pathological genes. In the first episode patients, the most pronounced findings comprised the reduction of non-target and target N100s, prolongation of N200, prolongation and reduction of P300. In the sample of patients with illness duration more than 5 years, the anomalies comprised all ERP components, including non-target and target N100 reduction, P200 reduction, target N100, N200, P300 prolongation, P300 reduction. The findings suggest that non-target N100 and target P300 reduction can be found prior to the disease. It is in line with the interpretation of P300 as the component associated with cognitive processes of selective attention. Non-target N100 reduction here can be considered as an index of vigilance level or functional or/and morphological ability of the corresponding neural substrate to process highly repeated stimuli. The data in the first-episode patients stress the more marked involvement of the processes connected with the target information processing. **CONCLUSIONS:** The data emphasize the role of that auditory non-target N100 and target P300 reduction as the possible markers of genetic liability to schizophrenia and stress the deterioration of auditory information processing along with schizophrenia progress.

INVOLUNTARY SELF-REGULATION BASED ON EEG-ACOUSTIC BIOFEEDBACK FOR CORRECTION OF BEHAVIOR AND IMPAIRMENTS ATTENTION FUNCTION OF CHILDREN WITH ADHS. VN Trushina, KV Konstantinov, VM Klimenko. Institute for Experimental Medicine RAMS, St. Petersburg, Russia

INTRODUCTION: Attention Deficit with Hyperactivity Syndrome (ADHS) of children is actual medico-social problem now, because of its spread in population (5-10%). ADHS can be diagnosed (male 4 time frequenter female) in early childhood, than it progress during school study and 30-70% of patients save it in adult. The syndrome points to risk factor of addictive and deviant behaviors development in adolescent. The methods of adoptive self-regulation based on functional feedback correction of bioelectrical activity of the brain have become popular in recent years. The strategy of involuntary self-regulation of EEG parameters, directed on integrative restoration of functional condition, realized in method of EEG-acoustic correction. The correction is achieving by procedures of patients hearing the acoustic image of their own EEGs. The acoustic image was created by computer transformation of the current EEG recording and was presented to the patient in the real-time mode. This method of EEG transformation saves all proportions of principal parameters of EEG (amplitudes, frequencies and phases in whole physiological range of signal) as well as integrality of EEG spatial-temporal structure in the acoustic signal. The purpose of this study was efficiency evaluation of

adoptive involuntary self-regulation of functional brain condition under EEG-acoustic biofeedback for rehabilitation of children with ADHS. **METHODS:** The sample comprised 23 children (18 male and 5 female) aged 10.5 ± 1.5 years. All patients were right-handed, without chronic diseases and did not receiving any pharmacotherapy. All patients had attention deficit hyperactivity disorder and behavioral disorders. The diagnosis was based on the results of neurological, psychological, and psychiatric examinations. In the work were registered dynamics of clinical symptoms number according to 3 symptoms complexes: inattention (6 symptoms), impulsivity (4 symptoms), hyperactivity (4 symptoms) before and after treatment. To evaluate level of attention we have registered spend time and errors number in proof correction test before and after treatment. Healthy children of control group aged 9-11 years have performed test for 12-15 min and number of errors was in range of 10-16. The treatment consisted of 10--12 sessions of adaptive self-regulation with a duration of 8 - 12 min each in the beginning and 15 – 20 min to the end of course. **RESULTS AND DISCUSSION:** At the very beginning of bioacoustic treatment the number of clinical symptoms was maximal. All patients have showed decrease of the indicators after course of bioacoustic procedures: inattention from $5.52 \pm .51$ to $2.61 \pm .71$ ($p < .01$), impulsivity from $3.39 \pm .90$ to $1.30 \pm .32$ ($p < .01$) and hyperactivity from $3.65 \pm .43$ ($p < .01$). Testing of attention function revealed that before treatment 7 patients have spend 27-32 min for proof-sheet test and have perpetrated 18-25 errors, 9 patients have spend time for test less 20 min, but have perpetrated 28-32 errors and 5 of children have made not more 30% of whole test. After the treatment 17 patients of 23 have spend same time and made errors number as children of control group, 4 patents have spend the same time, but errors number was enhanced and only 2 of them have exceed the data of control group. In the course of EEG-BAC procedures, the cerebral bioelectrical activity was reorganized, which was mainly expressed in a decreased proportion of slow-wave components of the EEG and a decreased interhemispheric asymmetry. The proportion of the alpha rhythm tended to increase (the average increase was from 43.3 ± 11.1 to $53.4 \pm 14.2\%$). Regarding the theta band, the proportion of oscillations decreased from 30.2 ± 5.3 to $24.8 \pm 5.1\%$ ($p < .05$). The interhemispheric asymmetry of the cerebral bioelectrical activity evaluated by the difference between the right- and left-hemispheric EEG periodograms was decreased from $.197 \pm .052$ to $.138 \pm .041$. **CONCLUSIONS:** Our data suggest high effectiveness of involuntary self-regulation under EEG-acoustic biofeedback for treatment of children with attention deficit and feebleness of will. The use of involuntary bioacoustic correction leads to reorganization of EEG structure, decrease of clinical symptoms of inattention, impulsivity and hyperactivity number as well as to improving of attention function of children with ADHS. Decreased hemispheric asymmetry and normalization of EEG rhythmic structure were revealed after treatment.

MICROELEMENTOSIS OF SCHOOL CHILDREN CAUSED BY CHRONICAL INFLUENCE OF CHEMICAL FACTORS OF ENVIRONMENT AND THEIR INFLUENCE ON PSYCHOSOMATIC HEALTH AND BEHAVIOR. LI Gubareva, GV Ermolenko, SP Popova, VV Potapenko. Department of Psychophysiology, State University, Stavropol, Russia

Chemical homeostasis is the necessary component of psychosomatic health preservation and of adequate behavior but the surplus or insufficient level of microelements content in organism may be the index of the health state and characteristic of ecological trouble of the surrounding (Chesnokova 2004), of chronic anthropogene stress. The group of investigators carried out all round study of 143 teenagers of 12-13 years old, living in the industrial zone (concentration of harmful chemical substances such us – nitric oxide (IV), cadmium lead, xylo, fenol, formaldehyde – 3-8 times exceeded limit of concentration (LC)) and 141 children living in Stavropol in ecologically favourable region (concentration of harmful chemical substances didn't exceed LC). The content of Pb, Cd, Zn, Fe and Cu in derivatives of epidermis (hair, nails) was determined by atom-absorption spectrophotometer Perkin-Elmer 2280 (USA). The investigators judged the state of cardiac-vascular system by indexes of variational pulsometry, hypothalamo-hypophyseal-adrenocortical – by level of peripheral adaptive hormone – cortisol, hypothalamo-hypophyseal-gonadal - by level of sexual steroids - testosterone, estradiol, which were determined by immune-ferment method, about the state of nervous system – by indexes of chronoreflexmeter. The estimation of psychoemotional status was conducted by experimental – psychological methods – the method of determination of neurotic and psychopathological state (Bazhin et al 1976), by the test "Scale of anxiety" (Rogov 1995). Besides the level of school motivation was determined. With the help of individual-typological questionnaire were studied individual-typological properties of a person; with the help of the method of determination the communicative and organization inclinations (COI - 2) were determined communicative and organization inclinations of teenagers' personality. The results were processed statistically. Chemical

pollution of surroundings leads to the balance breach of microelements in organism, which can be exposed by the concentration of metals in biosubstrats (hair and nails). Teenagers of 13, living under the conditions of chemical pollutions of the surroundings, have increase in the derivatives of epidermis of Pb and Cd concentration and decrease of content of Fe and Zn essential element. Hair is more informative biosubstrat in comparison with nails. Life of teenagers of 13 under conditions of chemical pollution of the surroundings, including Pb and Cd leads to the decrease functional resources of cardio-respirator system and the tension of the main mechanisms of regulation of heart rhythms and in the first place sympathetic section of vegetative nervous system. It is determined that teenagers living under conditions of chemical pollution of the surroundings, have higher functional activity of hypothalamo-hypophyseal-adrenocortical and hypothalamo-hypophyseal-gonadal systems. It can be determined by higher level of cortisol (C), testosterone (T), estradiol (E). The girls of test group have correlation of T/E higher than the girls of the group under control. Tension of functional activity of central links of vegetative nervous system, increase of C-level and breach of T/E correlation, which have teenagers living in chemically polluted regions, leads to the decrease of functional lability and breach of processes of internal inhibition in central nervous system, to decrease level of school motivation. Teenagers of 13, living under condition of chemical pollution of the surroundings in comparison with such teenagers, living in ecologically favourable regions, are characterized by changes of emotional state, i.e. by increase or decrease of level of school, selfestimating and interpersonal anxiety which are more expressed in the age group of teenagers; by increase of neurotic and psychopathological level by change of personal-typological features (decrease of indices according to the aggravation scale, increase of indices according spontaneous and aggressive scales). All these influence the formation and display of communicative and organizational features, leadership qualities and outcast and dictate the necessity of working out and using of adequate personality-oriented methods of correction. Correlation analysis showed that disbalance of microelements (Pb, Cd, Fe, Zn and Cu) is the reason of breaches of psychosomatic health, which exposed during out studies. Investigation is supported by Grant RHSF 06-06-18005e.

CONTROL OF THE ROSTRAL ANTERIOR CINGULATE OVER ACTIVITY IN THE AMYGDALA: A NEUROBIOLOGICAL MODEL OF PANIC DISORDER TESTED BY LONGITUDINAL FMRI. N Chechko, M Czisch, A Erhardt, D Hohn, R Wehrle, PG Samann. Max Planck Institute of Psychiatry, Munich, Nuclear Magnetic Resonance Research Group and Clinical Department of Psychiatry

INTRODUCTION: The anterior cingulate cortex (ACC) has been shown to be activated by the cognitive and emotional versions of the Stroop paradigm, supporting the hypothesis that it is recruited to allocate attentional resources and to be involved in response selection, and, also, when confronted with competing information-processing streams (Bush et al 1998, Whalen et al 1999). The amygdala, on the other hand, has been characterized as part of a conflict monitoring network at the junction of perception and stress response regulation (Gorman et al 2000). Close coupling of the ACC with amygdalar activity and neuroendocrine response renders the ACC an important mediating node in a network of stress response. Findings from healthy subjects show that the emotional conflict resolution paradigm as first presented by Etkin et al (2006) allows to dissociate the generation and monitoring phases of an emotional conflict from its resolution. In healthy subjects, successful emotional conflict resolution is paralleled by increased rostral anterior cingulate (rACC) activity, which reversely attenuates amygdalar response (Etkin et al 2006). Increased amygdalar and reduced rACC activities, mostly investigated separately, are features of a variety of stress-related disorders (posttraumatic stress disorder, anxiety and depression, panic disorder [PD]), suggesting that the rACC/amygdala interaction should be further explored for its potential to serve as a model of conflict resolution. We probe this general hypothesis by picking up the emotional conflict fMRI paradigm and applying it to two groups of patients with panic disorder. **STUDY DESIGN AND METHODS:** The first patient group comprises 15 persons with newly diagnosed PD who are exposed to the emotional conflict fMRI paradigm before treatment, during initiation with SSRI treatment and after symptom resolution to investigate the effect of medication on amygdalar and ACC activities and the connectivity between the two regions. The second group consists of 15 patients with PD under treatment who are partially or fully remitted. In parallel, 15 healthy volunteers are repeatedly scanned to monitor potential learning and habituation effects. Behaviorally, reaction times and error rates are obtained. Statistical parametric mapping on 1st and 2nd levels as well as dynamic causal modeling is performed to compare high versus low conflict resolution activation and rACC / amygdala connectivity. MR sequence, paradigm and statistical analysis: 1.5 Tesla clinical GE scanner; echoplanar imaging, 25 slices, thickness 3 mm, 1 mm gap. 152 face/word pairs with congruent (CON) or incongruent (INCON)

face/word combinations presented in 4 blocks of 38 pairs; within each block randomization for subject, emotional valence of face, word and order. Jittered stimulus interval of mean 4 s. TR of 2000 ms. Subjects were instructed to answer to the face expression (happy/anxious) with a response button. After motion, slice time correction, normalization and smoothing (FWHM 8 mm) a GLM was set with the following regressors: stimulus onset times of the four order types (CON-CON, INC-CON, CON-INC, INC-INC) convoluted with the canonical HR, error and post-error trials with HRF convolution, motion correction parameters and global intensity. First level T-contrast maps of INC-INC versus CON-INC comparison (ref. to as high > low conflict resolution) and the inverse contrast maps were taken to a second level random effect analysis and displayed at $p < .05$, hereby using a region-of-interest mask covering the prefrontal cortex. **HYPOTHESES:** (1) Patients with clinically symptomatic PD show a disturbance of conflict monitoring itself and a disturbance of the transition of conflict monitoring to conflict resolution. (2) In addition, the feedback control of rACC over amygdala may be disturbed. Furthermore, the degree of disturbances is related to clinical symptoms. (3) During therapy with SSRI, both types of disturbances [see (1) and (2)] are attenuated and may reach the level of healthy controls. (4). The prediction potential of the rACC / amygdala connectivity at the first follow-up scan for final treatment outcome is analyzed exploratively. **PRELIMINARY RESULTS AND CONCLUSIONS:** So far, 10 healthy subjects have been investigated. Preliminary results from the reaction time analysis confirm that emotional conflict resolution paradigm leads to robust behavioral effect, based on reaction time, in healthy subjects. All 10 healthy control subjects (2 males, 8 females; average age 24.9 years [SD 2.16 years]) show longer reaction times [RT] for incongruent image/word pairs ($p = .01$). Subjects demonstrate faster RT ($p = .009$, t-test) for high resolution (incongruent trials that follow incongruent ones) vs. low resolution trials (incongruent trials that follow congruent ones), suggesting the activation of an anticipatory mechanism by the preceding incongruent trial which aids conflict resolution in the current incongruent trial. fMRI analysis showed that increased activation of the rostral ACC and adjacent medial prefrontal cortex of BA 10 was seen for the high > low condition (1st cluster: peak voxel $p = .002$, cluster extent 235 voxels) in addition to a smaller more frontopolar cluster (304 voxels, peak voxel $p = .001$). The inverse contrast of low > high conflict resolution revealed bilateral prefrontal cortex activation locating to the right BA 46 and BA 47, left BA 47, bilateral BA 9 and left BA 10. In conclusion, the BOLD activation pattern and the behavioral effects of the high > low conflict and the inverse contrast were reproducible in a different sample and under different experimental conditions when compared with the results of Etkin et al (2006), confirming its potential usefulness for applications in clinical samples. Data from patients with panic disorder will be presented and discussed.

NEW PSYCHOTECHNIQUE FOR CORRECTING PERSONALITY, FEAR AND ANXIETY DISORDERS, AND DEVIATIONS (ACM). SR Sokolovsky. Department of Practical Psychology, Pyatigorsk Linguistic State University, Pyatigorsk, Russia

INTRODUCTION: Personality disorders and deviations, according to the reflection theory, are the most complicated combinations of conditioned and unconditioned reflexes. For instance, the personality aggressiveness includes both the inherent component, conditioned by the human metabolism peculiarities and biochemistry, and the acquired one as the means of affirmation his/her personality in a certain social environment. Psychologists and psychotherapists, engaged in the work with clients, try to break the psychology chain at the expense of forming new conditioned reflexes verbally during the individual sessions. With that, rational, emotional and training methods are used. A substantially weak link of the psychological influence is the attempt to generate new reflector forms of behavior on the basis of conditioned reflexes that are always weaker than the unconditioned ones. As the result of the psychologist's work, the newly formed conditioned reflexes of behavior may die away quickly without systematic support and, more often than not, become much weaker than the unconditioned one (the hormonal component). Just with that moments are connected the failures in psychological treatment of the patient when following the success there appears a return of bygone disorders. That is clearly represented in the works of Leo Tolstoy "Devil", F.M. Dostoevsky "Gambler", when, realizing and cursing their incorrect behavior, the 'heroes' magically repeat it again and again. Professionally speaking, the 'relapse' of disarrangement is bound with the insufficient motivation level, insufficient patient's knowledge about the disorders of his/her own psycho-emotional sphere, insufficient suppression of previous reflex bonds, low effectiveness of cognitive re-structurization and insufficient support for the new behavioral model. From the position of psychophysiology, a pathological behavior is obsessive-compulsive and is beyond the personality's control. It is very difficult to tear that exclusive circle, at times it is impossible, and the possible solution of the

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personality's "Karmic questions" looks for the solution in the investigations on the junction of physiology, clinical psychology and applied religious practices approved by thousand years of human history. Speaking of psychological influence in the cases of personality disorders and deviations, we apply new tools of interference together with the old ones and just that combination or the multimodality of methods brings to a more stable result. **METHODS:** We studied effectiveness of treatment of anxiety disorders in 43 people with different anxiety, depression and other behavior disorders by our method ACM (Applied Creative Meditation), 21 persons (experimental group) and Cognitive Behavior Therapy by EU protocol, 22 persons (control group). The choice of patients was carried out by a technique of random numbers in the general population of sick patients. Time and speed of approach remission consequence of treatment were estimated, also rates of approach remission. Depression was estimated on scale A. Beck-depression inventory, level of anxiety by Spielberger's scale, level of neurothismus - by Aizenk's scale. For Applied Creative Meditation simultaneously are used a multimodal combination of sensor deprivation, muscular, vascular, respiratory, nervous, mental emotional, spiritual relaxation. The postures correspond to the relaxation and meditation techniques. Some discomfort in the posture or position intensifies the outer deprivation. Mental movement - from the legs to the head. The psychologist works with the client according to the decimal scheme: P - identification of problems; A - analysis and priority of problems; U - scientifically grounded clinical - psychological understanding of the problems; I - correct intention influencing the motivation is being formed; S - clinically prognosticated correct speech; A - initiation of correct deeds; WL - formation and rehearsal of the new way of life. E - efforts are initiated by studying and identification of the pathology; T - turn of the mind is retained by the frequency 5-7 times a day); C - concentration is retained by frequency and self-monitoring, preventive discerning and cognitive restructuring. The psychologist give the patients: a) how the disorder proceeds; b) how it proceeds in general; c) the key cognitive-behavioral making up the remission; d) how the clinical-psychological remission should proceed in him/her personally; e) what is the connecting link between the ailment and remission. The effectiveness of re-structurization and following mastering the behavior is stimulated by joint, new models, use of unconditioned vegetal-tropical reflexes of carotid sinus, Göring-Breuer reflexes, Aschner, Valsalva, Magnus-Klein, reflexes controlled by hypoxia and other parasympathetic reflexes. The psychologist determines the bounds and eliminates excessive illusions, disbelief, rituals, malicious will, deceptions of senses, thirst for external, excessive materialism, arrogance, anxiety, and depression in understanding the veritable reality of the problem. The client is given a clinical perspective. Since inhalation activates the sympathetic nerve system, an implementation of negative modules is carried out during inhalation. Exhalation activates the vague parasympathetic reflexes and an implementation of positive modules is carried out during exhalation. More often it is necessary to work according to the method with exhalation. In the process of work one should count on egoism, as one of the deep biological senses. The patient's concentration on him/herself the best excludes subconscious and conscious resistance to the psychotherapist. On finishing the séances, the patient goes over to the program of self-help, freely regulating it depending on circumstances. Cognitive re-structurization used through primacy of feelings, re-realization, filtration and encouragement of emotions, change of interpersonally communication, creative regulated purposeful activity through the unconditioned vegetal-tropical reflexes, mantra and positively tinted meditation on oneself. **RESULTS AND DISCUSSION:** ACM without medical therapy after 8 month showed $50\% \pm 3$, 5% increase of effectiveness treatment of personality, anxiety, depression and fear disorders. The total estimation was spent on weight reduction, reduction of waist and normalization of standard analyses, better, than in the control group. Level of anxiety ACM-group after treatment was lower (by 23 ± 1 score), depression and neurothismus - 10 ± 2 and 12 ± 1 , accordingly. The difference in control and experimental groups answered criteria of reliability. The subjective level of satisfaction of treatment, and adherence to treatment in ACM group was considerably above. **CONCLUSIONS:** Psychological method ACM is effective in correction of anxiety, depression, fear, behavioral disorders.

Symposium 4. Experimental models of stress – II. Chairs: MI Aghajanov, TN Sollertinskaya, VM Klimenko

- SOCIAL HIERARCHY DYNAMICS AND STRESS-INDUCED ALTERATIONS IN COMMUNICATIVE BEHAVIOR IN RATS DEPENDS ON THEIR SPONTANEOUS

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LOCOMOTOR ACTIVITY. AA Polyakova, VI Liudyno, OE Zubareva. Institute For Experimental Medicine RAMS, St. Petersburg, Russia

- MODIFICATIONS OF BEHAVIOR IN THE MICE SELECTED FOR THE HIGH PREDISPOSITION TO CATALEPSY. DV Bazovkina, EM Kondaurova, AV Kulikov, NK Popova. Institute of Cytology and Genetics SBRAS, Novosibirsk, Russia
- VULNERABILITY TO CHRONIC DEPRESSION IN HETEROZYGOUS SEROTONIN TRANSPORTER KNOCKOUT MICE AS A MODEL RELEVANT TO HUMAN GENETIC POLYMORPHISMS. AV Kalueff, Center for Physiology and Biochemical Research, Moscow, Russia, Bethesda, MD, USA
- OVER-EXPRESSED HUMAN AMYLOID PRECURSOR PROTEIN INHIBITS M-CHOLINERGIC RECEPTOR BINDING IN SH-SY5Y CELLS. R Can-Jun, S Wang, GH Du, L Sun. Institute of Basic Medical Sciences, Institute of Materia Medica, Chinese Academy of Medical Sciences, Peking Union Medical College, Beijing, China
- DESINTEGRATION OF BRAIN REGULATORY MECHANISMS UNDER ACUTE HYPOXIA. SI Soroko, SS Bekshaev, VP Rozhkov. Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia

SOCIAL HIERARCHY DYNAMICS AND STRESS-INDUCED ALTERATIONS IN COMMUNICATIVE BEHAVIOR IN RATS DEPENDS ON THEIR SPONTANEOUS LOCOMOTOR ACTIVITY. AA Polyakova, VI Liudyno, OE Zubareva. Institute For Experimental Medicine RAMS, St. Petersburg, Russia

INTRODUCTION: Individual and typological characteristics play an essential role in resistance to negative environmental factors. In particular the stress-reactivity determines intensity, duration and consequences of stress-reaction, with other conditions being equal. The aim of this study was to investigate alterations of social behavior under conditions of acute physical or chronic social stresses in rats, which varied in spontaneous locomotor activity. The effect of the M35 – receptor antagonist of galanin (stress limiting peptide) on social behavior under stress conditions has been also investigated.

METHODS: The experiments were carried out in adult Wistar and Sprague-Dawley male rats. The rats were classified into three groups: high active (HA), moderate active (MD) and low active (LA), according to their locomotor activity in illuminated (500-Wt lamp) open field test. The locomotor activity was estimated by the number of lines crossed during 3 min. It was supposed that locomotor activity in highlighted open field was inversely proportional to stress-reactivity. Rats were exposed to chronic social stress (animal colony formation) (experiment 1) or acute physical stress (forced swimming) (experiment 2). The animal colony (experiment 1) was formed of three male rats (HA, MA and LA) and two females. Modified visible burrow system (Blanchard and Blanchard, 1991) was used to observe a dynamics of the rat colony formation and the development of social hierarchy among the male rats. Round-the-clock videomonitoring was performed to detect the male agonistic behavior during 7 days. A social position was evaluated by the victories/defeats ratio. Forced swimming (5 min) was used as a physical stress (experiment 2). Communicative and aggressive behavior was estimated in "intruder-resident" test (adult intruder) 1 day before the stress and in 1 hour after. Galanin receptor antagonist M35 was administered to HA and LA rats both intact and stressed. Statistical analysis has been made by Fisher test and ANOVA/MANOVA. **RESULTS AND**

DISCUSSION: Experiment 1. During the first 2 days of habitation LA rats were characterized by high level of aggression and high social status. As social hierarchy developed, since the third day of habitation, HA and MA rats demonstrated increasing of aggression. Thus, their social status elevated while the social status of LA rats decreased. Some differences have been revealed in the motivation of aggressive behavior: LA rats demonstrated higher level of aggression in fighting for water and fenced compartment; HA and MA rats revealed this behavior in competition for females. Experiment 2. The number of aggressive rats in LA group was higher than in HA group initially. However, the differences in aggressive behavior between HA and LA rats disappeared after swimming stress. The basal level of communication did not differ between HA and LA rats. Acute stress influenced the communicative behavior of HA- and LA-rats in different ways: the stress-induced reduction of communicative activity was observed in LA rats while in HA rats the communicative behavior increased as a result of stress. The difference in effects of galanin receptors antagonist on behavior of LA and HA animals was revealed. M35 elevated the aggressive behavior in intact HA rats but reduced it in stressed HA rats. The influence of M35 was not revealed in LA rats. Thus, the correlation between rat locomotor activity and stress-induced changes of communicative behavior has been found. Galanin receptor antagonist influenced differently the HA- and LA-rats under stress conditions.

MODIFICATIONS OF BEHAVIOR IN THE MICE SELECTED FOR THE HIGH PREDISPOSITION TO CATALEPSY. DV Bazovkina, EM Kondaurova, AV Kulikov, NK Popova. Institute of Cytology and Genetics SBRAS, Novosibirsk, Russia

INTRODUCTION: Catalepsy (freezing reaction, tonic immobility) is the state of pronounced motor inhibition, characterized by the failure to correct abnormal or awkward posture. The phenomenon represents passive defensive behavior and it is usually associated with fear and manifested as freezing in response to appearance of a predator or other threatening and stressful factors, as an alternative to flight. In human catalepsy is a syndrome of grave nervous or mental diseases. In laboratory mice, exaggerated freezing reaction is very rare phenomenon. Only the CBA inbred mouse strain show the genetically defined predisposition to catalepsy with incomplete penetrance (50%). The selection for catalepsy was begun from backcrosses (CBAX(CBAXAKR), received from the crossing between sensitive and resistant to catalepsy inbred strains (CBA and AKR, respectively). ASC mouse strain (Antidepressants Sensitive Cataleptics) is the result of this selective breeding, the percentage of cataleptics became 80% that is significant higher in comparison with the CBA mice (50%, $p < .001$). The main aim of the present investigation is to evaluate the association between freezing reaction and such kinds of behavior like aggressiveness, fear, anxiety and depressiveness. For that we have studied the effect of selection for high predisposition to catalepsy on these above-named kinds of behavior in intermale aggression test, acoustic startle reflex, light-dark, open field tests and forced swimming, tail suspension tests. **METHODS:** Adult mice males of CBA, AKR and ASC strains were used in the experiments. Open field, light-dark test, startle reflex, forced swimming test, tail suspension test and intermale aggression test are carried out according to commonly accepted protocols. Catalepsy is estimated by the time during which an animal maintained an immobile posture on parallel bars, with the forepaws at a 45° angle above the hind legs. **RESULTS AND DISCUSSION:** Selection for high predisposition to catalepsy does not affect mouse anxiety in the open field and light-dark tests. However, the ASC mice are characterized by decreased motor activity in the open-field test and increased immobility in the forced swim and tail suspension tests in comparison with the CBA and AKR mice, which is interpreted as the increase in "depressiveness." The results indicate that genetically determined catalepsy is related to depressive-like characteristics of defensive behavior. Moreover, it was found the positive association between high predisposition to catalepsy and startle reflex amplitude. So the ASC mice react more strongly to the unexpected sound stimulus than the parental strains. Besides, the cataleptic ASC strain is characterized by the significant decrease of aggressive behavior. The marked reduction in the percentage of aggressive animals in the mice selected for high predisposition to catalepsy is consistent with the notion that aggression and catalepsy represent two alternative kinds of behavior in intermale conflicts. The serotonin receptor 5-HT_{1A} seems to be the most probable molecular unit that assures the link between all these behavioral features. There are data on the involvement of 5-HT_{1A} receptors in different types of behavior including catalepsy, depression, startle reflex and aggressive behavior. Moreover, using QTL-analysis we have mapped the major gene of catalepsy on the distal part of mouse chromosome 13, near the gene encoding 5-HT_{1A} receptor. **CONCLUSIONS:** Selective breeding for high predisposition to catalepsy in mice led to increased startle reflex amplitude, reinforcement of the depressive-like features and decrease in the aggressiveness but does not affect anxiety. The demonstration of correlative features in the selected mice seems to be related to the alteration of serotonin 5-HT_{1A} receptor activity. This study was supported by Russian Foundation for Basic Research (grant №05-04-48124), Russian Research Program 'Integrative mechanisms of the regulation of function in the organism' (grants 5.2 and 427) and Russian Leading Scientific School (grant 1516.2004.4).

VULNERABILITY TO CHRONIC DEPRESSION IN HETEROZYGOUS SEROTONIN TRANSPORTER KNOCKOUT MICE AS A MODEL RELEVANT TO HUMAN GENETIC POLYMORPHISMS. AV Kalueff, Center for Physiology and Biochemical Research, Moscow, Russia, Bethesda, MD, USA

INTRODUCTION: Gene x Environment interactions are an important aspect of neuropsychiatric disorders (Caspi et al Science, 2003). Although serotonin and high-affinity serotonin transporter (SERT) have long been implicated in pathogenesis of depression, the role of SERT gene and its variants in depression remains unclear. Recent clinical studies have yielded conflicting results, with both negative and positive findings. While differences in objects and assessment methods may contribute to some of these discrepancies, human psychiatric genetics data may also be also

confounded by socio-psychological factors unrelated to depression (Kalueff et al 2007; Kaufman et al 2007; Biol Psych). Collectively, this emphasizes the importance of further biological research in this field, including experimental (animal) behavioral models of stress. Gene-targeted mice may provide further important insights, helping elucidate the link between SERT genetic polymorphisms and depression. Although SERT knockout (-/-) mice are a useful tool to assess the role of SERT in brain disorders, abolished SERT functions are very rare in human populations. In contrast, reduced SERT function due to genetic polymorphisms is common in human populations, suggesting that heterozygous (+/-) SERT mutant mice, relevant to human s/s and s/l genotypes (Kalueff et al TIPS, 2007), may enable a better focus on the role of SERT in pathogenesis of depression. **METHODS:** In the present study, we wanted to replicate Caspi et al human 2003 study in mice, examining whether SERT+/- mice have altered vulnerability to depression, induced by repeated psychological stress, such as 2-week experience of daily rat exposures. Overall, SERT+/+ and +/- mice of both sexes display similar baseline levels of anxiety and depression-like behaviors. In contrast, 2-week chronic stress evoked pronounced depression-like state in both male groups, whereas SERT+/- female mice were more reactive than SERT+/+ female mice. **RESULTS:** In general, our results corroborate clinical studies showing unaltered depression scores in "unstressed" carriers of s and l SERT alleles, and are also consistent with many reports showing interactions between human SERT polymorphisms and life stressors in female (but not male) carriers of s allele. **CONCLUSIONS:** Our data support the role of SERT in pathogenesis of female depression, and emphasize the importance of sex x gene x environment interactions in affective disorders. These data are also clinically relevant, as they specifically target female subjects (known for their higher vulnerability to stress-precipitated neuropsychiatric mood disorders). Finally, our study may have key practical implications, supporting the idea that sexes should be compared (rather than combined, as done in many previously published studies) in order to obtain more valid and reliable data on the role of SERT genetic variants in depression and other brain disorders.

OVER-EXPRESSED HUMAN AMYLOID PRECURSOR PROTEIN INHIBITS M-CHOLINERGIC RECEPTOR BINDING IN SH-SY5Y CELLS. R Can-Jun, S Wang, GH Du, L Sun. Institute of Basic Medical Sciences, Institute of Materia Medica, Chinese Academy of Medical Sciences, Peking Union Medical College, Beijing, China

INTRODUCTION: Our aim was to observe the effect of over-expressed amyloid precursor protein (APP) gene, one of AD-related genes and overproduction of β -amyloid (A β) peptides, on the cholinergic receptor binding and the ChAT activity in human neuroblastoma cell line SH-SY5Y. **METHODS:** SH-SY5Y cells were stably transfected with pCMV695 plasmid containing wild type human APP₆₉₅ gene by Lipofectamine 2000 method. The expression of APP was detected by western blot. A β contents were test by ELISA assay in over-expression SH-SY5Y cell clones (SH-SY5Y-APP). The special binding of muscarinic and nicotinic cholinergic receptors in those A β -overproducing cell clones were determined by radio-ligand binding method. The cholinergic acetyl transferase (ChAT) activity was assayed by radio-immunoassay. **RESULTS:** No evident morphologic changes of cytotoxicity were detected after transfection. When A β production was 2-2.6 times (< 115-150 pmol/L) as much as that of normal cells, muscarinic receptor binding was decreased from 18.5% to 21.9% (P<.05) compared with normal cells. However, no marked alterations in nicotinic receptor binding and the ChAT activity were found. **CONCLUSIONS:** In this experiment, we found that muscarinic receptor binding inhibition was showed before cytotoxicity, nicotinic receptor binding and ChAT activity changes in SH-SY5Y-APP. It is suggested that the increase of A β production could independently caused the cholinergic dysfunction in early stage of AD brain tissues by muscarinic receptor binding inhibition.

DESINTEGRATION OF BRAIN REGULATORY MECHANISMS UNDER ACUTE HYPOXIA. SI Soroko, SS Bekshaev, VP Rozhkov. Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia

Acute hypoxia is known to be a strong stress factor. Sustained hypoxic state under extremal environmental conditions leads to cognitive-mental processes deterioration before vital function could be affected. One of the most difficult and unsolved problems is a search for neurophysiological markers that permit to assess functional brain reserve and obtain early signs of central nervous system regulatory function destabilization as well as partial or overall functional desintegration. Characteristics of intercentral relationships adaptive reorganization and indices of system interactions disturbance degree were studied in healthy males under 15-25 minute 8% O₂ exposition

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by means of: a) EEG wave interaction structure temporal organization analysis; b) brain biopotential field local and spatially synchronous processes topical distribution evaluation based on EEG interarea crosscorrelation analysis (including factor analysis); c) normal and abnormal EEG waveforms intracranial localization and spreading assessment using original computer stereotaxic tomographic method of equivalent electrical dipole source (EEDS) localization. Our results show functional disturbances of the native structure of the brain electrical activity interregional relationships, that form a basis of either partial or general desintegration of the brain system activity. These alterations lead to arising of "the dynamic morphological equivalent" the brain activity directed to integrative mechanisms reorganization and formation of the adaptive brain reactions. EEDS tomography data reveals basic brain EEG rhythms "sources" that are mainly related to thalamic structures in normal conditions. Initial hypoxic stages bring intracranial EEDS redistribution with EEDS density increase into slices that include hypothalamic region, basal forebrain nuclei as well as basal and anterior medial temporal lobe regions of the left and the right hemisphere. Hypoxia strengthening cause EEDS bilateral spreading into basal and medial frontal lobe regions. Main targets of hypoxic action are in this period both superficial and deep regions of cerebral hemisphere frontal lobes. Stage of pronounced CNS functional alterations under strong hypoxia is characterized by appearance of hypersynchronous generalized paroxysmal EEG activities, that is accompanied by multiple EEDS foci traveling phenomenon, first of all through the basal and medial regions of frontal and temporal cerebral hemisphere lobes as well as limbic system structures. Sustained acute hypoxic state leads to functional separation between brain structures that constitute different central nervous system integration levels, in particular, neocortical and limbic-diencephalon ones. This process is accompanied by brain functional potentialities diminution, regulatory function destabilization and system brain activity desintegration at last.

Day 2. May 17, 2007. Venue: Oktyabrskaya Hotel, Ligovsky Prospect, 10

Symposium 5. Clinical Psychiatry and Psychology – III. Chairs: VM Klimenko, AV Kalueff, N Tolmacha

- FRUSTRATION OF ADAPTATION AT MENTALLY SICK SENIOR AGE GROUPS DIRECTED ON COMPULSORY TREATMENT. ER Kunafina. Faculty of Psychiatry and Narcology, Bashkir State Medical University, Ufa, Russia
- EPIDEMIOLOGY OF MYOTONIC DYSTROPHY IN KRASNOYARSK. LA Sviderskaya, EA Kozulina, N A Shnaider. Krasnoyarsk State Medical Academy, Krasnoyarsk, Russia
- ANALYSIS OF BRAIN BIOELECTRICAL ACTIVITY AND BEHAVIOR CORRECTION OF HYPERACTIVE CHILDREN. J Porozovs, N Tolmacha, J Vandans. Riga Teacher Training and Educational Management Academy, Psychoneurophysiological and Bioregulation Investigation Centre, Riga, Latvia
- OCD AND PTSD: TWO CASE REPORTS. Z Pires, M Lobo, S Mendes, S Fernandes. Hospital Nossa Senhora do Rosario, Barreiro, Portugal
- CHANGES OF THE HEART RATE CONTROL DURING PUPIL'S EXAMINATIONS. ES Gevorkyan, SM Minasyan, NN Ksadjikyan, AV Dayan, Tsl Adamyan. Yerevan State University, Yerevan, Armenia
- SOURCES OF PATIENTS' STRESS: BEDSIDE CASE PRESENTATION. S Omidvari, A Montazeri, AM Harirchi, H Soori. Iranian Institute for Health Sciences Research, University of Social Welfare and Rehabilitation Sciences, Beheshti University of Medical Sciences, Tehran, Iran

FRUSTRATION OF ADAPTATION IN MENTALLY SICK SENIOR AGE GROUPS ON A COMPULSORY TREATMENT. ER Kunafina. Faculty of Psychiatry and Narcology, Bashkir State Medical University, Ufa, Russia

INTRODUCTION: About 70% patients who made socially dangerous actions (SDA) and being on compulsory monitoring do not receive intensive medicamentous therapy. In the elderly patients with SDA, efficiency of medication depends on a degree of adaptation of patients to conditions of a hospital. Hospitalization sharply changes their way of life, breaks years-developed stereotype, alters social communications. Therefore, in a clinical practice the exact and adequate estimation of a condition of the patient, his/her reaction to medical rehabilitation, is necessary. **METHODS:** Reactions

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to hospitalization in 69 mentally sick seniors (men) have been investigated, including 23 schizophrenics and crazy frustration (33%); and 46 patients with organic mental disorder (67%). According to the International classification of illnesses-10 following clinical forms of frustration of adaptation are allocated: short-term depressive reaction (F43.20) - 12 (17,4%); mixed disturbing and depressive reaction (F43.22) - 19 (27,5%); with prevalence of infringement of other emotions (F43.23) - 9 (13%); with prevalence of infringement of behavior (F43.24) - 10 (14,5%). Short-term depressive reaction did not exceed 1 month. In reactions with prevalence of infringement of other emotions displays of alarm, depression, anxiety, intensity and anger took place. In a clinical picture of reactions with prevalence of infringements of behavior prevailed aggressive behavior. The age of patients varied from 52 to 78 years. For an estimation of development and expressivenesses of psychopathological parameters were used the standardized questionnaires: the Zung self-rating depression scale for a self-estimation of alarm and depression, Scale of a self-estimation functional conditions (DIGNITY) for an estimation of state of health, activity, mood, and Luscher colortest. Results of research are processed by a method of variational statistics. **RESULTS AND DISCUSSION:** 19 patients (27,5%) were adequately treated and quickly adapted. In 50 elderly patients, staying in a hospital for long time was a stressful situation, as broke the generated vital stereotypes (habitual conditions, the environment, house rituals), limited communication with relatives, and aggravated mental and somatic conditions, such as poor adaptation, sleep disorders, ischemic illness, hypertonicity or vascular brain insufficiency. Clinical and psychological studies revealed disturbed security (27,5%), protest (13%), passive-indifferent behavior (23,2%), and conversion frustration (8,8%) ($p < .05$). **CONCLUSIONS:** It is important to come into the first contact to patients at hospitalization, to prepare them for specific conditions of psychiatric branch, and to explain the purposes and problems of compulsory treatment.

EPIDEMIOLOGY OF MYOTONIC DYSTROPHY IN KRASNOYARSK. LA Sviderskaya, EA Kozulina, NA Shnaider. Krasnoyarsk State Medical Academy, Krasnoyarsk, Russia

INTRODUCTION: Myotonic dystrophy (DM) is one of the most frequent inherited pathologies in the nervous system. It often causes patient's invalidization and death in early age. Taking into account geographical and historical peculiarities of Siberia we can assume that the prevalence of DM could be differ from other Russian regions. The aim of our research was to determine epidemiological and clinical peculiarities of DM in Krasnoyarsk (by the database of Krasnoyarsk city hospital № 5). **METHODS:** 4969 patients were followed-up for 6 years between 2000 and 2005. 4627 patients case histories which have had hospitalized from 1990 till 1999 years were analyzed. Among them there were 1.2% patients with inherit pathologies and 4.0% of patient's relatives. Neurological, neurophysiological and genetic examinations were carried out. All of the patients consulted cardiologist and ophthalmologist. Ultra sound abdomen investigation was also performed. The mean age at the moment of studying constituted 32 ± 17 [95% confidence interval: 17-44] years old. The period while the patients were observed varied from 1 to 15 years. **RESULTS:** The mean age of the patients with DM was 35.7 ± 16.5 years old. The age of manifestation varied from 6 to 37 years, the average value was 19.6 ± 10.4 [95% confidence interval: 5-22] years old. We noted a significant phenotypic polymorphism of DM, including polymorphism within family. Monosymptomatic, latent, and effaced forms also happened, that made difficulties in disease recognition and estimation of inheritance type. We revealed disorders of the heart rhythm almost in half of the patients (41.7%). Intra-ventricular block was the most frequent (13.6%) pathology, in 4.5% cases antrioventricular block was noted. Sick sinus syndrome was observed in 3% patients. The disturbances of repolarization were found out in 1.5% patients. In echocardiography examination cardiomyopathy was the most frequent pathology (41.7%). We observed mitral valve incompetence in 14.3% cases. Abdomen ultra sound examination determined that almost every patient (90.9%) had some kind of pathology. Gastro-intestinal diseases were frequently noted. Disorders in pancreas and hepar ductus were in 45.5% and hypokinesia of the gallbladder in 4.5% cases. Nephropathology was at the second place. We determined nephroptosis in 31.8% of patients, double kidney in 9.1%, urolithiasis – 4.5%. Ophthalmologist examined 89.4% of patients. The most frequent eye pathology in DM was angiopathy (57.1%), cataract and myopia were revealed in 28.6% and 14.3% of cases respectively. The studied group of people belonged to 120 000 population of a city district. It allows us to evaluate DM disease rate in the city of Krasnoyarsk. The occurrence of DM is 14.7 per 100 000. **CONCLUSIONS:** The high occurrence of DM in this region can be related with the historical peculiarities of Siberian and Krasnoyarsk region colonization. They are the establishment of territorially isolated population of migrants, a high migration level especially from Kavkaz region where

a lot of inbreeding marriages still happen. The differences between Western Siberia (Novokuznesk, Tomsk) and Eastern Siberia (presented data) could be also explained by peculiarities of assimilation in this area in the past.

ANALYSIS OF BRAIN BIOELECTRICAL ACTIVITY AND BEHAVIOR CORRECTION OF HYPERACTIVE CHILDREN. J Porozovs, N Tolmacha, J Vandans. Riga Teacher Training and Educational Management Academy, Psychoneurophysiological and Bioregulation Investigation Centre, Riga, Latvia

INTRODUCTION: Hyperactivity with deficit of attention is a serious problem in our society. The characteristic symptoms of hyperactive children are inability to pay attention for a long time, weakness of self-regulation processes, impulsiveness and anxiety. These primary symptoms cause secondary symptoms: problems with self-estimation, excessive risk behavior, difficulties with coming into contact with other people and difficulties in learning. The effective method which allows to improve the psycho emotional sphere of people with different functional disorders of nervous system and to make correction work with them is functional bioregulation with biofeedback. Patients find out the way how to regulate the physiological processes of their organism using this method. It gives ability to improve the functional state of organism. The aim of the work was to determine the peculiarities of brain bioelectrical activity of hyperactive children and to make correction of their behavior using the method of functional bioregulation with biofeedback. **METHODS:** 32 hyperactive children with attention deficiency were observed. Children were 6 – 8 years old. Electroencephalograms (EEG) of hyperactive children were registered. The behavior correction of hyperactive children with attention deficiency by the method of functional bioregulation with biofeedback was carried out. Two kinds of trainings were used to hyperactive children depending from the parameters of brain bioelectrical activity of child: 1) relaxation from parameters of EEG (procedure directed to the increase of α rhythm in EEG); 2) changes of the rhythm ratio in EEG (procedure directed to the increase of ratio between quantity of β and θ rhythms). 12 – 15 training performances were carried out to every child. The endurance of one performance was 20 – 30 minutes. **RESULTS AND DISCUSSION:** The main deviations from the norm in the EEG of hyperactive children were following: 1. The decreased quantity of α rhythm mainly in the occipital lobes. 2. The considerable increase of slow θ rhythm in EEG. 3. Increased quantities of θ rhythm and decreased quantities of β rhythm mainly in the central and top of the head regions. Difficulties in the study process at school and attention concentration, decreased level of memory and declined work abilities have hyperactive children with these changes in EEG. The majority of hyperactive children trained by functional bioregulation with biofeedback procedure directed to the increase of α rhythm in EEG had the significant increase of α rhythm at the 7th till the 10th training performance but some of them already at the 2nd or the 3rd training performance. The majority of hyperactive children trained by functional bioregulation with biofeedback procedure directed to the increase of ratio between quantity of β and θ rhythms had significant increase of the quantity of β rhythm and it gets closer to the characteristic age norm at the 10th till 12th training performance. A decrease of behavior impulsiveness of hyperactive children, an improvement of abilities to concentrate attention to the work at school, an increase of self-estimation and an improvement of coming into contact with other children and parents after training procedures of functional bioregulation with biofeedback was observed. **CONCLUSIONS:** 1. Hyperactive children had various changes in EEG. Main of them were: the decreased quantity of α rhythm mainly in the occipital lobes, the considerable increase of θ rhythm and increased quantities of θ rhythm and decreased quantities of β rhythm mainly in the central and top of the head regions. 2. The training performances of functional bioregulation with biofeedback normalized EEG of hyperactive children: the increase of α rhythm for one group of hyperactive children and the increase of β rhythm index and decrease of θ rhythm index in the second group of hyperactive children was observed. 3. An improvement of behavior peculiarities of hyperactive children and contacts with other people after functional bioregulation with biofeedback procedures was observed.

OCD AND PTSD: TWO CASE REPORTS. Z Pires, M Lobo, S Mendes, S Fernandes. Hospital Nossa Senhora do Rosario, Barreiro, Portugal

CASE I. OCD AND ADOLESCENCE. OCD is characterised by the presence of obsessive ideas and/or compulsive rituals. The first are recurrent and persistent thoughts, urges or images, felt as inappropriate and intrusive, that cause intense anxiety or disturbance, in some moment of the disease. The patient tries to ignore or move against them, while recognising them as his own.

Compulsions are repetitive behaviors or mental exercises the patient feels compelled to execute as a response to the obsessions. These behaviors are intended to prevent or diminish the anxiety associated to the obsessions. This disturbance begins usually in adolescence or first years of adulthood, and appears earlier in the male gender. We present a case report that illustrates the early appearance of this disease with a good outcome. The case presented showed a very favourable outcome, being one of the 5% cases that stay asymptomatic or with minimal symptoms. The therapeutic choice has been recognised as efficient, with the use of higher doses in some patients or in association with other antidepressants. The association with some kind of psychotherapy, especially cognitive-behavioral therapy, has proved to improve the prognosis in this patient. The case presented here illustrates this multifaceted disease, and allows the authors to reflect in the prognosis and therapeutic weapons available today.

CASE II. PTSD AND PATHOLOGICAL GAMBLING. Posttraumatic stress disorder (PTSD) is an anxiety disorder that develops in some people following exposure to an overwhelming, frightening or distressing event. It is one of a range of serious psychological reactions you can have following a traumatic incident such as an accident, sexual assault or violence, a natural disaster, war or torture. Classified as a disorder of impulse control, pathological gambling is characterized by a loss of control over gambling and a driving need for the "rush" gambling provides. The association of PTSD and pathological gambling has been reported for some years now. Many symptoms of PTSD parallel the symptoms of late stage problem gambling. In both disorders symptoms of increased arousal, persistent and recurrent behavior, and self-destructive and impulsive behavior, are often high. These features are highlighted by the co morbid problems found in both disorders. Associated disorders such as depression, anxiety and related phobias, obsessive-compulsive, suicidal ideation and substance abuse, are common. We present a case report that illustrates the association of PTSD following civil war and pathological gambling in a patient that seeks help only nearly 30 years after the onset of the disease. The case presented here showed a very favourable outcome. Although the patient was not asymptomatic, there has been a large improvement both in his gambling and his PTSD symptoms. The therapeutic choice has been recognised as efficient, and the association with some kind of psychotherapy, as coping skills and problem-solving training, counselling and other trauma therapies has proved to improve the prognosis in this patient. Although some association of these two disorders have been reported, some say that there are no real relationships between them. More studies will be needed to gather some consensus and enlarge our knowledge about this matter. In Portugal, this association needs to be more reported, as there are very few case reports on a very common association.

CHANGES OF THE HEART RATE CONTROL DURING PUPIL'S EXAMINATIONS. ES Gevorkyan, SM Minasyan, NN Ksadjikyan, AV Dayan, Tsl Adamyan. Yerevan State University, Yerevan, Armenia
INTRODUCTION: Situations such as academic examinations can be strong stressors. Difficult syllabi, and chronic time pressure associated with the need to assimilate large amounts of information are attributes of education in modern society and may lead to nervous breakdowns. The tonic action of stress on the homeostatic systems of the body upsets the harmony of intersystem relationships and even to develop into autonomic dysfunctions. Cardiovascular changes are an integral component of the general stress response. The most convenient and informative tool for studying the cardiovascular system is time series analysis of heart rate variability. Temperament and some specific personality traits have a psycho emotional characteristic of individuals, shaping their behavior in difficult situations, including examinations. The goal of this study was to assess the level of strain in the operation of mechanisms regulating the heart rate in pupils of X class during the period of examinations. **METHODS:** To assess the mechanisms of heart rate control, the electrocardiogram (ECG) was recorded and fed directly into an IBM 486 computer for processing. In each ECG, a segment of 100 cardiac cycles was analyzed. Mathematical time series analysis of heart rate variability was performed as described by Baevsky et al using the Cardio computer program. This program automatically determined and analyzed the R-R intervals. Specifically, we determined the distribution an index of humoral regulations of the heart rate (mode, M_o); the sympathetic activity index (mode amplitude, AM_o); the variation range (ΔX). In addition, the following autonomic indices were calculated the stress index (SI), defined as $AM_o/2\Delta X M_o$, which is informative as a measure of the stress-induced strain in the operation of the compensatory mechanisms of the body and of the activity of the central circuit in the regulation of the heart rate. The autocorrelation function was calculated and plotted for each RR time series to reveal the periodicities contained in that series. There are makes it possible to assess how the central circuit of heart rate control affects the

peripheral circuit. His or her state was self-assessed using the Well-being-Activity-Mood (WAM) test. This psychological test was administered to the subjects before every ECG recording session. The subjects were studied 1 month before examinations period (base-line data), before and after examinations. **RESULTS:** Testing of pupils before their examinations indicate the self-rated well-being, activity, and mood were 4.74 ± 0.19 , 4.48 ± 0.19 , and 4.94 ± 0.17 , respectively. By the SI, we classified 27.8% of the subjects as vagotonics ($SI < 60$) and the other as normotonics ($60 \geq SI \leq 180$). None of the subjects were sympatotonics. As the examinations approached, the SI increased in 61.1% of subjects (sympathetic response type, group I) and decreased in the other 38.9% (parasympathetic response type, II group). In group I, the SI increased by an average of 26.1% as compared with its baseline value ($p < 0.05$). The AMo increased by 12.7% ($p < 0.05$). Obviously, the autonomic balance was tipped slightly in favor of sympathetic activity, indicating that the degree of central regulation in the heart rate control began to increase. A moderate increase in sympathetic activity in the central circuit of cardiac control suggested by the increases in the SI and AMo was accompanied by a small reduction in ΔX , which is an index of parasympathetic activity. The humoral control (Mo) remained unchanged. Similar changes were observed in group II. The SI decreased by 15.6% relative to their baseline values. The fact that sympathetic tone was diminished in this group might result from activation of the humoral control and an increase in cardiac parasympathetic activity (ΔX and Mo). The variability RR cardiointervals was large in these subjects, suggesting a relatively low degree of central regulations and a predominance of parasympathetic activity in the heart rate control. Before the examinations the proportion of normotonics decreased, the vagotonic and sympathicotonic group increased in size by 33.3 and 22.2%, respectively. The WAM scale mean decreased to 4.34 ± 0.15 , because all items of this questionnaire were scored lower in this period (well-being, 4.26 ± 0.22 ; activity, 4.02 ± 0.24 ; mood, 4.71 ± 0.18). After the examinations, the proportion of normotonics increased to 55.5%; vagotonics and sympathicotonics accounted for 38.9 and 5.6% of the subjects. The WAM scale mean was 4.36 ± 0.19 , remaining at the preexamination level, as a result of fatigue and emotional exhaustion. In two groups the AMo and SI decreased to some extent but did not reach their base-line values. The increase in the SI and the changes in psychological parameters suggest that examination stress produces a serious strain in the operation of the regulatory systems of the body. **CONCLUSIONS:** The examination period is a significant psychoemotional stress factor for pupils and changes the functional state of the body at the level of psychophysiological parameters used to describe the sympathetic and parasympathetic mechanism of the autonomic nervous system.

SOURCES OF PATIENTS' STRESS: BEDSIDE CASE PRESENTATION. S Omidvari, A Montazeri, AM Harirchi, H Soori. Iranian Institute for Health Sciences Research, University of Social Welfare and Rehabilitation Sciences, Beheshti University of Medical Sciences, Tehran, Iran

INTRODUCTION: Bedside case presentation and bedside clinical teaching are declining. Several barriers have been reported to contribute to such decline. The concern that bedside presentation may provoke distress in patients is one of them. Here we study patients' perception on bedside case presentation. **METHODS:** A descriptive study was conducted to assess patients' perceptions towards bedside case presentation at eight medical wards of a large teaching hospital in Tehran, Iran. Patients who had experienced at least two bedside case presentations were randomly selected and entered into the study. To assess patients' perceptions, a questionnaire consisting of 14 items covering four topics (privacy, visit duration, stress, and physician-patient relationship) was administered to patients. Data were analyzed descriptively. **RESULTS AND DISCUSSION:** Total 120 patients were studied. The mean age of patients was 36.5 years, and mostly were female (54%), married (56%) and had secondary educational level (53%). With regard to privacy, 37% of patients stated that aloud case-presentation in the presence of other patients was distressing, and 51% of patients stated that disclosure of their economic status was very annoying. The results also indicated that most patients (63%) claimed that during bedside presentation physicians did not spend enough time for them and using medical terminology was found to be the source of a considerable anxiety (47%). Finally, concerning patient-physician relationship it was found that 37% of patients believed physicians did not understand them. The study findings confirm earlier reports that bedside case presentation in spite of some advantages may have some disadvantages. **CONCLUSIONS:** The study findings indicate that bedside case presentations might breach privacy, provoke anxiety and impair physician-patient relationship. The study outlines some aspects of bedside case presentation that needs to be improved.

Symposium 6. PSYCHOPHYSIOLOGICAL APPROACHES TO MONITORING AND BIOFEEDBACK TREATMENT OF STRESS-RELATED SYMPTOMS. Chairs: E Lyskov, B von Scheele

- WHAT DOES RESPIRATORY SINUS ARRHYTHMIA PATTERNS TELL US? B von Scheele. PBM Stress Medicine AB, Sweden
- MONITORING OF STRESS RELATED PHYSIOLOGICAL PROCESSES IN AMBULANCE PERSONNEL. E Lyskov. Centre for Musculoskeletal Research, University of Gavle, Gavle, Sweden.
- PLANS FOR BALTIC SOCIETY FOR INTEGRATED PSYCHOPHYSIOLOGY. B von Scheele. PBM Stress Medicine AB, Sweden

WHAT DOES RESPIRATORY SINUS ARRHYTHMIA PATTERNS TELL US? B von Scheele. PBM Stress Medicine AB, Sweden

In clinical work, we often observe different patterns in Respiratory Sinus Arrhythmia (RSA). I have during the years discussed this at different meetings but have not got any substantial responses. One reason might be that not many clinicians have been working with patient in normal clinical settings using RSA as a tool (von Scheele, 1995) for understanding, communicating and training RSA, which I have done during many years. Clinical experience also leads to analysing metabolic behaviors (von Scheele and von Scheele, 1999) when breathing behaviors are influenced externally, which often is the case with RSA – biofeedback. I will show some specific RSA pattern characteristics and features from clinical work as an illustration what can be observed as well as discuss its clinical significance. RSA is a kind of “mirror” of complex systems integration processes and is never without meaning when properly measured even if we do not understand fully its functional significance.

MONITORING OF STRESS RELATED PHYSIOLOGICAL PROCESSES IN AMBULANCE PERSONNEL. N Kalezic, U Aasa, M Barnekow-Bergkvist, E Lyskov. Centre for Musculoskeletal Research, University of Gavle, Gavle, Sweden.

The autonomic nervous system (ANS) provides linkage between the brain and skeletal muscles and play a role in regulation of local circulation, metabolism and in perception of muscle afferent signals. Several clinical studies reported involvement of ANS in development of musculoskeletal disorders (MSD) however it is still difficult to define an origin of autonomous symptoms and their predictive value in MSD. Partly, discrepancy in results may be related to variety of methods that have been utilized to describe and evaluate autonomous functioning of subjects with MSD. Combination of laboratory tests and longitudinal (24-72 hours) monitoring of ANS may provide better description of autonomous involvement in MSD. Musculoskeletal and stress related complaints are common among health care personnel. The aim of the present study was to assess physiological and subjective stress markers during a 24-hour ambulance work shift and during the next two work-free days, and relate these parameters to self-reported health complaints. Twenty-six ambulance personnel were followed during a 24-hour work shift and during the next two work-free days with Holter ambulatory ECG records, cortisol assessments and diary notes. The ambulance personnel also performed tests of autonomic reactivity before and at the end of the work shift. The subjects were categorized into two groups according to their number of health complaints. In general, stress markers did not show differences between the work shift and leisure time. However, statistically significant deviation in heart rate variability pattern and higher morning cortisol values during work in comparison with work-free days were observed in personnel with stress related health complaints. Subjective and physiological characteristics of ambulance personnel did not indicate distinctive stress during the 24-hour work shift. However there exist indications of ANS and neuro-hormonal involvement in subgroup of subjects with frequent health complaints..

PLANS FOR BALTIC SOCIETY FOR INTEGRATED PSYCHOPHYSIOLOGY. B von Scheele. PBM Stress Medicine AB, Sweden

We plan to develop a Baltic Sea State Society for Integrated Psychophysiology (Baltic SIP) in cooperation with AAPB (Association of Applied Psychophysiology and Feedback; www.aapb.org). As the President of the International section of AAPB, I have anchored this plan in our organization (AAPB), and have full support from our main board as well. The Baltic SIP aims at integrating and hosting different multidisciplinary

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systems approaches within fields related to human development with specific focus on performance and health as well as the development of unhealth. We invite basic scientists, clinicians and laymen to join the organization. More details will be given during and after the presentation.

Symposium 7. Clinical and Experimental Psychopharmacology. Chairs: PD Shabanov, VM Klimenko

- PHARMACOLOGICAL STUDIES ON A TIBETAN HERBAL MEDICINE AGAINST DEMENTIA. JT Zhang J, LY Zhang, JG Shi. Institute of Materia Medica, CAMS, Beijing, China
- SALVIANOLIC ACID B, A NEW TYPE OF ANTI-DEMENTIA AGENT. Zhi-wei Qu, Ming-ke Tang, Wen-jie Zhao, Jun-tian Zhang, Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical University, Beijing, China
- PHARMACOLOGICAL CORRECTION OF POSTTRAUMATIC AND POST-WITHDRAWAL DISORDERS BY METABOLIC ACTIVATORS. IV Zarubina, TV Pavlova, PD Shabanov. Department of Pharmacology, Military Medical Academy, St. Petersburg, Russia
- BACOPA MONNIERA MASKS AMNESIC EFFECTS OF NO SYNTHASE INHIBITOR INDEPENDENT OF NMDA MEDIATED LTP INDUCTION IN MICE. A Anand, MK Saraf, S Prabhakar. Department of Neurology, Post-graduate Institute of Medical Education and Research, Chandigarh, India
- EMOTIONAL STATUS AND PECULIARITIES OF THE BEHAVIOR IN RAT FROM MOTHERS TREATED WITH CADMIUM SULFIDE. L Gubareva, H Agarkova. Department of Psychophysiology, State University, Stavropol, Russia

PHARMACOLOGICAL STUDIES ON A TIBETAN HERBAL MEDICINE AGAINST DEMENTIA. J Zhang J, LY Zhang, JG Shi. Institute of Materia Medica, CAMS, Beijing, China

INTRODUCTION: Wangla, rhizome of *Coeloglossum viride* (L.) Hartm. Var. bracteatum, is one of commonly used traditional Tibetan herbal medicines. Traditional applications of Wangla are multiple, such as invigorating vital energy, promoting the production of body fluid, tranquilizing and enhancing intelligence. The chemical isolation and structure identification of its active compounds in Wangla were performed, and the memory enhancing activity was discovered with a specific fraction (CE) and its active compounds. Both extract CE and single component W6 can improved, not only the memory impairment of animal models of Alzheimer's disease, but also the memory loss induced by ischemia and hypoxia. The CE and W6 are also effective enhancing the learning and memory function in young normal mice. The study demonstrated that W6 can stimulate brain choline acetyltransferase in vitro and in vivo, but W6 has no inhibitory effect on acetylcholinesterase. W6 can protect neurons against oxidative damage induced by A β or H₂O₂ in SH-SY5Y cell. CE and W6 have actions of large spectrum for memory enhancing in animal through potentiating ChAT activity and protecting neurons from oxidative damage. The mechanism of CE seems to be different from AchE inhibitors approved by USA FDA for treatment of AD. Moreover, CE and W6 are very safe (LD₅₀>5 g/kg, po in mice). This work is protected by PCT patent. CE is a new hopeful candidate drug for treating amnesia-related diseases such as AD. **RESULTS AND DISCUSSION:** Compared with naive mice, orally administration of CE (1.25-5 mg/kg, po) could shorten the escape latency and decrease the error number significantly in water-maze test, indicating that CE can enhance the capacity of learning and memory in normal mice. Scopolamine, a muscarinic cholinergic receptor antagonist, has been shown to impair memory retention when given to mice shortly before training in passive avoidance task, the scopolamine-amnesia test is widely used as primary screening test for so-called anti-Alzheimer drugs. CE (.1-10 mg/kg) and W6 (.03-10mg/kg) can attenuate the scopolamine-induced impairment of passive avoidance behaviors. CE (.4mg/kg) is as potent as HupA (.4 mg/kg) and Donepezil (6 mg/kg) on this experiment. W6 (5 and 20 mg/kg) has no inhibition on activity of AChE in rat brain. It indicates that the improvement of W6 on cognitive function in animal is not mediated via inhibition of cholinesterase pathway. CE and W6 active choline acetyltransferase (ChAT) in vitro (10⁻⁹M-10⁻⁷M) and in vivo (increase the production of ³H-ACh by 41.5% in CE (5 mg/kg) treated mouse brain). In the homogenization of mouse forebrain treated with W6 (.2-5 mg/kg, po), DA and 5-HT level increased, however their main metabolites DOPAC and 5-HIAA level decreased markedly. The ratio of DOPAC/DA and 5-HIAA/5-HT reduced in dose dependent manner. These results suggest that W6

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might had inhibitory action in metabolizing of monoamines transmitters in mice brain. Cycloheximide is an inhibitor of protein synthesis. It can impair the performance of experimental animals in a wide variety of learning and memory tasks, including passive avoidance. CE, at doses of 2.5mg/kg and 10mg/kg, significantly reversed the cycloheximide-induced reduction of step-through latency, and decreased the number of errors, indicating that CE can ameliorate impairments of passive avoidance induced by cycloheximide. Treatment of mice with CE (1.25-10 mg/kg, po) and W6 (1mg/kg, po) for 2 weeks significantly blocked the Abeta (1-42)-induced impairment in passive avoidance performance, also significantly improved Abeta (1-42)-induced deficit in mouse spatial working memory. These findings suggest that CE and W6 may have preventive effect against memory impairment related with Abeta of Alzheimer's disease. The efficacy of CE and W6 are stronger than piracetam (300 mg/kg). W6 (10^{-5} M- 10^{-8} M) significantly elevated the viability of SH-SY5Y cells and inhibited the LDH release induced by Abeta (30 μ M). Four week's cerebral hypoperfusion in mice and rats caused deficits of learning and memory (observed in step-down test and water-maze test). Long term treatment with CE (1.25-10 mg/kg, po) or W6 (1mg/kg, po) significantly alleviated these changes in behavioral. Our data suggest the beneficial role of CE and W6 in cerebrovascular insufficiency states and dementia. The efficacy of CE and W6 are stronger than piracetam (300 mg/kg). CE (1.25-10 mg/kg) could improve the memory dysfunction and other ageing symptom induced by consecutive injections of D-Galactose and NaNO₂. CE (1.25-10 mg/kg) significantly reduced the number of injured neurons in mouse hippocampus induced by repeatedly injections of D-galactose and NaNO₂. CE promoted remarkably the activities of GSH-px, SOD, ATPase and the content of GSH, and decreased significantly the content of MDA in mouse brain. The immunohistochemical results showed that CE significantly inhibited the increases in Caspase-3 and Bax positive neurons, as well as the reductions in NT-3 and Bcl-2 positive neurons induced by repeatedly injections of D-galactose and NaNO₂ in mice. From HPLC chromatogram we found that the main components W6-W9 can be clearly observed in CE treated mice brain. Thus, W6 and related compounds can pass through the blood-brain-barrier and reach brain in mice. After orally administered a single dose of CE at 5 g/kg, no significant differences in animal behavior was observed, and there is no animal dead and the body weights of animals increase as normal mice. The result suggests that CE has very low acute toxicity in mice.

SALVIANOLIC ACID B, A NEW TYPE OF ANTI-DEMENTIA AGENT. Zhi-wei Qu, Ming-ke Tang, Wen-jie Zhao, Jun-tian Zhang. Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical University, Beijing, China

Salvianolic acid B (Sal B) isolated from Radix Salvia Miltiorhizae was shown to have anti-dementia effects. Many evidences indicate that β -amyloid(A β) plays a critical role in the pathogenesis of AD. But A β exerts its toxicity only in the form of aggregation and fiber formation. Sal B was cultured with A β_{1-40} at room temperature for 30hr, Sal B could inhibit aggregation and fibril formation completely at 10^{-6} - 10^{-8} mol/L, suggesting that Sal B block A β toxicity at very early stage. Sal B could also inhibit A β -induced neuronal apoptosis. The anti-apoptotic effect of Sal B was mediated by inhibiting Par-4 and caspase-3 activity which are responsible for inducing apoptosis. Neurodegenerative diseases were divided into acute and chronic neurodegenerative diseases, cerebral ischemia/glucose and energy metabolism impairment is considered as acute neurodegenerative disease, therefore Sal B was used in MCAO model for its anti-cerebral ischemia effect. Our results show that Sal B had good effects in decreasing infarct volume and brain edema as well as improved neurological deficit. It is interesting that besides scavenging of free radicals, increase of blood flow, antithrombosis, protection of mitochondrial function, Sal B can also increase angiogenesis and neurogenesis which are the key mechanisms underlying the anti-cerebral ischemia effect of Sal B, and as we know there is no any other drug or compound to have such effects. In addition, comparison of pharmacology between Sal B and EGb-761 was carried out. The parameters used include cell protection against various insults, antioxidant activity, anti-apoptotic effect, inhibition of A β aggregation and fibril formation etc. In these parameters, the effective concentration of Sal B and EGb-761 were .007-.07mg/ml and 50-100mg/ml respectively, indicating that Sal B is much better than EGb-761 for treatment of cerebral vascular disorders.

PHARMACOLOGICAL CORRECTION OF POSTTRAUMATIC AND POSTWITHDRAWAL DISORDERS BY MEANS OF METABOLIC ACTIVATORS. IV Zarubina, TV Pavlova, PD Shabanov. Department of Pharmacology, Military Medical Academy, St. Petersburg, Russia

INTRODUCTION: The brain injury is known to be the main reason in human disability due to traumatization of the nervous system. The long recovery period after brain injury is characterized by

formation of psychopathological syndrome with asthenic features. Clinical investigations demonstrate, that the symptoms of delayed posttraumatic period are the same as in depression; both emotional and personality disorders are strengthening in such patients, and it suggests the search of new approaches for the pharmacological correction of posttraumatic cerebrasthenias. Alcoholization is shown to strengthen emotional disorders due to brain injury. Forasmuch the neurodynamic disorders of hypoxic type are prevailed in pathogenesis of both brain injury alone and alcoholism complicated with brain injury, we used bemithyl, a new antihypoxant of metabolic type, in combination with antidepressant pyrazidol to reduce asthenic symptoms in posttraumatic period in rats and humans. **METHODS, RESULTS AND DISCUSSION: EXPERIMENTAL INVESTIGATIONS.** Prior to the pharmacological experiments all rats were subdivided for two groups: with high (HR) and low resistance (LR) to hypoxia. The rats of both groups received pyrazidol (1 mg/kg) + bemithyl (25 mg/kg) i.p. for 20 days after mechanic brain injury. This combination of drugs harmonized behavioral reactions of phenotypically different rats (HR and LR) in terms of motor, explorative, emotional activity and anxiety level. All behavioral parameters in injured rats treated with the combination of drugs were the same as in control ones. Pyrazidol (1 mg/kg) + bemithyl (25 mg/kg) supported metabolic status of the brain in injured rats on the level of intact animals. The optimal effect on the level of lipid peroxidation, superoxide dismutase activity and macroergs content was obtained in LR in comparison with HR rats. **CLINICAL INVESTIGATION 1.** 45 patients, males aged 18-50, with consequences of brain injury of moderate degree (asthenoneurotic, asthenovegetative syndromes preferably) were treated with combination of pyrazidol (50 mg per day) and bemithyl (250 mg per day) for 15 days. The psychological testing was assessed by the M.Lusher color scale of personal sense. The reduction of asthenic features, psychophysiological mobilization, moderate psychic activation with high orientation and adaptation velocity as well as the expediency and successfulness in actions were registered after course of therapy. **CLINICAL INVESTIGATION 2.** 40 patients, males aged 32-37, with alcohol dependence (alcoholism of the second stage) and brain injury of moderate degree in anamnesis were treated with combination of pyrazidol (50 mg per day) and bemithyl (250 mg per day) for 15 days. The psychological testing was assessed by a battery of tests: Holmes and Rage scale of stress resistance, Wasserman neurotization test, Hospital anxiety and depression scale (HADS), MMPI 7th scale (scale of psychasthenia), Hamilton depression scale (HDRS), Spilberger anxiety scale, test for alcohol motivation. The reduction of emotional disorders such as depression, anxiety, sensitivity to stress and alcohol motivation (-68%) was registered after course of therapy. **CONCLUSIONS:** Therefore, combination of pyrazidol and bemithyl can be estimated as an effective antiasthenic tool in posttraumatic period after mechanic brain injury and in patients with alcohol dependence.

BACOPA MONNIERA MASKS AMNESIC EFFECTS OF NO SYNTHASE INHIBITOR INDEPENDENT OF NMDA MEDIATED LTP INDUCTION IN MICE. A Anand, MK Saraf, S Prabhakar. Department of Neurology, Post-graduate Institute of Medical Education and Research, Chandigarh, India

INTRODUCTION: NMDA receptor activation is essential for Long term potentiation (LTP) while nitric oxide, synthesized by activation of nitric oxide synthase, is required for sustaining LTP. NMDA receptor antagonists such as MK 801, AP5 and nitric oxide synthase inhibitor such as N_ω-Nitro-L-arginine methyl ester produces amnesia and have been used in many experimental models for studying several anti-amnesic agents. Bacopa monniera Linn (Syn. Brahmi), a herbal Indian drug, has been known to be an anti-amnesic agent in the ancient Indian medical system. **METHODS AND RESULTS:** We applied Morris water maze scale in order to discern the mechanism of action of this drug by studying the degree of reversal of effect of MK801, a NMDA receptor antagonist and N_ω-Nitro-L-arginine (L-NNA), a nitric oxide synthase inhibitors which induces anterograde and retrograde amnesia in mice. Male Swiss albino mice were subjected to muscle incoordination test before performing water maze tasks. Our data revealed that standardized extract of Bacopa monniera neither attenuated the MK 801 induced anterograde amnesia nor improved MK 801 induced retrograde amnesia. On the other hand, L-NNA induced anterograde amnesia was remarkably reversed by this extract. Bacopa monniera (80 mg/kg oral) extract, however, partially attenuated L-NNA induced retrograde amnesia. **CONCLUSIONS:** This report represents the first description of Bacopa monniera's anti-amnesic effect through reversal of L-NNA induced anterograde amnesia.

EMOTIONAL STATUS AND PECULIARITIES OF THE BEHAVIOR IN RAT POSTERITY OF MOTHERS, SUBJECTED THE INFLUENCE OF CADMIUM SULFIDE. L Gubareva, H Agarkova. Department of Psychophysiology, State University, Stavropol, Russia

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According to the European Charter "Surroundings and the Health Protection (1990)", the main task is the forecasting of the far after-effects of anthropogenic influences. The problem of modification of adaptive behaviors by environmental factors is not yet fully studied. The aim of this study was to investigate the influence of chronic effect of threshold dose of cadmium sulfide (CdS) on mother before pregnancy on the endocrine and emotional status, motive and research components of inborn behavior of her posterity. The study of the components of inborn behavior at rats was conducted with the help of multiparametric method (Rodina et al 1993) and the "Open field" test. Level of sexual hormones (testosterone, estradiol) in blood was determined immunoenzymatically, level of 11-oxycorticosteroids - by fluorescentmeter, level of ACTH and CL-activity of hypothalamus - by method of biological test. The posterity was studied in the critical period of ontogenesis 45, 60, 90 and 180 days. The certain volume of physiological solution was introduced to the group of animals under the control. The results were processed statistically. According to the received data, the posterity of the control group felt the highest feeling of fear while reacting on the ethologically inadequate stimuli of living and nonliving nature during all periods of ontogeny. Inadequate stimuli caused the reaction of passive avoiding but adequate stimuli caused active avoiding. It was discovered that 90 - days old rats had strictly expressed sexual differences of integral index of anxiety (IIA). During the period of early sexual maturity the anxiety level of female rats was higher than male rats have. Influence of cadmium sulfide (CdS) on female rats before coming of pregnancy led to the change of anxious-phobic status of the posterity of rats. According to IIA posterity of experimental group had much higher level of anxiety ($P < .05$), starting from the period of sexual maturity when a rat becomes older, its anxiety and fear and a number of stimuli, which provoke them are rising. When experimental rats were 45 days old their state of fear appeared only in answer to more stressogen irritant such as a hand of investigator. When they were 60 and 90 days old they reacted on more or less stressogen lifeless irritants, which revealed their reaction on new conditions. It must be noted that 60-days old rats had predominant reactions of passive avoiding. 90-days old rats beside the reaction of aggression. Sexual differences in reactions on the ethological adequate test-stimuli in experimental rats appeared earlier than in rats of control group. The same results were received during examining the rats' behavior in the conditions of "The open field". Influence of cadmium sulfide on female rats before coming of pregnancy leads to the increase of duration of stay in the central square, decrease of grooming and increase of defecation quantity, which witnesses about increase of fear reaction and oppression of emotion state. Higher indexes of latent period of leaving the centre of square by experimental rats, starting from pubertate period, combined with lower indexes of number of crossed lines. The revealed dynamics says about decrease of motive activity of the posterity from experimental group, in contrast to the posterity from the group under control, which is clearly expressed among rats with sexual maturity ($P < .01$). Vertical research activity of the posterity from experimental group at the end of pubertate period was also lower than activity of the posterity from the group under control. It must be noted that more significant changes were found in number of vertical poles without support. One must pay attention to the fact that inversion of age dynamics of such indexes as duration of staying in the central square, number of washing and defecation, number of crossed lines took place in the period of sexual maturity, which makes higher demands to organism and is great functional loading. All these points out at the decrease of functional reserves of adaptive systems of experimental posterity. The value of emotional, moving and research behavior components correlated when the level of hormones in the central, intermediate and far sections of hypothalamo-hypophyseal-adrenocortical system. So the hormonal disbalance and decrease of reserve possibilities of leading adaptive systems of posterity taken from their mothers, which were influenced by cadmium sulfide, led to the great formation of emotional status and unconditioned reflex behavior. The most significant changes revealed such indexes of unconditioned approximate reaction on novelty as a number of vertical posts without support, the quantity of defecation, the duration of stay in the centre of "The open field". All these points out at their high informative value.

Symposium 8. S.A. Chepurinov's Memorial Symposium on Psychoneuroendocrinology and Biochemistry of Stress. Chairs: YuF Pastuhov, VM Klimenko, AV Kalueff, SG Tsikunov

- IN MEMORIAM: PROFESSOR SERGEI A. CHEPURINOV (1936-2007)
- THE INFLUENCE OF THE MENTAL TRAUMA ON THE BEHAVIOR AND LIPID METABOLISM IN FEMALE RATS. SG Tsikunov, AG Pshenichnaya, AG Kusov, NN Klyueva. Institute for Experimental Medicine RAMS, St. Petersburg, Russia

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- PSYCHONEUROENDOCRINE PECULIARITIES OF PRISONERS CONVICTED ACCORDING ARTICLE 158 CRIMINAL CODE OF THE RUSSIAN FEDERATION. EV Buhantseva, LI Gubareva. Department of Psychophysiology, State University, Stavropol, Russia
- ECTOPIC GROWTH-HORMONE SECRETING PITUITARY ADENOMA: POTENTIAL ROLE OF MULTIVOXEL MR SPECTROSCOPY. D Kozic, M Medic Stojanoska, J Ostojic, L Popovic, N Vuckovic. Institute of Oncology, Diagnostic Imaging Center, Sremska Kamenica; Clinic of Endocrinology and Metabolic Disorders; Clinic of Neurosurgery, Clinical Center of Voivodina; Department of Pathology, University of Novi Sad, Faculty of Medicine, Novi Sad, Serbia
- FROM BIOCHEMISTRY TO BEHAVIOR: PROBLEMS WITH CURRENT TRANSLATIONAL RESEARCH. AV Kalueff, Center for Physiology and Biochemical Research, Moscow, Russia, Bethesda, MD, USA

THE INFLUENCE OF THE MENTAL TRAUMA ON THE BEHAVIOR AND LIPID METABOLISM IN FEMALE RATS. SG Tsikunov, AG Pshenichnaya, AG Kusov, NN Klyueva. Institute for Experimental Medicine RAMS, St. Petersburg, Russia

INTRODUCTION: During the last years, mental diseases, such as depression and posttraumatic stress disorder (PTSD) have become a serious and prevalent problem. Stress plays a key role in pathogenesis of these disorders. Despite a numerous number of investigations on the problem, the neurophysiological mechanisms underlying pathophysiology of stress-related disturbances remain to clear. During the past decades, the data on interconnections of depression, anxiety and PTSD and lipid metabolism disturbance are appeared. However, much of the investigations refer to clinical studies and are contradicted. Most of the neurobiological studies of the consequences of severe psychological stress are performed in male animals. At the same time, there are reports demonstrating sex differences in responses to stress. The clinical observations found that 31% of women and 19% of men develop PTSD when exposed to severe trauma. Studies in rats have shown that female rats appear to be more sensitive to the effects of traumatic stress. These differences depend on fluctuation of the neuroendocrine status in female of mammals. Numerous data suggest about changes of gonadal steroid levels occurring during the reproductive cycle and about influence of estrous cycle not only on reproductive function but non-reproductive behavior. Consequently, stress-related changes in reproductive system activity can enhance the risk of the development of psychopathology. The aim of the present investigation was to characterize behavior reactions and changes of lipid spectrum in blood serum in Wistar female rats survived acute psychological stress that was induced by predator actions. **METHODS:** For research of an emotional disturbances in rats was used a model of mental trauma – the experience of circumstances of death of the partner from predator (python) actions. A group of female rats (200 – 250 g) was exposed to predator for 25 min, and rats who survived this situation were returned to their regular cages thereafter. The emotional state of the animals that have survived a mental trauma of threat of life estimated from 1 to 10 days after psychotraumatic event. The following tests were used: “open field test”, “elevated plus-maze test”, “intruder-resident test” and Porsolt’s test. Every day vaginal secretion of each female rat was collected and observed using microscope to determinate the estrous cycle phase. On the 10-th days after mental trauma the rats were sacrificed by decapitation and a levels of total cholesterol, of α -cholesterol and triglycerides in the blood serum were measured. **RESULTS:** One day after mental trauma in “open field test”, female rats demonstrated signs of depression-like behavior – decreased ambulatory activity and very few number of hole explorations as well as increasing of the appearance of short grooming. On the 2-th day after psychological stress a significant increase in anxiety level in female rats in the “elevated plus-maze” test was revealed. 3-5 days after predator exposure, we revealed changes of behavior in the “intruder-resident” test - decrease of communicative behavior and increase of aggression level. 7-9 days after mental trauma, the rats demonstrated increased immobility in the Porsolt’s test (vs. controls). In the second part of experiment on the 10-th day after psychical trauma lipid spectrum of blood serum of rats was analyzed. The increased concentrations of total cholesterol, of α -cholesterol and of triglycerides in blood serum were revealed in experimental animals in comparing with the intact control group ($p < .05$). After determination of the estrous cycle phase, the rats were separated on four groups (proestrus, estrus, metestrus and diestrus). Analysis of the data showed that more significant changes of the behavior in response to mental stress were present in rats then estrus phase. The enhanced concentrations of total cholesterol and of triglycerides in blood after psychotraumatic event were found only in rats in the proestrus and diestrus

phases. An increased level of α -cholesterol was revealed only in rats in the phase of diestrus. **CONCLUSIONS:** The results of the present study demonstrate the stress-related changes in behavior in female rats that have survived a mental trauma. The rats exhibit a decrease of locomotor activity, investigative behavior, communication and an increase of immobility in Porsolt's test that, according to DSM-IV criteria for depression, could be characterized as depressive behavior or depressive-like state. However a number of behaviors such as the high level of anxiety and aggression developed as a result of mental trauma remind human posttraumatic stress disorder. The main reason of PTSD is mental trauma caused by threat of life. After of the psychical trauma appear the changes of lipids metabolism. The disorders in female rats are remained during not less than 10 days and depend on the estrous cycle phase. Thus, the data suggest specific role of gonadal steroids in regulation of response to stress in female rats.

PSYCHONEUROENDOCRINE PECULIARITIES OF PRISONERS CONVICTED ACCORDING ARTICLE 158 CRIMINAL CODE OF THE RUSSIAN FEDERATION. EV Buhantseva, LI Gubareva.

Department of Psychophysiology, State University, Stavropol, Russia

INTRODUCTION: Every day a man comes across various socially undesirable behavior, i.e. aggression, hooliganism, illegal actions. What are the motives of such behavior? What makes a person do harm to himself and to people again and again? What are the consequences of antisocial behavior for a society? Thus, the study of personality deformation under the conditions of changeable environment (territorial, local conflicts, economic and social instability of a society) is of particular importance. Taking into account all which were said above, it must be noted that the study of endocrine and psychophysiological peculiarities of prisoners is of great importance because the role of hormones in the formation of a prisoner's personality is badly studied. Under the conditions of natural experiment, we studied individual-typological peculiarities of a person and peculiarities of hormone status of male prisoners convicted according to article (par.) 158 (p.1 – larceny; p.2 – group larceny or repeated; p.3 – larceny performed by organized group or a person who was convicted before) CCRF. Control group comprised healthy male students of Stavropol State University. The hormone level in saliva (cortisol, testosterone, estradiol) was determined by immune-ferment method. Personal-typological peculiarities were studied by a number of psychological methods "Bass-Darky", "Taylor". The results were processed statistically. **RESULTS, DISCUSSION AND CONCLUSIONS:** The prisoners convicted according to par 158, p.1 had reduced cortisol levels ($10,1 \pm 5$ nmol/l); par 158, p.2 ($17,9 \pm 1,0$ nmol/l) and par 158, p.3 ($12,0 \pm 1,1$ nmol/l) vs. control group ($20,6 \pm 1,5$ nmol/l). Importantly, compared to controls ($3,1 \pm 4$ nmol/l), prisoners with different cortisol levels have changes in the content of testosterone: par 158, p.1 ($2,6 \pm 7$ nmol/l), par 158, p.2 ($2,5 \pm 9$ nmol/l), par 158, p.3 ($4,8 \pm 1,0$ nmol/l), respectively. In this situation, all prisoners have much higher levels of thyroxin than in the control group. Increase of thyroxin may conduct to the violent behavior, to the unwillingness to make monotonous activities. And the prisoners had higher level of estradiol in comparison with the group under control. The prisoners convicted according to par 158, p.3 have higher physical aggression, hostility, anxiety level in comparison with the prisoners convicted according to par 158, p.1 and 158, p.2. Our data show the important role of glucocorticoadrenal and sexual hormones in the formation of constitutional and personal-typological peculiarities. It is proposed that the change of constitutional-typological peculiarities is the base for the choice of that asocial environment, which is the developing factor of criminal stereotype of behavior.

ECTOPIC GROWTH-HORMONE SECRETING PITUITARY ADENOMA: POTENTIAL ROLE OF MULTIVOXEL MR SPECTROSCOPY. D Kozic, M Medic Stojanoska, J Ostojic, L Popovic, N Vuckovic. Institute of Oncology, Diagnostic Imaging Center, Sremska Kamenica; Clinic of Endocrinology and Metabolic Disorders; Clinic of Neurosurgery, Clinical Center of Voivodina; Department of Pathology, University of Novi Sad, Faculty of Medicine, Novi Sad, Serbia

INTRODUCTION: Ectopic pituitary adenomas are rare neoplasms, most frequently arising along the cranio-pharyngeal migration path of the Rathke's pouch. Only several reports of patients with growth hormone (GH) producing extrapituitary adenoma have been reported. Numerous studies regarding MR spectroscopic characteristics of malignant brain tumors are available in the literature. MR spectroscopic features of hormonally active pituitary adenomas are however unknown. The purpose of this report is to present the appearance of MR spectrum of ectopic GH secreting macroadenoma before and after the lanreotide treatment, and to show the potential advantages of multivoxel MR spectroscopy (3D chemical shift imaging technique) in order to detect hormonally active segments of the tumor. **METHODS:** Detailed, one year long clinical, hormonal, MR imaging and MR spectroscopic

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pretreatment and posttreatment follow-up was performed in a patient with ectopic growth hormone pituitary adenoma. **RESULTS:** A 41-year-old man noticed gradual enlargement of his nose, lips, hands and feet over the past 7 years. He also complained on headaches and infrequent periods of blurred vision. Physical examination revealed the acromegalic appearance and the presence of hypertension (160/80mmHg). Other clinical findings were unremarkable. Laboratory examination revealed the presence of GH and IGF – I elevation. Absence of GH suppression during oral glucose tolerance test (54.3-43.3-44.8-39.1 ng/ml) was evident. Low-normal levels of follicle-stimulating hormone (FSH) and luteinising hormone (LH) were found, associated with decreased level of testosterone, suggesting the presence of central hypogonadism. The remaining hormonal activity of the adenohypophysis was preserved. No functional abnormalities of neurohypophysis were detected. The visual acuity and visual fields were normal. MR examination revealed the presence of a huge mass involving the sellar floor, invading the clivus and extending into the sphenoid sinus and the region of the posterior ethmoid cells, measuring 40mm in antero-posterior and 53mm in oblique cranio-caudal dimension. Bilateral parasellar spreading of the tumor was seen with dislocation of the cavernous segments of the internal carotid arteries, more prominent on the left, associated with no consequent disturbance of the blood flow. The pituitary stalk was deviated to the left. The tissue of the pituitary gland was completely intact and clearly demarcated from the tumor. The tumor was partly extirpated via a trans-sphenoidal approach. The presence of unaffected pituitary tissue was confirmed during the procedure. The histological examination of the obtained specimen showed the features of pituitary adenoma. No clinical improvement was noted after the partial tumor reduction. Slightly decreased, but still high levels of GH and IGF – I and the signs of central hypogonadism were evident. The remaining hormonal activity of the adenohypophysis was normal. Slightly decreased, but still high levels of GH and IGF – I and the signs of central hypogonadism without any signs of clinical improvement were also evident thirty days after conformal radiation therapy (total dose 54Gy/30 fractions). MR examination, performed after surgical procedure and radiation therapy revealed partial reduction of the tumor size, measuring 33mm in antero-posterior and 43mm in oblique cranio-caudal dimension. Application of the single voxel spectroscopy SE 135 technique with voxel size 11x11x11 mm, revealed the elevated choline peak in the paramedial aspect of the tumor. According to persistent acromegaly and no signs of clinical improvement, the treatment with long-acting somatostatin analogue (Lanreotide, Somatulín autogel 120mg subcutaneously/4weeks) was initiated. Marked clinical improvement with significant regression of acromegaly, associated with marked decrease of GH and IGF-I levels was observed after 11 months of treatment. Improvement of FSH, LH and testosterone levels was also evident. No side effects of treatment were detected. MR examination revealed the presence of marked shrinkage of the tumor associated with cystic degeneration of the adenoma, consistent with positive effect of the medical treatment. Application of the single voxel MR spectroscopy (MRS) SE 135 technique with voxel (size 11x11x11 mm) positioned at the place of previously elevated choline peak, revealed electronic noise only (complete lack of any metabolites). 3D chemical shift imaging technique that allows small voxel sizes was additionally performed. Multivoxel spectroscopic data were obtained using 3D SE 135 sequence, with voxel size 5 x 5 x 5 mm, FOV 80x80x80 mm and volume of interest 40x40x40mm, 4 averages. The presence of "choline only" spectrum was identified on few locations within the lesion. **CONCLUSIONS:** Although single voxel MRS is useful and relatively rapid method for obtaining the information regarding the metabolic activity, it is unable to contribute in defining the spatial heterogeneity of the mass. However, multivoxel MRS is able to add new information relevant for not only the diagnosis, but also clinical management. The importance of multivoxel MRS in routine practice is still under investigation, however there is a reason to expect that this modality could provide information relevant for choosing adequate treatment in individual patients, like targeting of active portions of the tumor during radiosurgery.

Day 3. May 18, 2007. Venue: Oktyabrskaya Hotel, Ligovsky Prospect, 10

Symposium 9. Translational research in stress neuroscience and biological psychiatry. Chairs: VM Klimenko, IV Ekimova

- CHANGES IN THE BASIC PARAMETERS OF THE NEURONAL ACTIVITY OF THE MEDIAL SEPTAL COMPLEX IN THE BRAIN OF ANIMALS WITH A MODEL OF TEMPORAL LOBE

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EPILEPSY. AE Malkov, IYu Popova, Institute of Theoretical and Experimental Biophysics RAS, Pushchino, Russia

- TENOTEN AMELIORATES MEMORY IMPAIRMENTS AND IMPROVE IMPULSIVE AND INADEQUATE BEHAVIOR OF IMMATURE RATS IN EXPERIMENTAL MODEL OF ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD). TA Voronina, AV Volkova, ES Zhavbert, IA Kheyfets, JL Dugina, SA Sergeeva, OI Epstein. Materia Medica Holding, State Zakusov Institute of Pharmacology, Moscow, Russia
- THE ROLE OF SEROTONINERGIC BRAIN STRUCTURES IN NEUROTENSIN INFLUENCE MECHANISM ON DEFENSIVE BEHAVIOR IN RATS. NP Shugalev, AV Stavrovskaja, S Olshanskij, G Hartmann, L Lenard. State Research Center of Neurology RAMS, Moscow, Russia; Institute of Physiology, Pecs University, Pecs, Hungary
- EXPOSURE TO ELECTROMAGNETIC FIELDS AND DEPRESSION. F Partovi Rad, M Sattari. Iran Water and Power Resources Development Co, Tehran, Iran
- REACTIONS OF NEURONS OF THE NUCLEUS TRACTUS SOLITARIUS TO CHRONIC VIBRATION. SH Sarkisyan, SM Minasyan, ML Yeghazaryan, AM Haroutyunyan. Yerevan State University, Yerevan, Vanadzor State Pedagogical Institute, Vanadzor, Armenia

CHANGES IN THE BASIC PARAMETERS OF THE NEURONAL ACTIVITY OF THE MEDIAL SEPTAL COMPLEX IN THE BRAIN OF ANIMALS WITH A MODEL OF TEMPORAL LOBE EPILEPSY. AE Malkov, IYu Popova, Institute of Theoretical and Experimental Biophysics RAS, Pushchino, Russia

INTRODUCTION: Temporal lobe epilepsy (TLE) is one of the most widespread and drug-resistant neurological diseases. Most studies of temporal lobe epilepsy have been focused on the properties of the hippocampus (locus of principal changes) and the hippocampal-entorhinal circuitry. However, it is known that the activity and excitability of the hippocampus are modulated not only by the neocortical (via entorhinal cortex), but also the subcortical input (via medial septal nucleus-diagonal band of Broca complex, MS-DB). At present, the role of the septum, a pacemaker of the hippocampal theta rhythm, in the development of TLE remains unknown. Investigations along this line are very important for understanding the mechanisms of formation of epileptiform activity in the hippocampus. The aim of this study was to analyse the basic parameters of activity of MS-DB neurons in epileptic animals in comparison with control ones. **MATERIALS AND METHODS:** The experiments were performed on two groups of guinea pigs: control (n=5) and epileptic (n=6). The model of TLE was created by injection of kainic acid (.6 µg/.3 µl) into the ventral hippocampus, which induced the status epilepticus. After three months, the extracellular recording of the spontaneous neuronal activity was performed in vitro on slices taken from the MS-DB. The pacemaker properties of neurons were revealed by synaptic transmission blockade. **RESULTS AND DISCUSSION:** In the control group (n=43), the mean frequency of neuronal discharges was 9.0 (.96 imp/s). Three groups of neurons depending on activity pattern were distinguished: regular cells (n=24, 54.8%), irregular cells (n=15, 34.9%), and rhythmic burst cells (n=4, 9.3%). The mean frequencies in the groups were 9.65 (1.16, 6.17 (1.33 and 15.38 (3.39 imp/s, respectively). Most of the burst neurons (3 cells, 75%) fired by short bursts with a frequency of 1.74 (.25 Hz, and one cell (25%) possessed a very slow burst activity with a frequency of .29 Hz. All burst neurons (4 cells) were endogenous pacemakers. In the group of epileptic animals, 47 neurons were registered. The mean firing frequency in this group was substantially higher (17.1 (1.63 imp/s) compared with the control (P<.01). The distribution of neurons by activity pattern changed: 43.75% of regular cells (n=21), 29.17% of irregular cells (n=14), and 27.08% of rhythmic burst cells (n=13). The mean frequencies of activity in these groups were 16.47 (1.76, 16.99 (3.95 and 18.34 (3.45 imp/s, respectively). An analysis of mean firing frequency in each group showed that the increase in the total activity of septal neurons in the epileptic brain results from an increase in the frequency in regular and irregular cells. The number of neurons with the rhythmic burst activity sharply increased in the epileptic brain (12 cells, 25.5%) compared to the control. According to burst frequency, these neurons were divided into two groups, which corresponded to the groups in normal animals: cells with a burst frequency of 2.48 (.45 Hz (8 cells, 67%) and .26 (.02 Hz (4 cells, 33%). However, it should be noted that 4 of 12 burst neurons had no endogenous pacemaker properties. A comparative analysis of the basic characteristics of MS-DB neurons of control and epileptic animals revealed essential differences between these groups. In the epileptic brain, the total neuronal activity strongly increased (from 9.0 to 17.1 imp/s), indicating a weakening of inhibitory processes in the MS-DB. This is consistent with morphological data showing that inhibitory (GABAergic) septal neurons, which normally control the excitability of all MS-DB neuronal populations, are partly lost in the

epileptic brain (Colom et al 2006). It is known that MS-DB includes three groups of interrelated neurons, which differ in neurochemical and electrophysiological properties: GABAergic, glutamatergic, and cholinergic cells. A part of GABAergic and glutamatergic neurons are endogenous burst pacemakers, though the pacemaker potential is less expressed in glutamatergic cells. Cholinergic neurons do not exhibit any pacemaker potential. The decrease in the number of inhibitory cells can lead to intraseptal changes, in particular, to the sprouting of cholinergic and glutamatergic axon collaterals, and consequently, an increase in the excitability of remaining neurons. In the analysis of electrophysiological parameters of MS-DB, special consideration should be given to burst activity, which is known to make an important contribution to the generation of the hippocampal theta rhythm. The data obtained showed the essential increase in the number of burst neurons in MS-DB of the epileptic brain (25.5% vs. 9.3% in control). This fact can be partly explained by that neurons possessing no endogenous pacemaker properties become involved into burst activity. Indeed, a quarter of burst neurons (putative cholinergic and/or glutamatergic neurons) completely stop firing under the blockade of synaptic transmission. However, the portion of pacemaker burst neurons also increased, probably due to the enhancement of the burst activity of glutamatergic neurons as a consequence of the weakening of tonic inhibitory influence. **CONCLUSION:** Essential changes in the basic parameters of spontaneous activity of MS-DB neurons in the epileptic brain were revealed for the first time. The data obtained can extend our understanding of the mechanisms of TLE and provide a basis for new ways of treatment of this disease. The work was supported by the Russian Foundation for Basic Research, grant 06-04-48637.

TENOTEN AMELIORATES MEMORY IMPAIRMENTS AND IMPROVE IMPULSIVE AND INADEQUATE BEHAVIOR OF IMMATURE RATS IN EXPERIMENTAL MODEL OF ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD). TA Voronina, AV Volkova, ES Zhavbert, IA Kheyfets, JL Dugina, SA Sergeeva, OI Epstein. NPF Materia Medica Holding, State Zakusov Institute of Pharmacology, Moscow, Russia

INTRODUCTION: ADHD is one of the most common neurobehavioral disorders of childhood; its prevalence is variably estimated to be between 4 and 10%. About 50 per cent of patients having ADHD keep its symptoms and signs in adulthood. Among clinical presentations of ADHD there is physical agitation, impulsive behavior and thought, inattention, inability to concentrate, talkativeness, distractibility etc. Currently used medications such as psychostimulants, tricyclic antidepressants, nootropics, anxiolytics have many registered side effects and should be subject to careful prescription. Taking into account the young age of the patients suffering from ADHD, the design and development of novel and safe drugs with the best benefit/risk ratio for the treatment of ADHD is an unmet medical need. The aim of the present work was to study the efficacy of tenoten, a novel anxiolytic proved effective in the treatment of anxiety disorders in adults, in rat "model" of ADHD in comparison with phenibut and evaluate memory-enhancing activity of tenoten in passive avoidance conditioned reflex (PACR) in comparison with piracetam. **METHODS:** 105 young (30-35 days old) hyperactive outbred male and female rats with impulsive and inadequate behavior were involved in the study of tenoten efficacy in ADHD "model". The open-field test, Brady and Nauta scales were used to estimate the locomotory and exploratory activity and impulsive inadequate behavior of rats. The rats were divided into 3 groups: 1) tenoten (n=28; 2.5 ml/kg); 2) phenibut (n=20; 125 ml/kg) 3) distilled water (control; n=49; 2.5 ml/kg). Rats were given respective compounds once a day intragastrically for 7 days. The cognitive functions of rats were evaluated in PACR test (the entrance into dark chamber was punished by a series of 5 foot shocks (1s; .45 mA); the interval between shocks was 2 s). Emotional status and locomotory activity were estimated in the Elevated Plus Maze (EPM) test. A number of entries into the open and closed arms, a number of entries to the central square, time spent in the central square and in the open arms were registered. 112 young (30-35 days of age) outbred male and female rats were used in the study of tenoten and piracetam nootropic activity in PACR test. The rats were divided into 4 experimental groups: 1) intact animals (n=28); 2) tenoten (n=28; 2.5 ml/kg); 3) piracetam (n=28; 400 mg/kg in volume 2.5 ml/kg); 4) distilled water (control; n=28; 2.5 ml/kg). Rats were given respective compounds once a day intragastrically for 10 days. 56 of them were twice subcutaneously injected with scopolamine (1.4 ml/kg), and then tested in PACR test. The rest of the animals were involved in the suboptimal negative passive avoidance conditioned reflex test (PACR/sn). Rats received 8 punishing electrical shocks (1s; .6 mA) with 2 s interval in PACR test and 5 punishing electrical shocks (1s; .45 mA) with 2 s interval in PACR/sn. Nootropic effects of medications were assessed by the increase in the latency to enter the dark chamber. **RESULTS:** After 7-day treatment with tenoten or phenibut, the young hyperactive rats

showed 3-fold increase in the latency to enter the dark chamber. 40% rats of tenoten group and 20% of piracetam group did not enter the dark chamber. In EPM test, tenoten and phenibut caused 5.2- and 3.6-fold increase in a number of entries into the open arms respectively ($p < .05$), and 2- and 3.3-fold increase in a number of entries to the central square respectively ($p < .05$). Compared with tenoten, the anxiolytic activity of phenibut was more pronounced: phenibut showed a 2-fold increase in time spent in the central square and a 1.3-fold in time spent in the open arms ($p < .05$ vs tenoten). However, tenoten was significantly superior to phenibut in reducing the locomotory activity of hyperactive rats in EPM. In PACR test, as a result of scopolamine injection, the latency to enter the dark chamber in the control group decreased by 6.2 times ($p < .05$ vs intact group). On 10-day administration tenoten showed a memory-enhancing activity: the latency to enter the dark chamber was 4.3-fold higher than in control ($p < .05$). In piracetam group, the latency to enter the dark chamber was only a 3.3-fold higher ($p < .05$ vs control). In PACR/sn test, we confirmed nootropic activity of tenoten on 10-day administration: 2.5-fold increase in the latency to enter the dark chamber was registered in tenoten group ($p < .05$, vs control), 1.4-fold increase – in piracetam group ($p < .05$ vs control). **CONCLUSIONS:** Tenoten improved memory and impulsive and inadequate behavior of immature rats in experimental "model" of ADHD. Although anxiolytic activity of tenoten was slightly weaker than that of phenibut, nootropic and anti-amnesic effects of tenoten surpassed the effects of piracetam on 10-day administration.

THE ROLE OF SEROTONINERGIC BRAIN STRUCTURES IN NEUROTENSIN INFLUENCE MECHANISM ON DEFENSIVE BEHAVIOR IN RATS.

NP Shugalev, AV Stavrovskaja, S Olshanskij, G Hartmann, L Lenard. State Research Centre of Neurology RAMS, Moscow, Russia; Neurophysiology Research Group, Institute of Physiology, Pecs University, Pecs, Hungary

INTRODUCTION: Out of the literature it is known about reciprocal attitudes between catecholamine- and serotonergic (5-HT) structures of a brain in maintenance of defensive behavior. Increasing of dopaminergic system activity causes deterioration of a conditioned reflex of passive avoidance with its subsequent acceleration of extinction. On the other hand, serotonin synthesis inhibitor administration, para-chlorophenylalanine, on the contrary, facilitated development of active avoidance performance in rats. Infringement of development of a conditioned reflex of active avoidance in rats was observed after neurotensin administration into lateral ventricles of a brain. Such action of this neuropeptide is explained by its oppressing influence on dopaminergic brain structures. However, the specified neurotensin effects can speak its influence on function not only dopamin-, but also 5-HT structures of a brain and besides depend on a place of its administration in CNS. The main aim of research is finding-out of a role of 5-HT brain system in mechanisms of neurotensin influence on behavior after the painful stress in rats. **METHODS:** Male Wistar rats weighing 250-300g were used in the experiment. Intensity of escape reactions was estimated by latency of entering the dark chamber where the rats got a unavoidable electrical foot shock (2mA, 3s). Neurotensin (Sigma) or serotonin 1A receptor agonist, 8-hydroxydipropylaminotetralin (8-OH-DPAT) was injected into substantia nigra of the rat's brain (2,5µg in .7µl) 10 minutes before (or after) electrical shock presentation. Neurotensin microinjections were carried out 24 hours after electrical shock presentation too. The passive avoidance learning was tested for the next 4 days. Motor activity of the animals was studied in an "open field" and "elevated X-maze" tests. Influence of local neurotensin and 8-OH-DPAT microinjections into substantia nigra of a brain on behavior of rats with 5-HT neurons of dorsal raphe nucleus lesion was studied. The lesion was carried out by local administration of neurotoxin. The analysis of neurotensin and 8-OH-DPAT influences on recall of passive defensive reactions and also their influence on painful stimulation afteraction was spent. Serotonin and its metabolite 5-hydroxyindolacetic acid (5-HIAA) contents of the caudate nucleus (<50 mg) and hypothalamus of rat brain (<20 mg) were determined by HPLC. **RESULTS, DISCUSSION AND CONCLUSIONS:** We showed that lesion of 5-HT neurons led to increasing of intensity of passive avoidance reactions and motor activity in rats. The neurotensin microinjections into substantia nigra of a brain directly before or right after injuring of painful stimulation weakened effects of neurotoxin in rats with neurotoxic lesion of 5-HT neurons and restored parameters of intensity of passive avoidance reactions up to a control animal level. Such neurotensin microinjections also led to decreasing of latency of entering open arms of elevated X-maze and increasing of staying period in it. The behavioral effects of 8-OH-DPAT microinjections into substantia nigra were similar to neurotensin effects. In case of animals without lesion of 5-HT neurons the neurotensin microinjections led to infringement of recall of passive avoidance reactions and caused increase in motor activity. The administration of neurotensin in 24 hours after painful stimulation injuring directly before testing of a reflex did not weaken intensity of

passive avoidance reactions neither in rats with neurotoxic lesion nor in rats without it. The administration of neurotoxin was accompanied by decrease, and the administration of neurotensin, on the contrary - increase of the maintenance of serotonin and its metabolite, (5-HIAA), in caudate nucleus of rats brain. Behavioral effects of neurotensin in rats with deficiency of 5-HT neurons function are caused by its normalizing influence on an emotional condition of animals during formation the conditioned reflex that promotes increase of adaptive character of defensive behavior.

EXPOSURE TO ELECTROMAGNETIC FIELDS AND DEPRESSION. F Partovi Rad, M Sattari. Iran Water and Power Resources Development Co, Tehran Iran

INTRODUCTION: Since the nervous system is composed of electrically excitable tissues, it is plausible that they can be stimulated by electromagnetic fields (EMF). So the aim of this study was to assess the correlation between depression and exposure to 50Hz electromagnetic fields. **MATERIAL AND METHODS:** 50 male workers from electric power substations or power plants who had worked there for more than 3 years were selected as case group and 50 healthy men as control group. The level of depressive symptoms was measured with the 20-item center for epidemiologic studies depression (CESD-20) SCALE. **RESULTS AND DISCUSSION:** 38 workers (76%) fit criteria for significant depressive symptoms, while in control group, 18 individuals (36%) had significant depressive symptoms. Statistical analysis showed significant difference regarding depressive symptoms between case and control groups ($P < .05$). **CONCLUSIONS:** The data of this study provide some evidence for an association between occupational electromagnetic fields and depression that warrants further evaluation.

REACTIONS OF NEURONS OF THE NUCLEUS TRACTUS SOLITARIUS TO CHRONIC VIBRATION. SH Sarkisyan, SM Minasyan, ML Yeghazaryan, AM Haroutyunyan. Yerevan State University, Yerevan, Vanadzor State Pedagogical Institute, Vanadzor, Armenia

INTRODUCTION: The pathogenesis of vibration disease under common vibration has been determined by the complex of changing in the functional status of different part of nervous system. For account of complex labyrinthine-extralabyrinthine interaction of the afferent system in the reaction of the brain structures ensuring the central regulation of vegetative and somatic functions are involved. The vestibular apparatus has a dominant effect on the development of «moving disease», which is accompanied by a series of autonomic disturbances (drowsiness, cold sweats, nausea, vomiting, etc.) resulting from the interaction of the autonomic and somatic systems. A number of histomorphological studies demonstrate the direct projection of the vestibular nucleus to the structures of vagus complex. One of the perspective directions in studying of bulbar mechanisms of regulation vestibule-autonomic functions is finding out of a role in these processes neurons of nucleus tractus solitarius (NTS), on which terminate primary afferent fibers of n.vagus. The aim of the present work was to compare changes in background impulse activity (BIA) of neurons in the right and left NTS at different durations of exposure to vibration. **METHODS:** Experiments were performed in acute experimental conditions using rats weighing 230-250 g anesthetized with Nembutal (40 mg/kg, i.p.). Spike activity was recorded from neurons using extracellular glass microelectrodes. Animals were exposed to vibration using vibroplatform (frequency 60 Hz, amplitude .4mm) daily for 2 h/day. Spike activity from neurons in NTS was recorded after 5, 10 and 15 days of vibration. In control group was registered impulse activity of 134 neurons (54-right, 80-left), after 5 days – 145 neurons (83- right, 62-left), 10 days – 148 (73-right, 75-left), 15 days with sessions of vibration – 149 neurons (56-right, 93-left) of NTS. Recording and analysis of spike activity from neurons in the NTS were performed using a specially developed computer program. Sequential segment of interspike interval (ISI) including up to 1200 action potentials were analyzed. The non-parametric Kolmogorov-Smirnov test was used with sliding frequency plots to assess stationary BIA. When segments were stationary, normalized histograms of ISI and autocorrelograms were plotted. For stationary neurons we calculated the mean discharge frequency and coefficient of variation of ISI. Histograms of ISIs were classified as mono-, bi- and polymodal. According to the impulsation frequency, the neurons under study were divided into three groups, with a low (below 10Hz), medium (10 to 30Hz) and high (above 30Hz) frequency of BIA. NTS neurons were classified according to the level of regularity of spike flow (with a regular BIA, intermediate regularity of spiking, irregular discharging neurons). **RESULTS:** The comparative analysis of characteristics BIA of neurons in left and right NTS in intact animals revealed significant changes of distributions of ISI at type of dynamic activity, the value of average frequency of BIA and frequency distribution. Other parameters of the BIA generated by NTS neurons of both nuclei in the norm had no significantly distinctions. So in intact groups the average frequency BIA of NTS was

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composed on the right $15,4 \pm 2,2$ Hz, on the left $22,5 \pm 2,4$ Hz ($P < .05$). At the degree of regularity in both at right and left NTS the dominated neurons with unregulated ISI (51,8% and 50,0% respectively). The analysis of distributions of neurons at types of dynamic activity in intact animals the dominance of neurons of train-grouped activity (on the right 48,2%) and units with local changes in ISI (on the left - 43,8%) were revealed. As well as in right and left NTS were dominated the neurons with polymodal distribution of ISI (61,5% и 51,5% respectively). Long everyday vibration stimulation induced significant modifications of the BIA generated by NTS. The comparative analysis of parameters of average frequency of neurons in the left and right NTS has revealed significantly distinctions after 5- and 10-days long vibrating expositions ($10,9 \pm 0,8$ Hz, $17,8 \pm 1,1$ Hz, in the right and $17,0 \pm 1,5$ Hz; $14,2 \pm 1,1$ Hz in the left NTS respectively, $p < .05$). Frequency distributions of BIA in postvibration period statistically changes of both in 5-th (on the right low-frequency 55,5% and on the left mean grouped 60,6% $P < .01$), in 10-th (on the right and on the left mean grouped 66,2% and 56,0%, $P < .1$) days. Coefficient of variation of ISI significantly changed only after 15 days of long vibration influences ($79,5 \pm 3,1$; $69,8 \pm 2,1$ %). Vibration for 10 days led to definite imbalance in parameters at neurons of the right and left NTS at degree of regularity ($P < .01$). Vibration for 10 and 15 days produced significant changes of dynamic activity of neurons in the both NTS, where on the right were dominated the neurons with local and train-grouped BIA (50,7% and 78,6% respectively), on the left - only with train-grouped BIA (46,7% and 53,8% respectively, $P < .05$). The modality parameter of histograms of BIA of the right and left side of NTS neurons were significantly distinguished after 5-th ($P < .05$) and 10-th ($P < .01$) days vibration exposition. **CONCLUSIONS:** Under chronic vibration stress, the participation of vegetative components in reflexive reaction of organism is sharply increased and can lead to occurrence of tension reaction. At that all complex of protect-regenerative reactions of an organism, the decrease of functional stability of vestibular sensory system and its disturbance of accuracy of performance of body transfer of in space were included.

Symposium 10. Experimental models of stress – III. Chair: AV Kalueff

- EFFECT OF THERMAL PRECONDITIONING ON ANXIETY-RELATED BEHAVIOR IN RATS SUBJECTED TO ACUTE STRESS. MV Chernyshev, OA Sapach. Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia
- FEEDING INDUCED THROUGH MILD STRESS IN THE RAT. E-M Kim, E O'Hare. University of Ulster, Coleraine, Queens University, Belfast, Northern Ireland, UK
- THE EFFECTS OF QUERCETIN ON BEHAVIORAL PARAMETERS OF STRESSED RATS IN THE SUOK-TEST. I Tubaltseva, V Lozova, E Tukalenko, M Makarchuk. Kyiv National Taras Shevchenko University, Kyiv, Ukraine
- THE DEVELOPING UTILITY OF THE SUOK TEST IN ANXIETY PHARMACOLOGY AND BEHAVIORAL RESEARCH. AV Kalueff, A Minasyan, T Keisala, Y-R Lou, P Tuohimaa. University of Tampere and Tampere University Hospital, Tampere, Finland

EFFECT OF THERMAL PRECONDITIONING ON ANXIETY-RELATED BEHAVIOR IN RATS SUBJECTED TO ACUTE STRESS. MV Chernyshev, OA Sapach. Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia

INTRODUCTION: Stress protein, or heat shock protein, 70 kDa (HSP70) is one of the most conservative systems of cell and organism protection from various damaging factors (Pastukhov, Ekimova, 2005). The simplest method of the enhancement of HSP70 expression in various organs and tissues, including CNS, is a thermal preconditioning (TP) approach. Treating cells with TP results in realization of chaperone function of HSP70, associated with protection properties (Guzhova et al 2000; Ellis, 1990). Protective effects of TP have been elicited in cells and organisms subjected to a large number of different damaging factors such as superheating, hypoxia, radioactive emanation, heavy metals, ethyl alcohol, infectious and cytotoxic factors (Pockley, 2001; Ellis, 1990). A recent pilot investigation (Ekimova et al 2005) has revealed a positive effect of TP on the symptomatology of seizure convulsions in rats predisposed to audiogenic seizures. However, so far there is no literature data related to possible effects of TP on animal behavior after stress. The purpose of the present study was to examine an effect of TP on several indices of anxiety assessed in the elevated plus maze test in rats subjected to acute restraint stress. **METHODS:** Experiments were carried out in adult male Wistar ($n=30$) and Krushinsky-Molodkina ($n=15$) rats. Within each strain all the animals were divided into 2 groups, experimental and control (TP). The TP process was conducted inside a

thermal chamber (size 50x50 cm). Anesthetized with nembutal animal were placed inside the chamber (50° C constant temperature) and present there for 20 min since the moment of the rise of rectal temperature 42° C. Control group was also Anesthetized, but not placed inside the chamber. 24 h later both groups were subjected to restraint stress, staying within a rounded transparent plastic penal for 30 min. Immediately after the end of the restraint session behavior of the rats were evaluated in the elevated plus maze (EPM) test. The maze was elevated to a height of 50 cm and consisted of 2 closed arms (CA) and 2 open arms (OA), divided into 5 squares for each one. The animal was placed at the cross of the arms (central platform) to start a 5 min test session. The behavior of each animal in the maze was analyzed, based on standard spatiotemporal measures. Data obtained were analyzed by Mann-Whitney U-test. **RESULTS AND DISCUSSION:** Analysis of behavior in Wistar rats subjected to restraint permitted to find out a number of statistically significant differences between experimental group (treated with TP) and control group. It was found that animals of the experimental group exhibited a considerable increase in the level of the following behavioral parameters: (1) the number of head dipping toward the OA, (2) the number of entries onto the OA and (3) CA, (4) total time spent on the OA and (5) CA, (6) the number of head dipping down toward the floor, (7) the number of squares crossed within the OA, (8) the number of OA shifts and (9) CA, (10) percentage of time spent and the percentage of arm entries in the OA, as compared to control. Totally, the levels of these measures may indicate a balance between the 3 conflicting tendencies: anxiety (fear of unprotected open arms and a height), exploration and locomotor activity. A factor analysis of the behavioral repertoire in the EPM test has shown that any of the tendencies is contaminated with another one (Wall 2000). It carries a loading of a certain rate. Thus, measures related to OA entries are conventionally considered to have a predominant loading on anxiety. The less value of the measure is observed, the more amount of anxiety is presented. Data obtained in our experiment may indicate a great decrease in anxiety in animals treated with TP in comparison with control. It reflects the changes observed in parameter 2, 4, 6, 7, 8 and 10 ($p < .0001$), where the last one has been validated as best measure of anxiety (File 1992). It has a loading of 95% on this factor (Lister et al 1987). Changes found in parameters 1, 3, 4, 6, 9 may indicate a certain increase in the level of exploration and locomotor activity, where parameter 3 loads on locomotor activity with the maximum rate (File 2001). However, no changes in locomotor activity were observed in rearing activity, which disrupts the integrity of this behavior. No effect of TP was found in the number of defecations and urinations conventionally considered as an index of emotionality (Hall 1934). It is consistent with the fact that analysis of other emotionally loaded behaviors such as freezing, immobilization and grooming (correct and incorrect) revealed the same result. No differences were found in comparison of TP effects between Wistar and Krushinsky-Molodkina rats. The results of the present study showed that treatment of animals with TP greatly decreases the level of anxiety, increases the levels of exploration and a component of locomotor activity and reveals no effect on emotionality. Two different strains, Wistar and Krushinsky-Molodkina rats, showed the same tendencies of the effects. Thus, thermal preconditioning approach can be proposed to be a powerful method for correction of behavioral disorders.

FEEDING INDUCED THROUGH MILD STRESS IN THE RAT. E-M Kim, E O'Hare. University of Ulster, Coleraine, Queens University, Belfast, Northern Ireland, UK

INTRODUCTION: Mild stress is known to increase consummatory behavior, and applications of this observation have been employed by bar owners for many years. This phenomenon of increased consummatory behavior in the presence of mild stress has been studied in both human and non-human animals. The object of the current study was to investigate the mechanism by which mild stress enhances consummatory behavior. **METHODS:** Experimentally naïve male Sprague-Dawley rats were trained to respond under a cyclic-ratio operant schedule for .1 ml 5% sucrose reinforcers. Under this schedule, subjects were required to press a lever (over a range of ratio values) for each reinforcer. Subjects were trained with 70dB of background white noise playing in the test chamber, then tested for 6 days with 70dB or 90dB of background white noise playing in the chamber on alternate days. **RESULTS AND DISCUSSION:** The results of microanalysis of the data indicated no significant changes in running response rates resulting from the different intensities of background white noise. However, response rates were increased at all ratio values in the 90dB white noise condition, and the increase in running response rates was accompanied by an increase in post-reinforcement pause durations. When the cyclic-ratio molar regulatory model was applied, this indicated that the mild stressor of 90dB background increased consummatory behavior through a mechanism affecting the palatability of the reinforcer. **CONCLUSIONS:** Mild stress, in the form of

90dB background white noise, increases consumption through a mechanism affecting the perceived palatability of the ingestant.

THE EFFECTS OF QUERCETIN ON BEHAVIORAL PARAMETERS OF STRESSED RATS IN THE SUOK-TEST. I Tubaltseva, V Lozova, E Tukalenko, M Makarchuk. Kyiv National Taras Shevchenko University, Kyiv, Ukraine

INTRODUCTION: According to modern stress concepts, its adaptive character can turn into pathogeny in case of prolonged exposure to stressor. It has been proposed that initiation and development of stress reaction include an activation of free radical oxidation as a consequence of stress-related disturbances of redox-homeostasis with simultaneous attenuation of the cellular antioxidant defense systems. Oxidative stress and the products of lipid peroxidation are implicated in the pathophysiology of various neurological disorders including anxiety and depression. Therefore, treatment with antioxidants may theoretically prevent stress-related oxidative damages and improve the behavioral and cognition status of stressed organism. One of the most common and efficient due to their biochemical properties antioxidant agents are bioflavonoids, a naturally occurring phenolic compounds. The aim of this study was to assess the effect of pre-stress administration of bioflavonoid Quercetin (100 mg kg⁻¹) on the locomotive, exploratory and emotional activity of rats in the Suok test (Kalueff and Tuohimaa, 2005ab). **METHODS:** Male nonlinear rats (n=35, 5 months old) were used for this study. The animals were maintained under standard colony condition with ad libitum food and water throughout the experiment. The animals were divided into four groups. Rats of 1st and 2nd groups were subjected to chronic electric footshock of .8 mA intensity (10s duration with a 25±22s interval for 40 min) which supplies once in two days for 2 weeks. First and third rats groups obtained Quercetin (100 mg kg⁻¹) per os daily for 2 weeks before the stress exposure. Fourth group consist of control animals. All the animals were tested in the Suok ("rope-walking") test on 4th day to estimate the influence of stress factor on the behavioral repertoire of rats and its probable correction by the Quercetin. All data were analyzed by nonparametric Mann-Whitney U-test, results are presented as medians [lower quartiles; upper quartiles]. **RESULTS AND DISCUSSION:** Chronic footshock stress commonly depressed the behavioral activity of both stressed group, but quercetin administration evidently increased several measures of locomotor and exploratory behavior. Hereby, reliable distinction was found in amount of total stopping time between the "stress" group and both the control and quercetin administrated groups (255 [165;257] for "stress" group, 128 [60;173] (p=.04) for "control" group rats and 109 [30;183] (p=.02) for "quercetin" group, respectively). At the same time, stressed and quercetin-treated rats ("stress+quercetin" group) did not show significant stress-induced rise of total stopping time (161s [125;244], NS). Locomotor activity level (the number of crossed alley segments) of "stress" animals, but not "stress+quercetin" rats, was the lowest (11 [5;14] segments), significantly differing from "quercetine" group (29 [10;56] segments, p=.04). The same situation was found for other exploratory indices such as orientation reaction and looks down. Thus, "stress" rats demonstrated fewer looks down (2 [2;4]), significantly differing from "stress-quercetin" rats (6 [4;9], p=.02), Quercetin-treated rats (13 [3;15], p=.01) and control animals (8 [3;13], p=.01). Another measure of exploring behavior – orientation reaction – was the highest in the "Quercetin" group rats (12 [7;16]), markedly differing from the "stress" (5 [2;8], p=.02) and even control rats (3 [0;8], p=.04) groups. **CONCLUSIONS:** Our findings suggest that antioxidant administration can attenuate the developing of stress-related behavioral activity's inhibition, although misuse of bioflavonoid can lead to unpredictable consequences admittedly due to its capacity to impact the natural antioxidant balance of the organism appearing in the alteration of behavioral activity.

THE DEVELOPING UTILITY OF THE SUOK TEST IN ANXIETY PHARMACOLOGY AND BEHAVIORAL RESEARCH. AV Kalueff, A Minasyan, T Keisala, Y-R Lou, P Tuohimaa. University of Tampere and Tampere University Hospital, Tampere, Finland

Anxiety spectrum disorders show significant co-morbidity with vestibular dysfunctions in both animals and humans. We have recently introduced and psychogenetically/pharmacologically validated the Suok test in mice (Kalueff et al 2005; Brain Res Protocols, 14(2):87-99) and rats (Kalueff et al 2005; Behav Brain Res, 165(1):52-57), as the new animal model of anxiety disorder. The test is based on exposure of mice or rats to the elevated horizontal rod or alley, respectively, as well as to their half-dark half-light version (the light-dark Suok test, LDST), based on the animal's light-dark preferences on the Suok test apparatus. This model allows simultaneous assessment of 1) anxiety (by reduced rod exploration), 2) neurological phenotypes, 3) vestibular functions and 4) anxiety-evoked motorisensory disintegration. Behavioral endpoints in this model include: light, dark, total time spent, rod sectors

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visited, vertical rears, falls, missteps, defecation and urination episodes. In the present study, we pharmacologically validate the LDST in mice, showing the model's bidirectional selectivity to anxiogenic (PTZ) and anxiolytic (diazepam, ethanol) drugs. In Experiment 1, we first tested the strain baseline differences in the LDST performances. Overall, anxious BALB/c mice produced more anxiety, pronounced light aversion and increased motorisensory deficits in the 5-min test, compared to their non-anxious C57BL/6 counterparts (n=8 in each group). In Experiment 2, anxious mice of BALB/c strain and non-anxious NMR1 mice (n=16 each) showed reduced exploration, higher dark-vs.-light preference, and more vestibular disbalances following PTZ (20 mg/kg i.p.) vs. saline treatment. In Experiment 3, 129S1 and F1 hybrid C57BL/6-129S1 mice (n=16 each) showed predictably more exploration, higher light-vs.-dark preference, and fewer vestibular disbalances following ethanol (.75-1.5 g/kg) or diazepam (.05-.01 mg/kg) vs. saline treatment. In general, this study shows the utility of the LDST in behavioral neurogenetics and psychopharmacology research, as a new, high-throughput, fast and reliable experimental model targeting several distinct behavioral domains.

Symposium 11. Why do we need models of stress disorders? Chair: VM Klimenko

- EGIS-11150/S 36549: A NEW ANTIPSYCHOTIC AGENT WITH PROCOGNITIVE EFFICACY. H Kompagne, Sz Kertesz, LG Harsing, Gy Levay, I Gacsalyi. EGIS Pharmaceuticals Ltd, Division of Preclinical Research, Budapest, Hungary
- THE EFFECT OF I.C.V MICROINJECTION OF PEGANUM HARMALA SEEDS EXTRACT ON THE APPEARANCE OF FEAR BEHAVIOR IN ADULT MALE RATS. Gh Vaezi, L Etemadi, M Sabzali, Islamic Azad University, Damghan branch, Biology Department, Azad, Iran
- TREATMENT OF RATS WITH INTERLEUKINE-1B AT PERINATAL PERIOD RESULTS IN LONG-TERM DISTURBANCES OF COGNITIVE FUNCTIONS, WHICH ARE MORE EVIDENTIAL UNDER STRESS CONDITIONS. EB Fedotova, OE Zubareva, AS Simbirtsev, VM Klimenko. Institute of Experimental Medicine RAMS, Acmeological Institute, State Company of High Pure Preparations, St. Petersburg, Russia
- DO EARLIER DIAGNOSIS OF CANCER AND EARLIER STRESSFUL EVENTS INFLUENCE WOMEN'S STATE OF DISTRESS IN CANCER-RELATED SITUATION? B Korovljev, N Boskov. Zrenjanin Hospital, Zrenjanin, Serbia

EGIS-11150/S 36549: A NEW ANTIPSYCHOTIC AGENT WITH PROCOGNITIVE EFFICACY. H Kompagne, Sz Kertesz, LG Harsing, Gy Levay, I Gacsalyi. EGIS Pharmaceuticals Ltd, Division of Preclinical Research, Budapest, Hungary

INTRODUCTION: EGIS-11150/S 36549 is a putative atypical antipsychotic synthesized in the Chemical Division of EGIS Pharmaceuticals. The compound has a multireceptorial profile and displays massive antipsychotic effect in animal models of both positive and negative symptoms of schizophrenia, while is free of extrapyramidal effects in the therapeutic dose range. Examination of the side effect profile revealed that EGIS-11150 has a positive procognitive effect in various animal models of learning and memory. **METHODS:** Passive avoidance learning. The apparatus used is a 40X20X16 cm plastic box, divided into a lit (transparent walls) and a dark (black walls) compartment. The compartments are connected by a 7.5X8 cm opening, which can be closed by a computer-controlled sliding door. The floor of the dark compartment is of steel rods, through which electric shock can be administered. On the first day of the experiment male Wistar rats (weighing 200-220 g) were placed into the lit part of the test box. To avoid light, which is fearful for rodents, rats typically step through the gate. As soon as the animal was in the "safe" dark compartment, the sliding door was closed and rats received an unavoidable .4 mA foot shock (duration: 10 s). When animals are placed in the lit compartment 24 h later, they try to avoid electric shock by not stepping into the dark compartment. Increase of time spent in the lit area is considered as learning. Animals were treated by either vehicle, .005 mg/kg E-11150 or .005 mg/kg risperidone p/o on the second day. Object recognition. On day one 220-230 male SPRD rats were placed in a plastic box (70X50X40) where they could explore the environment freely. Two identical objects were presented to the rats in the same box on the second day. Time spent with examining the objects during a 5 min session was recorded. 24 h later one of the already familiar objects was replaced with a clearly different new one. Rats typically examine one object no longer than the other on this day, unless they have received a memory enhancer treatment. In that case, discrimination index (i. e. time of exploring) of the

unfamiliar object grows significantly. Increased discrimination index of the "new" object is considered to be a memory enhancing effect. Animals were given either vehicle or .01 mg/kg E-11150 po. on the third day. 8-arm radial maze. The apparatus consists of 8 transparent arms (70X9X11 cm) and a transparent central area (30X25 cm). In the experiment reported here, all arms were baited. 240-260 g male SPRD rats were kept on a low-calory diet for one week before experiment. During learning period animals were placed individually in the central zone and were left to explore for max. 5 min. Animals that fulfilled the task flawlessly on 3 consecutive days were chosen for testing. (Repeated visit of an arm and/or missing an arm were counted as mistake). 3 treatment groups were formed: C (control) animals received only vehicle (sc. and ip), S animals a combined .5 mg/kg scopolamine (sc.) and vehicle (ip.) and E rats both .5 mg/kg scopolamine and .01 mg/kg of E-11150 treatment (sc. and ip., respectively). Initial correct responses, working memory errors and total errors were counted. Statistics. All data were analysed by one-way ANOVA followed by Duncan-test, where appropriate. **RESULTS:** Passive avoidance learning. E-11150 had a significant effect on the latency of entry during retention trial, while risperidone failed to show any activity. ($F=23.78$ and $p<.001$ and $F=.038$, $p=.848$, respectively). Object recognition. E-11150 significantly prolonged the time of examining the "new" object even in this very low dose. ($F=37.548$, $p<.01$). Radial arm maze. E-11150 increased the number of initial correct responses compared to the scopolamine-vehicle treated group whereas risperidone had no such effect. ($F=27.39$ and $p<.001$, $F=.503$, $p=.490$, respectively). Number of working memory errors and total errors were decreased compared to scopolamine-vehicle treated group by E-11150. Risperidone was not effective. (Working memory errors: $F=6.384$ and $p=.025$ for E-11150, $F<.001$ and $p=.977$ for risperidone. Total errors: $F=11.340$ and $p=.005$ for E-11150, $F=.067$ and $p=.802$ for risperidone). **CONCLUSIONS:** EGIS-11150 is a potent antipsychotic with beneficial procognitive effects according to animal models. Due to these effects this drug may be efficient in disorders characterised by memory deficiencies or/and enhanced learning disabilities.

THE EFFECT OF I.C.V MICROINJECTION OF PEGANUM HARMALA SEEDS EXTRACT ON THE APPEARANCE OF FEAR BEHAVIOR IN ADULT MALE RATS. Gh Vaezi, L Etemadi, M Sabzali, Islamic Azad University, Damghan branch, Biology Department, Azad, Iran

INTRODUCTION: It is interesting to assess the effects of Peganum harmala seeds and fear-inducing and hallucinogenic effects on behavior. The influence of I.C.V injection were evaluated on adult male rats, using Peganum harmala seeds ethanol extract (ETE, 37%). **MATERIAL AND METHODS:** After surgical operation using stereotaxic methods, animals received 10, 20, 25, 50, 100 g/rat doses of extract (I.C.V) in groups separately ($n \leq 6$ in each groups). Plus-maze apparatus was used for evaluating the fear behavior. In the present study, pure harmaline (50 g/rat) - a hallucinogenic drug that causes fear and hallucination in animals as positive control group, and saline as sham, were used. HPLC testing showed that harmaline is the main alkaloid of Peganum harmala seeds extract. **RESULTS:** The results showed that administration of the ETE (10, 25, 50, 100 g/rat I.C.V) exhibited a significant different for fear behavioral in compare control group ($p < .05$). All doses had no effects on positive control group ($p > .05$). **CONCLUSIONS:** I.C.V. administration of Peganum harmala seeds ethanol extract at different doses caused fear-like behavior in rats, and its main composition (harmaline) with other alkaloids may cause these behavioral effects by various neural mechanisms, with the least effective dose of 10 g/rat.

TREATMENT OF RATS WITH INTERLEUKINE-1B AT PERINATAL PERIOD RESULTS IN LONG-TERM DISTURBANCES OF COGNITIVE FUNCTIONS, WHICH ARE MORE EVIDENTIAL UNDER STRESS CONDITIONS. EB Fedotova, OE Zubareva, AS Simbirtsev, VM Klimenko. Institute of Experimental Medicine RAMS, Acmeological Institute, State Company of High Pure Preparations, St. Petersburg, Russia

INTRODUCTION: Proinflammatory cytokine interleukine-1 β (IL-1 β) is known to play an important role in neuroimmune interaction. In adult rats IL-1 β treatment activates hypothalamus-pituitary-adrenal axis, mediates stress-reactivity, reduces the communicative and exploratory activity, damages memory. The mechanisms of high IL-1 β level influences cognitive function in early childhood are poorly investigated. **METHODS:** Wistar rat pups were injected i.p. with IL-1 β in doses 1 mcg/kg during the 3rd week of life. Control animals were injected with saline. Intact animals were also used as a control. The following tests were performed: "Open field" (the round "hole-board" was used), "Extinction of orientative-exploratory behavior in the Open Field" (animals were placed in Open Field for 5 min 3 days successively), "New object investigation", "Y-shaped maze training" (rats were trained to run into one of the maze arms by food reinforcement), "Active avoidance conditioning" (two-

level electric-flored box was used, light was used as a conditioned signal). The rats were tested with behavioral tests at the age of 45-70 days consequently with an interval 2-3 days). The behavioral patterns were registrated and analysed using the videorecording and computer ethological program developed in Pavlov Department of Physiology of IEM RAMS. The number of behavioral acts of animals treated with IL-1 β at early postnatal ontogenesis was increased during the first testing in "Open field" and averaged duration of contact with the holes was decreased to the age of 45 days. **RESULTS, DISCUSSION AND CONCLUSIONS:** The experimental rats if were repeatedly placed in "Open field" demonstrated decreased reaction of extinction of the exploratory behavior in comparing with control rats. Total duration of contacts with new objects when placed in a habitual environment did not differ in experimental and control rats, however the first ones performed more brief (for 1-2 s) approaches. Treatment with IL-1 β at an early age failed to impair the Y-shaped maze training but did disturb the active avoidance conditioning. Thus the elevation of IL-1 β level in blood at early postnatal ontogenesis results in abnormal exploratory behavior and memory impairment. The disturbances were more evidential under stress conditions (placing in a novel territory and use negative reinforcement). These differences could be explained by enhanced stress-reactivity of experimental rats. A severe stress-reaction to foot shock was shown in experiments with adult rats which have been exposed to IL-1 β treatment during the 3-d week of live time. Experimental rats have had more evident reduction of the "open-field" activity and higher levels of the blood corticosteron. In experimental animals compared to control ones the expression of mRNA of glucocorticoid receptors in hippocampus was less evident. Probably it might be accounted for by disturbance of one of feedback mechanisms of the stress-reaction control system. More strong reaction to stress may be related with disturbances of the brain neuromediator systems: in rats treated with IL-1 β (during the 3d week of livetime) the dopaminergic and serotonergic hypothalamic systems are activated more severely under stress conditions as compared to control rats. However, it is possible that stress-dependent mechanisms are not the only ones that underlie the cognitive dysfunction of animals treated with IL-1 β . The basal production of cFos mRNA involved in memory mechanisms was detected in hippocampus of experimental but not control rats. Less active extinction of exploratory behavior in the open field, observed in experimental animals, may be due not only to the impairment of memory mechanisms, but also due to disturbance of inhibitory brain systems caused by treatment with IL-1 β in early ontogenesis.

DO EARLIER DIAGNOSIS OF CANCER AND EARLIER STRESSFUL EVENTS INFLUENCE WOMEN'S STATE OF DISTRESS IN CANCER- RELATED SITUATION? B Korovljević, N Bosković, Zrenjanin Hospital, Zrenjanin, Serbia

INTRODUCTION: Breast cancer is the most common malign disease women can have. Confronting with cancer is always stressful. In case of breast cancer, the stress is intensified by the fear of losing a part of body that is very important in feminine sexuality. Cancer undoubtedly affects many aspects of life (the way patient see the life, himself etc.). The goal of this research was to reveal some of the factors that influence women's state of distress in the situations where they are about to hear whether they have a cancer or not, or was their therapy successful or not. The sample for this survey were women who were sent to "breast inspection" at Oncology section in Hospital in Zrenjanin, Serbia. They were tested while waiting to be invited to inspection, where a few doctors would examine them. The inspection was very stressful because the patients were expecting very important information about their health problems. Some of the patients were already at cancer therapy and they were waiting for news about success of therapy, whether they would have to prolong the same therapy, or to have different therapy with uncertain effects; whether the tumor growth was restrained or not; what health problems could they expect in the future or how long would they live; and, of course, was the therapy successful so they could go home and end their misery. Others, who considered themselves healthy, were afraid to hear that they have a cancer and that their suffering was just to begin. **METHODS:** 16 women were observed in stressful situation of breast inspection. The youngest patient was 19, and the oldest was 75. The average age of the sample was 57 years. 9 of them (56.2%) have been treated for cancer before. Average time they were under observation was 6.4 years. 6 of 9 (66.7%) patients, who have been treated before, have had complete breast amputation (mastectomy) and 3 of 9 (33.3%) have had operation without complete mastectomy. 7 of 16 (43.8%) had got the diagnosis of cancer for the first time and they were waiting for therapy plan. Since the state of distress can be measured by the state of depression and anxiety in stressful situation, the patients were examined with two questionnaires that explore current depression and anxiety. Independent variables were age, earlier diagnosis and treatment for cancer, treatment of patient's relatives and stressful

events in last year. Number and stressfulness of life events was measured by "The scale of life events" and other information were collected by additional questionnaire. In data analysis chi-square test was used in testing influence of most independent variables. In testing does patients with earlier diagnosis of cancer react different in stressful situation, t-test was used. **RESULTS AND DISCUSSION:** There have not been confirmed hypotheses that age, earlier diagnosis, treatment of relatives and stressful events influence stress reaction. Nevertheless, in group of women with earlier diagnosis of cancer, there was significant difference in depressive stress reaction between those who had been treated many years ago and those who had been treated in near past (chi square value was 4.29 with significance level .05). Women treated many years ago had stronger depressive reaction. **CONCLUSIONS:** Although this research didn't show significant connection between independent and dependent variables, it could be expected that, if the sample of patients had been bigger, some of the results might have been significant. An earlier research in similar situation supports that assumption. Stronger depression reaction of women who had been treated many years ago shows that those who had been treated in near past were more adapted and prepared for another treatment. Those who had been treated many years ago experienced the situation as a bigger loss, perhaps because after those years they hoped that cancer was gone for good.

Symposium 12. Behavioral and biological markers in stress research. Chair: AV Kalueff

- **ABERRANT BEHAVIORS, UNALTERED SENSORY, COGNITIVE FUNCTIONS AND HEDONIC RESPONSES IN VITAMIN D RECEPTOR MUTANT MICE.** A Minasyan, T Keisala, Y-R Lou, AV Kalueff, P Tuohimaa. University of Tampere and Tampere University Hospital, Tampere, Finland
- **SERUM LEPTIN LEVEL IN DEPRESSION.** S Mehrmofakham, M Sattari, H Darbandi. Shaheed Beheshti University of Medical Sciences, Tehran, Iran
- **NONLETHAL DOSES OF IONIZING RADIATION EFFECTS UPON INSTRUMENTAL BEHAVIOR OF RATS.** EV Tukulenko, VV Varetsky, AG Rakochi, MJU Makarchuk, IR Dmitrieva. Scientific Center for Radiation Medicine AMSU, Kyiv National Shevchenko University, Kyiv, Ukraine
- **CASPASE INHIBITORS PREVENT ISCHEMIC STRESS-INDUCED DECREMENTS IN LEARNING AND MEMORY IN GERBILS.** T Himi, Musashino University, Tokyo, Japan

ABERRANT BEHAVIORS, UNALTERED SENSORY, COGNITIVE FUNCTIONS AND HEDONIC RESPONSES IN VITAMIN D RECEPTOR MUTANT MICE. A Minasyan, T Keisala, Y-R Lou, AV Kalueff, P Tuohimaa. University of Tampere, Tampere University Hospital, Institute for Regenerative Medicine, Tampere, Finland.

INTRODUCTION: Several experimental and clinical studies suggest that vitamin D₃ active hormonal metabolites, especially 1,25-dihydroxyvitamin D (calcitriol) identified as active neurosteroid in adult and developed brain. The functions of vitamin D are mediated through nuclear vitamin D receptors (VDR, a member of the nuclear receptors superfamily of ligand-activated transcription factors) which are widely distributed through the nervous system. Genetic ablation of VDR has been performed in mice to show the role of vitamin D / VDR system in different tissues. We have recently shown that mutant mice lacking functional VDR display several behavioral abnormalities, including high anxiety and specific motor deficits, abnormal grooming activity and its sequence (Kalueff et al 2004a-c), suggesting the role of VDR in regulation of behavior. In line with this high VDR concentrations were found in the limbic system, the brain area which are involved in emotional behavior. **METHODS:** In the present study we further examine phenotype of these mice, testing their novelty responses as well as cognitive and sensory (olfactory, gustatory) functions in the novel food, two-trial Y-maze and tastant consumption tests. Since the high level of VDR have been detected in multiple hippocampal regions (Eyles et al 2003. Prufer et al 1999., Langub et al 2001) and VDR is widely distributed throughout the olfactory system (Glaser et al 1999). Also, vitamin D up-regulates transient receptor potential (Clapham et al 2003., Wood et al 2001), which represents cellular sensors to different stimuli and tastes (Clapham et al 2003., Wood et al 2001). The hippocampus is directly implicated in regulation of cognitive functions, and possibly elucidates the role of VDR in regulation of memory and learning processes and modulation of olfaction and gustation. In addition, we study depression-like behavior in these mice [using anhedonia-based sucrose preference test], as mounting clinical data show that vitamin D insufficiency increases depression in humans (Schneider et al 2000, Jorde et al

2006). **RESULTS AND CONCLUSIONS:** Overall, VDR mutant mice showed neophobic response in several different tests, but displayed unimpaired olfactory and gustatory functions, spatial memory and baseline hedonic responses. Collectively, these data confirm that mutation of VDR in mice leads to altered emotional/anxiety states, but does not play a major role in depression, as well as in the regulation of some sensory and cognitive processes. These results support the role of the vitamin D/VDR neuroendocrine system in the regulation of behavior, and may have clinical relevance, enabling a better focus on psychiatric and behavioral disorders associated with dysfunctions in this neuroendocrine system.

SERUM LEPTIN LEVEL IN DEPRESSION. S Mehrmofakham, M Sattari, H Darbandi. Shaheed Beheshti University of Medical Sciences, Tehran, Iran

INTRODUCTION: It is well documented that leptin is a circulating hormone that plays a key role in regulating food intake and body weight via its actions on specific hypothalamic nuclei. However leptin receptors are widely expressed in the CNS, in regions not generally associated with energy homeostasis, such as the hippocampus, cortex and cerebellum. Moreover, evidence is accumulating that leptin has widespread actions in the brain. In particular, recent studies have demonstrated that leptin markedly influences the excitability of hippocampal neurons, via its ability to activate large conductance Ca²⁺-activated K⁺ (BK) channels, and also to promote long-term depression (LTD) of excitatory synaptic transmission. Regarding some controversies about the exact role of leptin in depression, the aim of this study was to evaluate serum leptin and cortisol levels and assess its correlation with depression. **MATERIAL AND METHODS:** 38 depressed patients and 20 control subjects were enrolled. The level of depressive symptoms was measured with SCL-90-R. Serum leptin and cortisol levels were measured by ELISA. **RESULTS AND DISCUSSION:** We found significantly lower concentration of Leptin in depressed patients ($P < .05$) but not significant difference regarding cortisol level. **CONCLUSIONS:** Reduced leptins level might play important pathophysiological role in these psychiatric disorders.

NONLETHAL DOSES OF IONIZING RADIATION EFFECTS UPON INSTRUMENTAL BEHAVIOR OF RATS. EV Tukalenko, VV Varetsky, AG Rakochi, MJU Makarchuk, IR Dmitrieva. Scientific Center for Radiation Medicine AMSU, Kyiv National Shevchenko University, Kyiv, Ukraine

INTRODUCTION: Studies of radiation effects in radiobiology strongly focus on the dose-effect relationship. At the same time, available data on dose-dependence of radiation conditioned changes in the higher nervous activity and behavior are incomplete and frequently contradictory. The aim of this study was to find the dose-effect relationship of ionizing radiation effects at nonlethal dose range upon conditioned instrumental (operant) behavior of rats during two months after exposure. **METHODS:** The operant activity of white rats was studied after single total exposure to gamma-radiation (⁶⁰Co) in the dose range of .05 to 7 Gy. The rat performance was evaluated in shuttle boxes with negative painful enforcement (414 animals) and Skinner chamber with positive drink enforcement (146 animals) weekly during two months after the exposure. **RESULTS AND DISCUSSION:** Found dose dependence of all active avoidance indices in shuttle box had similar nonlinear pattern. At the doses below 1 Gy, certain instability of the effects was observed: deviations from the values in the control groups in different directions or absence of significant changes. In the dose range of 1 to 4 Gy, the increased level of performance as compared with the control groups with the maximum at the doses of 2 to 3 Gy; and at the doses of 6 to 7 Gy, progressive decline of the active avoidance performance as compared to the control rats was registered. With this, the changes observed at the doses above 5 Gy, tended to be more pronounced during prolonged time after the exposure. Such dose-dependent pattern can be explained by different levels of radiation injuries and compensatory mechanisms as well as their different relative contribution correspond to each dose (dose range). Besides, we assumed that the appearance of the dose dependence could be conditioned by superposition of damaging exposure effects and considerable stress loading which is caused by animals testing in a shuttle box. To verify this hypothesis, a more "soft" operant technique, Skinner chamber (with positive enforcement), was used. The comparison of the dose dependence of operant indices after exposure obtained in the Skinner boxes with the results of changes in the indices of active avoidance showed that in general the pattern of indices changes was similar in both cases. Thus, at the doses of .25 to 2.0 Gy the level of the operant activity in Skinner chamber increased, and at the larger doses decreased becoming significantly lower as compared to the control animals at the dose of 6.5 Gy. The main differences of the results obtained with different operant techniques were considerably more expressed changes of the active avoidance indices after the exposure, which is

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consistent with the hypothesis of the significance of the additional stress of the animals testing. **CONCLUSIONS:** Prolonged studies of the operant activity of the rats after exposure to ionizing radiation using different techniques showed rather complicated nonlinear dependence of the behavioral indices on the exposure dose. Similarity of the dose dependences obtained using both shuttle and Skinner chambers suggests the significance of interaction of effects of the additional stress factor of testing and irradiation in realization of radiation behavioral effects. Thus, the hypothesis, according to which exposure to ionizing radiation leads to dose dependent readiness to the response to additional stress, deserves future studies.

CASPASE INHIBITORS PREVENT ISCHEMIC STRESS-INDUCED DECREMENTS IN LEANING AND MEMORY IN GERBIL. T Himi. Musashino University, Tokyo, Japan

INTRODUCTION: Recent reports suggest that caspase family proteases play a critical role in the cell death machinery in various cell types. Here we show caspase inhibitors can protect neurons from delayed neuronal death caused by ischemic stress in gerbils. **METHODS:** Young adult gerbils were subjected to brief bilateral common carotid artery occlusion followed by reperfusion. Western blot analysis showed poly(ADP-ribose) polymerase (PARP), a known target of caspase-3 (CPP-32/YAMA), was cleaved in hippocampus at post-ischemic day 4. **RESULTS AND DISCUSSION:** Immediate post-ischemic administration of a caspase inhibitor, benzyloxycarbonyl-Asp-CH₂-dichlorobenzene (zD) significantly reduced the number of TUNEL-positive neurons at day 4 and suppressed the loss of CA1 pyramidal cells at day 8. This neuroprotective effect of zD was, however, not observed when administration was started 24 hr after the ischemic insult. Behavioral studies showed that zD-administered animals at the early stage showed higher scores in the passive avoidance tests, suggesting the functions of neurons protected by zD. On the other hand, the appearance of reactive astrocytes and the increase of reactive microglia were unchanged by zD, even administration was started at early onset of ischemia. **CONCLUSIONS:** These findings indicate that caspases play important roles in delayed neuronal death following transient global ischemia, and that this death can be suppressed by blocking caspases.

Day 4. May 19, 2007. Venue: IEM RAMS - Institute of Experimental Medicine RAMS, 69/71 Kamennooostrovsky Prospect

Special Plenary Symposium: Psychoneuroimmunology. Chairs: VM Klimenko, SG Tsikunov, AV Kalueff

- OPTIMIZATION OF ANTIPSYCHOTIC THERAPY BY ADJUVANT AGENTS. NP Dzhuga, VL Koslovskiy. Department of Clinical and Experimental Psychopharmacology, Bechterev Psycho-Neurology Institute, St. Petersburg, Russia
- HUMAN BRAIN TUMORS: MULTIDRUG-RESISTANCE P-GLYCOPROTEIN EXPRESSION IN TUMOR CELLS AND INTRATUMORAL CAPILLARY ENDOTHELIAL CELLS. S Fattori, F Becherini, M Cianfriglia, G Parenti, A Romanini, M Castagna. Pathological Anatomy III, Department of Surgery, Department of Neurosurgery, University of Pisa, Pisa; Department of Drug Research and Evaluation, Istituto Superiore di Sanita, Rome; Division of Medical Oncology and Plastic Surgery, University Hospital, Pisa, Italy
- FUNCTIONAL RESERVES AND REACTIVITY OF BLOOD LEUKOCYTES DURING OXIDATIVE STRESS INDUCED BY INTOXICATION BY NITROGEN-CONTAINING SUBSTANCES. EM Tsoy, RI Kovalenko, AA Petenkova. Department of General Physiology, St. Petersburg State University, St. Petersburg, Russia
- NEUROPEPTIDES AND INDUCTION OF NEUTROPHIL DEATH. B Khajehnoori, M Sattari, S Mehrmofakham, H Darbandi, S Taheri. Shaheed Beheshti University of Medical Sciences, Tehran, Iran
- NEUROPEPTIDES AND INFLAMMATION IN GINGIVA. M Sattari, S Mehrmofakham, H Darbandi. Shaheed Beheshti University of Medical Sciences, Tehran, Iran

OPTIMIZATION OF ANTIPSYCHOTIC THERAPY BY ADJUVANT AGENTS. NP Dzhuga, VL Koslovskiy. Department of Clinical and Experimental Psychopharmacology, Bekhterev Psycho-Neurology Institute, St. Petersburg, Russia

It is well known that, on the cellular level, all manifestations of vital activity, such as motion, digestion, contractions, perception, emotions and hallucinations, are due to depolarization and hyperpolarization of neurons, and the integrative interaction of these processes in CNS cells populations determines the condition of certain function. It is also known that Ca^{++} may be regarded as a secondary messenger, which determines the development of physiological and pathological reactions. The blockade of voltage-dependent Ca^{++} channels (CC) of L-type by Nifedipine, while reducing intracellular Ca^{++} concentration during cells stimulation, may modulate physiological functions. On the other hand, Ca^{++} channels antagonists demonstrate considerable effect in conditions of pathological excitement while showing minimal effect in the normal physiological processes. It is suggested that under normal conditions calcium voltage-dependent channels are in the passive state and do not bear such physiological load as they do under pathological conditions. Thus we believe that Ca^{++} channels antagonists may be effective in pathological cases without causing any side-effects. In other words, by preventing / modulating neurons' hyperactivity these drugs may act as psychostabilizers in the realization of higher functions. The present study examines the influence of nifedipine on the development of affective reactions and the level of neurocognitive functioning in patients with subacute schizophrenia. Fifty schizophrenic patients were included, mainly with episodic course of disorder. There were two phases in this study: the blind placebo-controlled one and the open one with atypical antipsychotic as an active comparator. In both phases standard antipsychotic therapy was supplemented by a daily dose of 60 mg of nifedipine. It was found that adjuvant nifedipine therapy was more effective in cases of acute psychotic conditions with pronounced non-specific excitement and "mental disintegration" during the maximal psychotic manifestation. Further investigations showed the positive effect of the drug in reducing negative symptoms of schizophrenia, together with its influence on the affective symptoms. These findings allow us to consider the combination of Nifedipine with a typical antipsychotic (haloperidol) as an alternative substitute for atypical antipsychotic (used in the control group).

HUMAN BRAIN TUMORS: MULTIDRUG-RESISTANCE P-GLYCOPROTEIN EXPRESSION IN TUMOR CELLS AND INTRATUMORAL CAPILLARY ENDOTHELIAL CELLS. S Fattori, F Becherini, M Cianfriglia, G Parenti, A Romanini, M Castagna. Pathological Anatomy III, Department of Surgery, Department of Neurosurgery, University of Pisa, Pisa; Department of Drug Research and Evaluation, Istituto Superiore di Sanita, Rome; Division of Medical Oncology and Plastic Surgery, University Hospital, Pisa, Italy

INTRODUCTION: Malignant brain tumor is a lethal disease with currently available treatment options having a limited impact on outcome. Nevertheless, novel therapeutic approaches combined with genetics prediction of chemosensitivity have in the last decade significantly improved clinical benefit for the treated patients. Since the pharmacological relevance of the drug transporter mechanisms in the unresponsiveness of solid tumours to chemotherapy, the fine characterization of the MDR1 gene encoding for P-glycoprotein (MDR1-Pgp) in brain tumors may be a crucial determinant for evaluating the long-term efficiency of specific anti cancer compounds. **METHODS:** Immunohistochemistry was performed on formalin fixed and paraffin formalin embedded tissue blocks from 83 patients with brain tumors. In order to determine the expression level of MDR1-Pgp in brain tumors we have used the MAb MM4.17 that has been shown to react with unique specificity and affinity. The study includes also formalin fixed and paraffin embedded brain tissue from 10 different regions of autopsy normal adult brain and from 10 fetal autopsy. **RESULTS AND DISCUSSION:** The MDR1-Pgp was immunodetected in 34 out of 43 grade IV, 6 out of 10 grade III, 24 out of 27 grade II and 1 out of 3 grade I brain tumors. Then, MDR1-Pgp resulted hyper-expressed both in vessels and in neoplastic cells from the majority of tumors examined, compared to normal parenchyma. This study demonstrates that the MDR1 gene can be detected in all grade tumor brain malignancies and in endothelial cells of newly formed capillaries, thus impairing drug access at the tumor cell level. Furthermore MDR1-Pgp expression was found into the endothelial, meningeal cells, in choroids plexus epithelium of both fetal and adult autaptic brain tissues; in the pyramidal neurons of different cortical areas in the adult autaptic brain and in the neuronal cells of ponto-mesencephalic nuclei in fetal brain. These results confirm that MDR1-Pgp may play an important role in the endothelial cells of the brain pumping out xenobiotics from endothelial cells into the lumen of capillaries for the protection of the brain parenchyma and protecting fetal brain against toxic agents or maternal metabolic products during the intrauterine development. **CONCLUSIONS:** Although the role of MDR1-Pgp in tumor blood vessels needs to be further examined and more clearly defined, drug resistance in malignant brain tumors may result from characteristics not only of tumor vasculature, but also of neoplastic cells. MDR1-Pgp

in this special localization can remove anticancer compounds from tumor cells located around the capillaries. These observations suggest that, after careful evaluation in well designed preclinical studies, combined chemotherapy consisting of MDR1-Pgp reversing agents and specific anticancer compounds may represent a novel and promising clinical approach for the treatment of malignant brain tumors.

FUNCTIONAL RESERVES AND REACTIVITY OF BLOOD LEUKOCYTES DURING OXIDATIVE STRESS INDUCED BY INTOXICATION BY NITROGEN-CONTAINING SUBSTANCES. EM Tsoy, RI Kovalenko, AA Petenkova. Department of General Physiology, St. Petersburg State University, St. Petersburg, Russia

INTRODUCTION: It is well known that stress is a standard adaptive response to various factors (intoxication, trauma, infectious process, prolonged physical and mental activities), which potentially threaten the organism's existence. Prooxidant-antioxidant shifts, more or less marked bloodstream centralization and selective redistribution of migratory streams of activated leukocyte populations to the immune organs and other strongly functioning tissues underlie protective and damaging reactions during different types of stress. Cytokines, free radicals and other inflammatory mediators, produced by immune cells, contribute considerably to the development of these processes. Neuromediators and hormones provide receptor-mediated control of the activity of functional leukocytes, especially their adhesive, migratory and secretory capacities. Neurotransmitter systems, participating in regulation of immune processes and in the initiation of lipid peroxidation as well as their role played in tissue damage during stress, are poorly known. The goal of this research is to examine the dependence of functional leukocytic activity as well as their reactivity to neuromediator signals on the level of lipid peroxidation intensification and high norepinephrine concentration during the alarm stage of the adaptation syndrome. **METHODS:** Stress was created by a single subcutaneous injection of sodium nitrite to Wistar rats at 3 mg per 100 g of body weight. Nitrite hypoxia, as one of the types of hemic hypoxia, is accompanied by oxidative stress. The features of nitrite hypoxia include: the transformation of haemoglobin into hemoglobin, the formation of haemoglobin complexes with nitric oxide or other nitrogen-containing substances and the inhibition of hem-containing antioxidant enzymes. Formed nitric oxide has various physiological functions, including vasodilatation and modulation of functional activity of leukocytes. In addition, this mediator of inflammation influences the neuroendocrinal system, thereby increasing the intensity of stress. Oxidative stress intensity was estimated by lipid peroxidation intensity, antioxidant enzyme catalase activity and the concentration of catecholamines in the blood. Lipid peroxidation intensity in tissues (brain, heart, liver and femoral muscle) was estimated by the concentration of active end products in the test with 2-thiobarbituric acid (TBA-active substances). Basal radical-producing activity of leukocytes as well as the activity stimulated by zymosan were determined by a nitroblue tetrazole reduction test. The quantity of cationic peptides was determined with the help of the lysosome-cation test. The cytokine-producing activity of lymphocytes was detected by the reaction of leukocyte migration inhibition with the mitogens concanavalin A and phytohemagglutinin in 5-pored capillaries. The capacity of leukocytes to respond to neuromediators was estimated by change in cell mobility during the addition of epinephrine and norepinephrine. The aforementioned parameters were measured at 15, 30, 60 and 90 minutes after sodium nitrite injection. **RESULTS AND DISCUSSION:** It was shown that in 30 minutes after NaNO_2 injection, the concentration of lipid peroxidation products in brain tissues as well as norepinephrine concentration in the blood were significantly higher in treated rats in comparison with control rats. In the presence of oxidative stress, the quantity of circulating leukocytes was decreased predominantly due to the reduction in the number of lymphocytes. The basal production of oxygen radicals by cells, as well as the production stimulated by zymosan, was not significantly changed during stress dynamics. Neither had we detected significant changes in cytokine production in response to mitogen application. In 1 hour after NaNO_2 injection, the quantity of cationic peptides and proteins in neutrophils were significantly decreased, which indicates granulopoiesis inhibition or a predominance of less mature neutrophil forms with low bactericidal action. Spontaneous mobility of blood leukocytes was increased in the first period of oxidative stress, which implies a likely decrease in adhesive properties and migration. At the same time, leukocytes had heightened sensitivity to NaNO_2 addition: the mobility of leukocytes in vitro was notably decreased in response to NaNO_2 (10^{-9} – 10^{-11} M) in comparison with the cells of control animals. Data received from in vitro experiments indicate that the level of locomotor activity in leukocytes is closely related to the balance of sympathetic and parasympathetic influences. At high norepinephrine concentrations in the blood (10^{-4} M), immune cells didn't react to the administration of physiological concentrations of this mediator,

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while α - and β -adrenoceptor antagonists (phentolamine and propranolol accordingly) resulted in a decrease of leukocyte mobility. Acetylcholine application (10^{-8} - 10^{-10} M) led to significantly reduced cell mobility. It can be assumed that norepinephrine increases and acetylcholine decreases cell mobility. The reduction in the number of circulating leukocytes due to monocytes and stab neutrophils as well as unchanged leukocytic reactivity to zymosan at 90 minutes after NaNO_2 injection supports our conclusion. **CONCLUSIONS:** The administration of a moderate dose of the nitrites leads to increase of lipid peroxidation in the brain, sympatho-adrenal system activation, increase of spontaneous immunocompetent cell mobility and an absence of changes in radical- and cytokine-production activity of leukocytes. Based on our research, we concluded that the sympathetic-parasympathetic balance plays a significant role in the regulation of leukocyte migratory capacity and reactivity.

NEUROPEPTIDES AND INDUCTION OF NEUTROPHIL DEATH. B Khajehnoori, M Sattari, S Mehrmofakham, H Darbandi, S Taheri. Shaheed Beheshti University of Medical Sciences, Tehran, Iran

INTRODUCTION: Neutrophil apoptosis is an important event in the resolution of inflammation. The role of substance P (SP) and calcitonin gene related peptide (CGRP) in neutrophil apoptosis has not been previously investigated. The aim of this study was to assess the effect of these neuropeptides on the neutrophil death. **MATERIAL AND METHODS:** Neutrophils were collected from heparinized blood from a healthy individual. Then the cells were incubated with two different doses of SP (.42 and .62 pg/ml) and CGRP (.01 and .11 pg/ml). Annexin V fluos staining was used for detecting the apoptotic and necrotic neutrophils under fluorescence microscope. **RESULTS AND DISCUSSION:** Both SP and CGRP significantly induce apoptosis in neutrophils in a dose dependent manner ($P < .05$). **CONCLUSIONS:** Both substance P and CGRP could induce apoptosis instead of necrosis in the neutrophils, thus could modulate inflammatory response by the nervous system.

NEUROPEPTIDES AND INFLAMMATION IN GINGIVA. M Sattari, S Mehrmofakham, H Darbandi. Shaheed Beheshti University of Medical Sciences, Tehran, Iran

INTRODUCTION: Recent advances in the analysis of neuropeptide receptors, have demonstrated that they are distributed not only in the cells of the neuronal system, but also in immune and peripheral cells. Therefore, the effect of neuropeptides is not limited to the nervous system. Neuropeptide receptors are widely distributed in gingiva. This wide distribution suggests that neuropeptides may directly modulate gingival tissue functions. The aims of the present study were to investigate whether the neuropeptides such as SP (Substance P) and CGRP (Calcitonin gene related peptide) were present in gingival crevicular fluid in both periodontal health and disease and to study the relationship with periodontal inflammation. **MATERIAL AND METHODS:** Gingival crevicular fluid (GCF) was collected from a healthy, a gingivitis and a chronic periodontitis site in 29 subjects (consisted of 20 females and 9 males with mean age of 36.3 years) by means of Periopaper from one interproximal site. Samples were analyzed for SP and CGRP using ELISA. **RESULTS AND DISCUSSION:** The level of SP in was significantly higher in periodontitis sites than gingivitis and its level in gingivitis sites was higher than healthy sites ($P < .05$). There was also a significant correlation between the level of SP and the amount of attachment loss (as an index for the destruction of gingival or periodontal tissues) in periodontitis ($P < .05$). In contrary to SP, we could not found CGRP in periodontitis sites and its level in healthy sites was higher than gingivitis sites ($P < .05$). **CONCLUSIONS:** Substance P may have a role in the pathogenesis of periodontal disease but CGRP may have some role in protection of gingiva and probably some components of GCF could be responsible for degrading this neuropeptide in diseased sites. Of course, further investigations could prove useful in clarifying the mechanisms through which neuropeptides could modulate periodontal health and disease.

Day 4. May 19, 2007. Venue: IEM RAMS - Institute of Experimental Medicine RAMS, 69/71 Kamennostrovsky Prospect

POSTER SESSION

- EVENT-RELATED POTENTIALS, STRESS AND ANXIETY ASSESSMENT IN PEOPLE COMPLAINING ABOUT IDIOPATHIC ENVIRONMENTAL INTOLERANCE (IEI) ATTRIBUTED TO ELECTROMAGNETIC FIELDS: A COMPARISON WITH CONTROLS

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MATCHED FOR AGE AND GENDER. M Crasson, P Papart, S Nevelsteen, M Anseau, J-J Legros. Belgian BioElectroMagnetic Group, Psychoneuroendocrinology Unit, Department of Psychiatry, University of Liege, Liege, Belgium

- COCAINE-INDUCED IMPAIRMENT OF LTP IN RAT DENTATE GYRUS AND INVOLVEMENT OF CORTICOSTERONE AND GLUCOCORTICOID RECEPTORS. M Grzegorzewska, G Hess. Institute of Pharmacology PAN, Krakow, Poland
- MONOAMINERGIC CORRELATES OF ANXIETY STATE AFTER CRONIC STRESS IMPACT IN RATS. AM Titkova, SV Utevskeya. Institute of Neurology, Psychiatry and Narcology of AMS of Ukraine, Kharkiv, Ukraine
- GENDER DIFFERENCES OF CYTOCHROME OXIDASE REACTIVITY IN THE HIPPOCAMPUS OF TOTAL SLEEP DEPRIVED RATS. Hung-Ming Chang and Chyn-Tair Lan. Chung Shan Medical University, Taichung, Taiwan
- CHRONIC CORTICOSTERONE-INDUCED INCREASE IN THE RESPONSIVENESS OF RAT HIPPOCAMPAL CIRCUITRY TO THE ACTIVATION OF 5-HT₇ RECEPTOR IS REVERSED BY IMIPRAMINE. P Pitra, G Hess. Institute of Pharmacology PAN, Krakow, Poland
- AFFECTIVE DISORDERS IN THE STRUCTURE OF MENTAL DISORDERS IN EPILEPSY: CLINICAL AND REHABILITATION ASPECTS. TV Kazennykh. Mental Health Research Institute TSC SB RAMS, Tomsk, Russia
- STRESS INDUCED BY HOUSING CONDITIONS AFFECTS VULNERABILITY TO DRUG RELAPSE IN MICE. MA Aguilar, J Lluch J, M Rodriguez-Arias, J Minarro. Psychobiology of Drug Dependence Research Unit, Department of Psychobiology, Faculty of Psychology, University of Valencia, Spain
- EVALUATION OF ATTENTION LEVEL AND COGNITIVE DYSFUNCTION IN PATIENTS WITH VALVULAR DISEASE OF THE HEART. AN Savostyanov, VG Postnov, MKh Kadochnikova, OV Zhukova. State Research Institute of Blood Circulation Pathology, State Research Institute of Physiology SB RASM, Novosibirsk, Russia
- LOCALIZATION OF CEREBRAL ISCHEMIA AS A FACTOR OF POST-STROKE DEPRESSION (PILOT STUDY) S Draca, D Kolar. Clinic Dr M.Zotovic, Belgrade, Serbia; Department of Psychiatry, McGill University, Montreal, Quebec, Canada
- LIFE STRESS EVALUATION WITH REGARDS TO SUICIDAL IDEATION AND FAMILY SUICIDE HISTORY IN RANDOM COHORT OF GENERAL POPULATION. ZhV Emyasheva, VA Rozanov. Odessa National Mechnikov University, Odessa, Ukraine
- GROUP THERAPY FOR BIPOLAR DISORDER: A SYSTEMATIC REVIEW. ID Segredou, MD Livaditis, CI Mitsonis, KI Liolios, KE Stamatopoulou, EE Maragkoudaki, M-NE Katsanou. Psychiatric Hospital of Athens, Athens; Democritus University of Thrace, Thrace, Greece

EVENT-RELATED POTENTIALS, STRESS AND ANXIETY ASSESSMENT IN PEOPLE COMPLAINING ABOUT IDIOPATHIC ENVIRONMENTAL INTOLERANCE (IEI) ATTRIBUTED TO ELECTROMAGNETIC FIELDS: A COMPARISON WITH CONTROLS MATCHED FOR AGE AND GENDER. M Crasson, P Papart, S Nevelsteen, M Anseau, J-J Legros. Belgian BioElectroMagnetic Group, Psychoneuroendocrinology Unit, Department of Psychiatry, University of Liege, Liege, Belgium

INTRODUCTION: A growing number of people report a variety of health problems, claiming that the reason for their adverse health symptoms is exposure to electric, magnetic or electromagnetic fields (EMF) from nearby electric installations or appliances. There are, to date, no objective clinical signs or biological markers that may be of value in reaching the diagnosis of hypersensitivity to electricity or electrosensitivity (EHS), as it is the case for other forms of environmental illnesses. The term Idiopathic Environmental Intolerance was suggested by World Health Organisation to describe a number of disorders sharing similar non-specific medically unexplained symptoms that adversely affect people, without any implication, in this case, of EMF susceptibility. Although the majority of provocation studies indicate that EHS individuals cannot detect EMF exposure any more accurately than non-EHS individuals, the symptoms are real and can vary widely in their severity. Some studies suggest an hyper reactivity in the central nervous system and imbalance in the autonomic nervous system with a trend towards sympathetic over activity and increased arousal (Sandström et al 1997, 2003, Lyskov et al 2001a,b). These results were interpreted as a physiological predisposition to stress vulnerability, increased sensitivity and lower tolerance to physical environmental factors. The symptoms most commonly reported include dermatological symptoms (redness, tingling, burning

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sensations) as well as neurasthenic and vegetative symptoms such as fatigue, tiredness, concentration difficulties, dizziness, nausea, heart palpitation and digestive disturbances. The goal of this study is to assess information processing through cognitive event-related potentials (i.e. CNV and P300) as well as anxiety and perceived stress in a group of EHS complaining persons, in comparison with a group of controls matched for sex and age. **SUBJECTS:** Perceived EHS people were recruited for their participation in a clinical evaluation. People were classified as perceived EHS if they answered yes at the question: "Do you think that your health problem are associated to electromagnetic fields?". They were recruited through action and support groups and personal contacts. The EHS group was matched for sex and age to a control group of healthy people without complaints attributed to electromagnetic fields. **METHODS:** Two event-related potentials (ERPs) recordings, related to attention and arousal functions, were chosen. Contingent Negative Variation (CNV) is an event-related potential that develops during a simple experimental situation associating a warning (S1: 1000 Hz, 50 ms tone) and an imperative stimuli (S2:18/s light flashes), presented one second later. The subject has to stop S2 by pushing a button. CNV amplitude is calculated as the voltage difference between the 1 s baseline before S1 and 200 ms before S2. P300 is a positive deflection which occurs when a subject detects an informative task-relevant stimulus. It reflects memory updating and context closure. An auditory oddball paradigm was chosen which consisted in the presentation of 120 frequent tones of 800 (15 dB, 40 ms) and 30 target tones of 1470 Hz (15 dB, 40 ms). The subjects were asked to press a button for the rare stimuli. P300 amplitude and latency were measured as the difference in voltage between baseline and the higher point between 280 and 450 ms after the stimulus. Subjects also completed psychological questionnaires: Perceived Stress Scale (Cohen & Williamson, 1983), STAI-Y (Spielberger, 1993), Hyperarousal Scale (Pavlova et al 2001). The occurrence of symptoms was recorded by a self administrated symptoms questionnaire. **RESULTS:** Data of about 15 EHS patients will be compared to an equal number of age and sex matched healthy controls. Data collection is under progress. **CONCLUSION:** With this study, we intend to get a better description of the psychophysiological profile of people who report symptoms that they attribute to exposure to electric and magnetic fields.

COCAINE-INDUCED IMPAIRMENT OF LTP IN RAT DENTATE GYRUS AND INVOLVEMENT OF CORTICOSTERONE AND GLUCOCORTICOID RECEPTORS. M Grzegorzewska, G Hess. Institute of Pharmacology PAN, Krakow, Poland

INTRODUCTION: Long-term potentiation (LTP) has been considered a plausible cellular mechanism of learning and memory. Changes in excitatory synapses underlying synaptic plasticity depend on rearrangements of cell-to-cell and extracellular matrix-to-cell interactions, which are mediated by recognition molecules. The neural cell adhesion molecule (NCAM) has been implicated in several cellular processes such as neurite growth, cell migration and synaptic plasticity. Alterations in the expression of PSA-NCAM may reveal plastic changes occurring in the adult brain. Recent data indicate that single administration of cocaine decreases expression of PSA-NCAM in rat dentate gyrus lasting up to 6 days after treatment. Changes in PSA-NCAM expression after cocaine treatment may, potentially, influence LTP in the dentate gyrus. Corticosterone level may influence the PSA-NCAM expression. Several lines of evidence indicate that exposure to various types of stressors, or stress hormones may increase or induce sensitization to psychostimulants. Corticosterone, the main glucocorticoid hormone in the rat, can modulate the behavioral effects of drugs of abuse. Glucocorticoids act on the mammalian brain through two main receptors, the mineralocorticoid receptor (MR) and the glucocorticoid receptor (GR). It has been known that administration of a GR antagonist dose-dependently reduced the motivation to self-administer cocaine. **METHODS:** To check the involvement of corticosterone and glucocorticoid receptors in the cocaine effect on LTP, brain slices were prepared 2 days after cocaine (15 mg/kg, i.p.) or saline administration to male young adult rats aged 6 to 8 weeks. The third experimental group received metyrapone, a corticosterone synthesis inhibitor (100 mg/kg, s.c.), 3 h before cocaine injection. The fourth group received RU 38486, an antagonist of glucocorticoid receptors (10 mg/kg, s.c.), 45 min before cocaine injection. The fifth group received spiro lactone, an antagonist of mineralocorticoid receptors (50 mg/kg s.c.), 1 h before cocaine injection. Ex vivo slices were incubated in standard conditions. Field excitatory postsynaptic potentials were evoked by stimulation of the medial perforant path and they were recorded from the middle molecular layer of the dentate gyrus. LTP was induced by high-frequency stimulation (HFS, 100Hz, 1s), delivered three times every 5 minutes. During HFS the intensity of stimulation was doubled. Each experiment was done in the presence of .3 μ M bicuculline. **RESULTS:** HFS resulted in a long-term increase of responses in slices obtained from control rats (n=11). A stable

response increase ($157 \pm 13\%$) was maintained for 90 min. LTP evoked in slices from rats receiving cocaine treatment was impaired ($119 \pm 12\%$, $n=11$, $p < .05$, ANOVA, control vs cocaine). Both metyrapone and RU 38486 reversed low level of LTP to control ($158 \pm 10\%$, $n=10$, $p < .05$, ANOVA; $159 \pm 11\%$, $n=10$, $p < .05$, ANOVA, respectively), whereas spiro lactone has no effect on reversal of LTP after cocaine treatment (96 ± 7 , $n=10$, the difference was not statistically significant). **CONCLUSIONS:** Single dose of cocaine attenuates LTP in the dentate gyrus. Cocaine treatment-related LTP impairment was reversed by metyrapone, a corticosterone synthesis inhibitor or RU 38486, an antagonist of GR, but not spiro lactone, a MR antagonist administration. These results suggest the involvement of corticosterone and GR, but not MR, in the inhibitory effect of cocaine on LTP.

MONOAMINERGIC CORRELATES OF ANXIETY STATE AFTER CRONIC STRESS IMPACT IN RATS. AM Titkova, SV Utevskaia. Institute of Neurology, Psychiatry and Narcology of AMS of Ukraine, Kharkiv, Ukraine

INTRODUCTION: It is well known that neurotic disorders in the majority of cases are of stress nature. However depending on the individual metabolic features of the organism, the type, force and duration of the stress impact different neurotic disorders are formed. There exist different approaches to modeling neurotic states. Some of them are used in our work [Vorobjova et al 2005, 2006; Titkova, 2007]. In this report we present the data of biochemical research of anxiety state in rats which results from the repeated unavoidable effect of the electric current of the threshold power. **METHODS:** The work is conducted in 23 male rats aged 4-5 months. To form the model of neurotic disorder the animals were put in the camera in pairs. To the floor of the camera there was given the electric current of threshold value in probabilistic mode. The influence lasted 1 hour a day during 20-22 days. The next day after the last influence the contents of biogenic monoamines was determined in the rat brain structures and blood [Endo, Ogura, 1975]. The glucose, pyruvate and lactate concentrations in the blood plasma were also determined on the standard kits. The statistic data processing and correlative analyses of the results obtained were conducted in the Excel program. **RESULTS, DISCUSSION AND CONCLUSIONS:** As a result of modeling the neurotic disorder the rats developed the anxiety state, which manifested itself in the animals' behavior. That is the increase in excitability, irritability, vocalization while handling, aggressive reactions. At the end of the experiment the animals showed the significant increase of the absolute and relative adrenal gland mass (1,46 and 1,38 times, accordingly). It testified to the fact that the rats were in the distress state, which was followed by enhanced activation of the pituitary adrenocortical system and increased corticosterone secretion. The studies of biogenic monoamines contents in blood demonstrated the dopamine level increase up to 250% and epinephrine level increase up to 217% in comparison with corresponding indexes in the intact animals. Norepinephrine contents decreased to 47%. Glucose and pyruvate concentration in rat blood did not undergo significant changes however lactate contents increased up to 140% in peripheral blood and up to 162% in the cerebral vessels blood. The revealed increase of the adrenocortical activity and adrenomedullary one combined with arising dissociation of neurosympathetic and adrenomedullary components of sympathoadrenomedullary system according to Henry (1993) corresponded to the states of anxiety and striving but not to depression yet. In rat brain structures there were observed the decrease of norepinephrine and serotonin contents in the hypothalamus and especially in the septum: norepinephrine - to 51%, serotonin - to 68%. The level of catecholamines decreased in neocortex: dopamine - to 52%, norepinephrine - to 51%. Serotonin level in this structure increased up to 165%. In the hippocampus dopamine level enhanced up to 177%, norepinephrine one - up to 174%. These findings testify to the appearance of the monoaminergic activity disbalance between the structures of cortical and subcortical formations. As shown earlier with regard to the cholinergic brain system during neurotic disorders formation [Titkova, 2007], as well as in this research the septum appears to be the key structure for these states. The contents of catecholamines in septum, hippocampus and neocortex were in the reverse correlative dependence on the glucose level, and serotonin - in the direct dependence on the lactate level in the brain. The catecholamine contents in hypothalamus correlated with the adrenal gland mass and the pyruvate and lactate levels in the rat peripheral blood as well. The data presented show that as a result of the formation of the neurotic state of anxiety in rats the decline in the peripheral carbohydrate and energetical metabolism connected with the activity of the hypothalamic neurotransmitter and hormonal systems was observed. In the brain structures against the background of the monoaminergic disbalance appearance of carbohydrate and energetical metabolism disbalance is developed. Along with it the organism tends to compensate the decline of catecholaminergic

influences and energetical metabolism at the neocortex level with the help of the intensification of these processes in the hippocampus.

GENDER DIFFERENCES OF CYTOCHROME OXIDASE REACTIVITY IN THE HIPPOCAMPUS OF TOTAL SLEEP DEPRIVED RATS. Hung-Ming Chang and Chyn-Tair Lan. Chung Shan Medical University, Taichung, Taiwan

INTRODUCTION: Sleep disorders are a common cause of neurocognitive impairment that has been implicated as a risk factor for neuropsychological disease. While both epidemiological and clinic-based studies indicate that neuropsychological diseases are more common in women than in men, the present study is aimed to determine whether there is any gender difference in the functional status of hippocampal neurons following severe sleep disturbance. **METHODS:** Sleep disturbance was achieved by subjecting the adult rats to five days of total sleep deprivation (TSD). The cytochrome oxidase (COX) histochemistry together with the NMDA receptor subunit 1 (NMDAR1) immunohistochemistry was used to detect the functional status of the hippocampus. **RESULTS AND DISCUSSION:** The results indicated that in normal rats, enhanced COX and NMDAR1 reactivities were detected in the entire region of hippocampus without gender difference. However, following TSD, the staining intensity of COX and NMDAR1 reactivities were drastically decreased in the hippocampus of both genders with a more significant dropping in females. Since COX and NMDAR1 reactivities could serve as the reliable marker for cellular endogenous metabolism and neuronal activity, respectively, the remarkable decreasing of COX and NMDAR1 reactivities following TSD may imply that TSD would suppress the functional status of hippocampal neurons. The pronounced reduction of COX and NMDAR1 expression observed in female rats than in male rats further suggests that TSD would exert a worsened effect on functional status of females' hippocampal neurons. **CONCLUSIONS:** We suggest that the present neurochemical finding might provide new insights into the pathophysiological mechanisms underpinning the gender difference susceptibility of sleep-related neuropsychological diseases.

CHRONIC CORTICOSTERONE-INDUCED INCREASE IN THE RESPONSIVENESS OF RAT HIPPOCAMPAL CIRCUITRY TO THE ACTIVATION OF 5-HT₇ RECEPTOR IS REVERSED BY IMIPRAMINE. P Pitra, G Hess. Institute of Pharmacology PAN, Krakow, Poland

INTRODUCTION: Perturbations of the hypothalamic-pituitary-adrenal (HPA) axis in animals can uncover cognitive and emotional disturbances in predisposed individuals that resemble some of the symptoms that are seen in human with depression. One of those is hypercortisolemia which can be mimicked by repetitive administration of corticosterone to rats and it has been suggested to represent one animal model to study the role of stress in depression. It has been established that serotonergic receptors are affected by stress and corticosterone. The effects of serotonin (5-hydroxytryptamine, 5-HT) in the central nervous system are mediated by multiple 5-HT receptors. The 5-HT₇ receptor has been implicated in various functions including circadian rhythmicity and sleep, disturbances of which are related to affective diseases. It is also could be a potential therapeutic target for treatment of psychiatric diseases such depression. Our previous study demonstrated that repetitive treatments of rats with antidepressant drugs (imipramine and citalopram) decrease the responsiveness of rat hippocampal CA3 neurons to the activation of 5-HT₇ receptor. However, these experiments have been conducted in naive animals. Therefore, in the present study we set out to evaluate whether imipramine treatment of rats repetitively receiving corticosterone will result in a reversal of corticosterone-induced changes in 5-HT₇ receptor-mediated modulation of epileptiform activity in *ex vivo* hippocampal slices.

METHODS: Young adult male rats were injected subcutaneously with corticosterone for 7 or 21 days (10 mg/kg, suspended in 1% Tween 80) twice daily. The third experimental group received corticosterone for 21 days and since the eighth day of corticosterone treatment, these animals additionally received imipramine for 14 days (10mg/kg, per os) twice daily. Each treated group had a matched control group receiving vehicle. Hippocampal slices (450 µm) were prepared two days after the last drug administration. Spontaneous epileptiform bursts were recorded extracellularly from CA3 area of slices in nominally Mg²⁺-free incubation conditions. 5-HT₇ receptor-mediated increase in bursting frequency was induced by bath application of 5-carboxamidotryptamine (5-CT) in the presence of N-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-N-2-pyridinylcyclohexanecarboxamide (WAY 100635), an antagonist of 5-HT_{1A} receptor. This effect was dose-dependent. **RESULTS AND DISCUSSION:** The effect of application of 100nM 5-CT induced increase in bursting frequency, which was significantly enhanced in slices prepared from animals treated repeatedly with corticosterone for

7 and 21 days ($74 \pm 3\%$ of basal frequency, $n=16$ and $86 \pm 9\%$, $n=12$ respectively, $p < .05$, ANOVA) compared to slices prepared from control rats received 1% Tween 80 for 7 and 21 days ($61 \pm 5\%$, $n=15$ and $66 \pm 5\%$, $n=9$ respectively). This enhancement was reversed by imipramine administrated concurrently with corticosterone ($56 \pm 5\%$, $n=15$, $p < .001$, ANOVA). Neither repeated administration corticosterone nor imipramine did not affected the mean basal bursting frequency, which was not different from the activity recorded in slices obtained from the control group of animals. The result of the present study confirm earlier data from this laboratory that repetitive corticosterone and imipramine treatments exert opposite effects on the reactivity 5-HT₇ and extend these findings in showing that imipramine administrated concurrently with corticosterone normalizes the response to agonist of 5-HT₇ receptor. Corticosterone- and imipramine-induced adaptative changes in the reactivity of hippocampal 5-HT₇ receptor remain less explored. To our knowledge, no data are available, regarding the influence of corticosterone and imipramine on the amount of hippocampal 5-HT₇ receptor. **CONCLUSIONS:** The results of the present study indicate that imipramine administrated concurrently with corticosterone normalizes the corticosterone-increased responsiveness of rat hippocampal circuitry to the activation of 5-HT₇ receptors. The mechanism by which long-term elevated corticosterone influences functions by imipramine remains open to further research.

AFFECTIVE DISORDERS IN THE STRUCTURE OF MENTAL DISORDERS IN EPILEPSY: CLINICAL AND REHABILITATION ASPECTS. TV Kazennykh. Mental Health Research Institute TSC SB RAMS, Tomsk, Russia

INTRODUCTION: Some authors regard depression as “an attribute of epilepsy just as it is” (Boglium et al 1997; Motta et al 1997) or speak about “high risk of depressive disorders in epilepsy” (Siffels et al 1997). On the other hand, presence of disease itself, diagnosis of epileptic illness often was very dramatic for the patient, was perceived as ruin of life plans, socially disadapted and promoted permanent psychological distress and as a result – decrease of quality of his/her life. Clinical, clinical-catamnestic, experimental-psychological methods were used in this study. **RESULTS AND DISCUSSION:** We assessed mental disorders in epileptic patients under observation at Interdisciplinary Center of prevention of paroxysmal states (ICPPS). In 632 epileptic patients among revealed mental disorders of affective sphere predominated (59,4%) in the kind of irritability, decreased mood, emotional lability, inclination for reactions of anxiety. Decreased mood in patients was accompanied by feeling of anguish, inclination for reactions of weak spirit. Great number of “somatic” complaints has been noted: headaches – various in character and intensity, feeling of fatigue, unpleasant sensations in various parts of the body, general weakness. 18,2% were constituted by cases of decreased mood with dysphoria and anxiety, in patients explosiveness, touchiness, whining were noted. In 43 patients (6,8%) cause of depression was psychogenic trigger, for 24 of them an absolute traumatizing factor was diagnosis of epilepsy, for the rest separation from their partners was dramatic and in 6 patients suicidal statements were revealed (female patients were admitted in mental hospital). Depressive mood, anxiety and uneasiness in this case were causally conditioned and according to ICD-10 state of patients may be diagnosed as depressive reaction associated with disorder of adaptation. We investigated quality of life of epileptic patients. To assess quality of life, we used Scale of Quality of Life according to Gundarov (1995), with evaluation according to 15 indices – position in the society, work, inner peace, family, children, health, conditions in area of living, housing conditions, material well-being, nutrition, sexual life, spiritual needs, communication with friends, recreation. Examination has shown decrease of indices of quality of life in all patients, especially according to scales “job”, “inner peace”, “family”, “children”, “health”, “material well-being”, “sexual life”, “spiritual needs” up to 0-2 scores. Predominance in the structure of mental disorders in epilepsy of disorders of affective domain required, in addition to correct antiepileptic therapy, addition to the scheme of treatment of antidepressants, “correctors of behavior”, tranquilizers. Purposefulness of their administration and dose were considered by the psychiatrist-epileptologist individually. However, significant role in complex treatment was played by psychotherapeutic activities directed at training the patient “to live with his life”, correctly react to various stressful situations what, in its turn, decreases risk of emerging the seizure. Catamnestic follow-up has revealed decrease of affective tension in 263 patients (70,3%), accompanied by reduction of paroxysmal seizures. One more assessment of quality of life has revealed positive dynamic of indices according to scales “family”, “children”, “health”, “material well-being”, “sexual life” up to 3-4 scores. **CONCLUSIONS:** Analysis of mental disorders comorbid with epilepsy in 632 patients of ICPPS, has shown that in structure of affective disorders in epilepsy, the depressive

character of affect is most typical. Conducted rehabilitative activities including medication and psychotherapy individual and familial) promoted better social including familial adaptation of epileptic patients what was clearly illustrated by positive dynamic of criteria of quality of life.

STRESS INDUCED BY HOUSING CONDITIONS AFFECTS VULNERABILITY TO DRUG RELAPSE IN MICE. MA Aguilar, J Lluch J, M Rodriguez-Arias, J Minarro. Psychobiology of Drug Dependence Research Unit, Department of Psychobiology, Faculty of Psychology, University of Valencia, Spain

INTRODUCTION: Social isolation induces profound and long-lasting effects on an animal's behavior. Studies that have evaluated the effects of housing manipulation on the rewarding properties of cocaine have obtained controversial results. In some, isolation did not affect animals' self-administration of cocaine (Boyle et al 1991; Bozarth et al 1989), while in others it enhanced sensitivity to the reinforcing properties of the drug, evaluated by the response rate to a conditioned stimulus and food (Smith et al 1997). Conversely, when the conditioned place preference (CPP) paradigm was employed in post-weaning isolated rats it showed that they were insensitive to cocaine and did not develop CPP (Schenk et al 1986). Two recent studies have evaluated the effects of neonatal isolation on the acquisition, extinction and reinstatement of cocaine self-administration in adult rats. Isolation increases acquisition, maintenance (Lynch et al 2005; Zhang et al 2005) and cue-induced reinstatement (Lynch et al 2005), without altering cocaine-induced reinstatement (Zhang et al 2005). In the present work we investigate the effects of stress induced by social deprivation (isolation housing) on the extinction and reinstatement of a previously acquired CPP induced by cocaine in adult mice. Our hypothesis is that isolated housing is a stress-inducing event that leaves animals more prone to reinstatement after extinction. **METHODS:** Male mice of the OF1 strain were housed in groups of four for 10 days previous to carrying out experiments and during the acquisition of CPP. Afterwards, animals were divided into 2 groups according to the conditions in which they had been housed during CPP extinction and reinstatement: 1) isolated before extinction and 2) grouped during extinction and isolated before reinstatement. The apparatus consisted of four identical plexiglas place-conditioning chambers containing two equally sized compartments (with different coloured walls and distinct floor textures), which were separated by a grey central area. The procedure of CPP acquisition, unbiased in terms of initial spontaneous preference, consisted of 3 phases. In the first phase (pre-conditioning) mice were allowed access to both compartments of the apparatus for 15 min each day over 3 days, and the time spent by an animal in each compartment was recorded. In the second phase (conditioning), which lasted 4 days, animals received an injection of physiological saline before being confined to the vehicle-paired compartment for 30 minutes. After an interval of 4 h, they were administered 50 mg/kg of cocaine and immediately confined to the cocaine-paired compartment for 30 minutes. During the third phase (post-conditioning), the time spent by untreated mice in each compartment was recorded over a timespan of 15 min. Following acquisition of CPP, animals were submitted to an extinction schedule consisting of a weekly 15 min test until CPP was confirmed to be extinguished. After extinction, the reinstating effects of decreasing doses of cocaine were evaluated. **RESULTS AND DISCUSSION:** In previous studies we have not found isolation rearing to have effects on cocaine CPP: isolated and grouped animals showed similar acquisition of CPP and reinstatement with a priming of cocaine (25 mg/kg). In the present study we demonstrate that isolation of animals prior to extinction (i.e., after acquisition of CPP) increased their resistance to extinction of CPP. Isolated animals maintained a significant cocaine-CPP five weeks after conditioning, while those that were grouped together maintained CPP for only two weeks. Moreover, isolated animals showed a stronger reinstatement response after a priming injection of a low dose of cocaine (6.25 mg/kg) than animals that were isolated only before reinstatement, suggesting that long-term isolation renders animals more sensitive to the reinstating effects of drug priming. **CONCLUSIONS:** These findings demonstrate that isolation stress has marked and enduring effects on cocaine-seeking behavior in adult mice, suggesting that stress interacts as a vulnerability factor in relapse into cocaine abuse. **ACKNOWLEDGEMENTS:** Ministerio de Sanidad y Consumo, Delegación del Gobierno para el Plan Nacional sobre Drogas (Proyectos de Investigación, 2004). Instituto de Salud "Carlos III" (FIS), RETICS, Red de Trastornos Adictivos (RD06/001/0016). Ministerio de Educación y Ciencia, Dirección General de Investigación and FEDER (SEJ2005-00316/PSIC) (Spain). Generalitat Valenciana. Agencia Valenciana de Salud. Dirección General de Drogodependencias (FEPAD).

EVALUATION OF ATTENTION LEVEL AND COGNITIVE DYSFUNCTION IN PATIENTS WITH VALVULAR DISEASE OF THE HEART. AN Savostyanov, VG Postnov, MKh Kadochnikova, OV

Conference Proceedings
10-th Jubilee Multidisciplinary International Conference of Biological Psychiatry
"Stress and Behavior", St-Petersburg, Russia, May 16-20, 2007

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Cardiological operations are accompanied by a number of surgical interventions in vital activity of organism, which have influences to functions of nervous system. Application of total anesthesia, artificial blood circulation and hypothermia in a number of cases can be the reason of violation of the highest psychical functions, and may induce long-time behavioral changes that may break social adaptation of a patient after surgical intervention. Besides, psychological stress in result of subjective emotions during intervention is a source of behavioral violations. However, neurological, psychophysiological and psychological results of cardiologycal surgical intervention are not enough clear. Here we study disturbances of attention arising in patients with valvular heart diseases, which had surgical intervention on open heart in conditions of artificial blood circulation. Patients (45-60 y.o.) who had interventions on heart in State Research Institute of Blood Circulation Pathology, have been surveyed. Results of patients' inspection were compared with the similar results received from healthy subjects. In our research, the dependence of attentional changes after surgical intervention on individual reactive anxiety levels, was analyzed. Psychological tests for detection of a level of personal and situational anxiety were used for the research. Besides, all subjects have been tested by means of system of computer tests of the program "MP-Psychotest" aimed to determination of an individual level of directed and not directed attention. After a psychological part of exploration, at its participants the acoustical evoked potentials of the brain which have been written down in paradigm P300 were registered. In result of research it has been shown, that cardiologycal surgical intervention did not lead to change of a directed attention level and speed of sensomotor reaction under absence additional noise handicaps. However, cardiologic patients showed essential change of reaction speed and execution accuracy under presence irrelevant stimuli accompanying to the primary goal. During switching from one task to another one, the patients had much greater quantity of errors in comparison with healthy subjects. The quantity of errors positively correlated with parameters of situational anxiety. Such finding can be interpreted as consequence of low stability of attention in result of factors of the operational period, and also psychological stress observable for 7-10 day after surgical intervention.

LOCALIZATION OF CEREBRAL ISCHEMIA AS A FACTOR OF POST-STROKE DEPRESSION (PILOT STUDY). S Draca, D Kolar. Clinic Dr M.Zotovic, Belgrade, Serbia; Department of Psychiatry, McGill University, Montreal, Quebec, Canada

INTRODUCTION: Common behavioral and cognitive sequale of stroke include depression, psychosis, anxiety, and personality change among others. Post-stroke depression (PSD) appears to be more than a reaction to the loss of function in stroke patients. Injury to specific brain areas appears to increase the risk of developing PSD, with hemispheric and antero-posterior asymmetries affecting mood states. Researches reported an increased frequency of indifference reactions in patients with right hemisphere lesions, while the lesions in the left hemisphere are more likely to be associated with PSD. **METHODS:** This study included a total of 24 first-stroke patients, ages 39-73 years, 2-18 months post-stroke, 46% of patients were female. The patients were subdivided in four groups (n=6/group): Group 1: left cortical frontal-temporal-parietal (FTP) lesions, Group 2: right cortical FTP lesions, Group 3: left sub-cortical (caudate-putamen) lesions, and Groups 4: right sub-cortical lesions. All patients were tested by self-rating depression scale Beck Depression Inventory (BDI)-II. BDI-II is a very useful screening instrument for a depression with a high reliability. The patients with depression before the stroke, as well as the patients with post-stroke cognitive decline or dysphasia, that was severe enough to prevent reliable communication, were excluded from the study. A one-way analysis of the variance (ANOVA) was used, while paired t-test was performed to evaluate differences between two groups. **RESULTS AND DISCUSSION:** Eight patients (30%) in our sample met a clinical criteria for depression. The patients with left hemisphere lesions, both cortical (Group 1) and sub-cortical (Group 3) had a significantly increased BDI-II scores compared to patients with right cortical (Group 2) lesions (Group 1 vs. Group 2, as well as Group 3 vs. Group 2 =probability value less than .05). Group 4 showed no significant difference compared to any other group. These results demonstrated an increased rate of PSD in patients with left hemisphere lesions (both cortical and sub-cortical) compared to patients with right cortical lesions. A group of post stroke patients with right sub-cortical lesions showed no difference compared to other groups. Numerous previous studies on the same topic suggested various underlying mechanisms, including difference in serotonin binding or hemisphere specialization for the perception of emotions. **CONCLUSIONS:** These results highlight a need for depressive symptoms screening in stroke patients. A further investigation regarding a

question why injuries of specific brain regions are more likely to produce depression, are with no doubt necessary.

LIFE STRESS EVALUATION WITH REGARDS TO SUICIDAL IDEATION AND FAMILY SUICIDE HISTORY IN RANDOM COHORT OF GENERAL POPULATION. ZhV Emyasheva, VA Rozanov. Odessa National Mechnikov University, Odessa, Ukraine

INTRODUCTION: Negative life events (NLE) have a great impact in precipitation of suicidal tendencies. Nevertheless there are few studies evaluating NLE in general, non-suicidal population. On the other hand evaluation of NLE may be of interest from the point of view of evaluation of life stress in the population, as well as possible links with suicidal tendencies. **METHODS:** We have studied NLE in the random group of Odessa residents, attendees of the medical courses for those seeking driving licenses. General number of respondents was 300 people, 120 men and 180 women, aged from 18 to 77 years. During testing confidentiality was provided. For life stress evaluation the NLE questionnaire developed by NASP (Swedish National Suicide Prevention Center) for the purposes of the "Swedish-Ukrainian suicide genetics" project was used. The questionnaire contained 29 questions about possible negative events, each question designed in a way to measure 3 dimensions: what happened, when happened and how often it happened. Respondents were also asked to range NLE by adverse impact on their life-being. They were also asked to report about positive events, which affected their lives in a positive manner. This instrument was supplemented with demographic information, family suicide history questionnaire and several questions revealing their own suicidal tendencies (suicide attempts and suicidal thoughts). NLE accumulation scores (life stress) were calculated using software developed in NASP, based on multiplication of individual answers scores (happened/not happened, when young/when old, once/several times) and with consideration of quality factor (QF), derived from previous studies, based on ranking of the NLE by random non-suicidal respondents. **RESULTS AND DISCUSSION:** General NLE scoring in the studied group was about 17,4; men and women had almost the same scoring (17,6 and 17,9 scores). On the other hand when looking at the age groups there were distinctions: women reported about higher life stress in the age groups 18-19, 40-49 and 60-69 years. In the age groups 20-29, 30-39 and especially 50-59 years men outscored women. This coincides with differences in suicide attempts frequency in the corresponding age groups of men and women in Odessa, registered during suicide attempts monitoring in the general population. Ranking of NLE by respondents showed, that loss of a close person by the reason of death was ranked first in 33,9% of cases, second highest rank event (25,2%) were relationship problems. These two problems can be combined together as "personal network problems", which means that about 60% of life stress is determined by this dimension. Next ranks were occupied by life threatening problems (security threats -12,2%), economical problems (10,4%), violence and abuse (7,4%) and loss of health (7,0%). It is remarkable that NLE ranking appeared different in age and gender groups. In the early age group "loss of a close person by reason of death" and "break of relationship" occupied first positions followed by "loneliness", in the middle age groups economic problems prevailed followed by "personal network problems", in the older age groups again "loss of close person" and "relationship problems" were prevailing followed by economic problems. Questioning about suicidal thoughts revealed that 25,6% of respondents (27,5% of men and 24,4% of women) reported about suicidal ideation. This reminds the known fact that in many animal species from 20 to 30% of animals has abnormally high reaction to stress. The biggest percent of suicidal thoughts was registered in the age group 20-29 years both in men and women. From 300 persons questioned 6 persons (2%) reported about suicide family history. Majority of them had NLE score higher than average for the whole group. **CONCLUSIONS:** It is likely that life stress (at least evaluated by NLE questioning) is equal in men and women, in both genders high frequency of suicidal thoughts coincides with the period of life when negative events are accumulating, age and gender differences between NLE accumulation during life span has the same profile as suicide attempts rate which confirms the role of life stress in provoking suicidal behaviors.

GROUP THERAPY FOR BIPOLAR DISORDER: A SYSTEMATIC REVIEW. ID Segredou, MD Livaditis, CI Mitsonis, KI Liolios, KE Stamatopoulou, EE Maragkoudaki, M-NE Katsanou. Psychiatric Hospital of Athens, Athens; Democritus University of Thrace, Thrace, Greece

INTRODUCTION: Bipolar (manic-depressive) disorder is a chronic psychiatric illness that results in significant psychosocial impairment, including diminished quality of life and functioning, despite aggressive pharmacotherapy. The review will consider the current evidence for effectiveness of group therapy as an adjunct to pharmacotherapy for bipolar disorder. In group psychotherapy the complexity

of communication is multiplied manifold. Interactions take place in relation to authority, to peers, or to the group as a whole. **METHODS:** We reviewed published outcome studies since 1985 identified in MEDLINE and PsycINFO searches, based on the following key variables: bipolar disorder, group therapy, psychoeducation, psychotherapy, psychosocial treatments, social skills training. **RESULTS AND DISCUSSION:** We identified 18 studies: 9 on psychoeducational interventions, 2 on group cognitive behavior therapy, 3 on interpersonal/ interactional and social rhythm therapy and 4 on psychoanalytic group psychotherapy. Controls were included in 3 and all studies included medication. The addition of group therapy to standard pharmacological treatment appear to benefit people with bipolar disorder. Many studies lack appropriate control groups, follow-up and standardised measures of symptoms and diagnosis. **CONCLUSIONS:** Adjunctive group therapy augment the benefits of pharmacotherapy and enhance social functioning in bipolar disorders. Better designed studies would reduce the risk of over-estimates of effect sizes. Few studies, small sample sizes, brief treatment durations, and nonstandardized assessment instruments may have contributed to the limited positive outcomes. Further developments of group therapy need to have a clear picture of what approach (e.g. psychoeducational, cognitive behavior, interpersonal) is most effective in what phase of the disorder. Also, there is as yet no clear indication of whether such subtypes (e.g. bipolar I or II, or rapid cycling) have differential responses to group therapy.

COMMUNICATIONS

COMPARATIVE ANALYSIS OF SPONTANEOUS ALTERATION BEHAVIOR FOLLOWING i.c.v. INJECTION OF A β (25-35) PEPTIDE AND EXPOSURE TO HYPOKINESIA. MI Aghajyanov, KB Yenkovyan, KS Safaryan, GA Navassardyan. Departments of Biochemistry and Pathophysiology, Yerevan M. Heratsi State Medical University, Yerevan, Armenia

INTRODUCTION: Hippocampal neurons are appeared to be impaired either by beta-amyloid peptide as by stress. Though effects of A β on learning and memory processes have been extensively studied using different experimental in vivo and in vitro approaches, the influence of A β on cognitive function is not completely understood. Cognitive deficit has been well documented both in transgenic mice overexpressing mutant human APP and in rodents with centrally administered A β . Most injection models were performed using synthetic peptideS A β (25-35), A β (1-40) or A β (1-42) analogous to peptides found in neuritic plaques in Alzheimer's Disease patients. Intracerebral injections of A β -related peptides to mice or rats impair the learning and retention of active or passive avoidance in elevated plus maze (X-maze), as well as discrimination learning in Y-maze. On the other hand the movement restriction is great social problem of contemporary population, which can be a main risk factor of the cognitive functions impairment. The aim of this study was a comparative analysis of hippocamp-dependent spatial alternation behavior and passive and active avoidance between rats subjected aggregated A β 25-35 peptide into each cerebral lateral ventricle and rats exposed to hypokinesia. **METHODS:** The experimental model of AD was created in rats by intracerebroventricular (i.c.v.) injection of 3.0 μ l aggregated A β (25-35) solution (1mg/ml) into each cerebral lateral ventricle at a rate of 1 μ l/min. Fifty young adult male rats, weighing 230-290g were divided into 2 groups: the control group consisted of vehicle treated animals injected with 3,0 μ l sterile bidistilled; the experimental group was i.c.v. injected with aggregated A β . The hypokinetic rats were exposed in hypokinesia 22 hour daily in narrow individual plexiglass cages, which restricted their movements in all directions. All experimental groups were tested in the spontaneous alternation performance in the Y-maze. We also studied behavioral changes in elevated plus maze in mentioned groups. **RESULTS:** The i.c.v. injection of aggregated A β (25-35) into the cerebral ventricles resulted in a significant decrease in spatial alteration behavior at 30, 60 and days after surgery, whenever hypokinetic rats showed non unidirectional changes along the restriction period. It should be mentioned that amyloid injected group shows progressive non cognitive behavior effect and not dependent on the time of observation. Since the decrease in alternation behavior did not depend on changes in general exploratory activity of rats measured as a number of entries it reflected the decline in memory function suffered by exposure of A β (25-35). In the elevated plus maze, which reflects the passive and active avoidance hypokinetic rats increased time in closed arms in all time point studies, while amyloid induced rats spent prevailed time in open arms. **CONCLUSIONS:** Our investigation showed that in different models used spatial alteration and avoidance changed indirectly in time dependent manner. It means that each pathway, which leads neuronal death even in the same structure has it's specific dependence on the pathogenesis, which is involved in the process.

SUCROSE TEST METHOD IN C57BL/6 MICE: FACTS, ARTEFACTS AND UTILITY FOR DEPRESSION MODELS. T Strekalova, O Dolgov. Animal Behavior Division, University of Aachen, Max-Planck Institute of Biophysical Chemistry, Goettingen, Germany; Institute of Normal Physiology RAS, Moscow, Russia

Sucrose test is believed to measure sensitivity to reward in rodents. As such, a reduction in sucrose intake and preference are taken to have face validity to anhedonia, a core feature of human depression and depressive-like endophenotype in animals. In mouse models of depression, the definition of anhedonia by a sucrose test parallels other depressive-like changes in experimental groups, while the characterization of inter-individual differences in depressive-like behaviors with this paradigm is problematic. We developed a sucrose test method in mice, which provides with such a possibility. It is based on the assessment of sucrose preference, instead of absolute sucrose intake, as a parameter of hedonic state and on the application of refined testing conditions. Proposed procedure enables to diminish an impact of physiological and physical confounding phenomena of the mouse sucrose test, such as side preference, neophobia, individual variability in circadian fluctuations and liquid consumption, interference with experience of stress and repeated access to sucrose solution, leakage of bottles due to physical effects. Validity of this methodology was confirmed in a chronic stress depression model, as among stressed mice only individuals with a decreased sucrose preference showed depressive-like behavioral, physiological and gene expression changes verified in vivo studies, and were sensitive to the antidepressant treatment (Strekalova et al 2004, 2006).

ANXIETY AS AN EMOTIONAL STATE TYPICAL FOR PATIENTS WITH ORGANIC AND FUNCTIONAL CNS PATHOLOGY. TN Reznikova, IU Terent'eva, NA Seliverstova, VI Semivolos. Institute of the Human Brain RAS, St. Petersburg, Russia

INTRODUCTION: One of the most important problems in a clinical psychologist's practice is to determine the degree of the emotional disorders manifestation, in particular the anxiety. According to the modern concepts the anxiety is a special emotional state representing as a reaction to stress under imbalance of personality-environment interaction. On the initial stage of its generation the anxiety plays the positive role because it contributes to the psychic spare capacities mobilization and makes more active the psychological defense mechanisms. However, under long-term exposure of unfavorable stress factors the anxiety intensifies the negative emotions and brings to psychic dysadaptation and psychosomatic disorders. Therefore research into the anxiety is of great importance in case of various functional CNS disorders when the anxiety appears to be the guiding symptom and also in case of severe incapacitating chronic diseases, such as multiple sclerosis (MS). Thus the objective of this investigation is the determination of the anxiety characteristics in patients with organic and functional CNS pathology requisite for carrying out the psychotherapy. **METHODS:** The psychological investigation was carried out with two groups of patients: patients with MS (48 patients – 17 male, 31 female, at the age of 17-52 years old, in remission, severity of disease - $3,73 \pm 1,7$ (EDSS scale)); patients with obsessive-compulsive neurosis (OCN) (30 patients – 10 male, 20 female, at the age of 19-55 years old, neurosis form - development). The following psychological techniques directed to the research of conscious and unconscious anxiety have been used: the "Taylor test", based upon patient's verbal estimation of their psychic state; the projective techniques, such as the "Lusher test" reflecting the actual emotional state and the drawing tests ("Myself", "My family", "Male and female", "The house, the tree, the man") detecting the reflected attitudes to various aspects of life activity and permitting to differentiate the attitudes to which the anxiety was directed. The total index of anxiety has been considered by the "Taylor test" and the "Lusher test". By the drawing test the analysis has been carried out with the help of our specially developed approach, based on transferring the qualitative adjectives of some personality characteristics (including the anxiety) reflecting in drawings to the quantitative adjectives, which have been compared with the group of control group of healthy people. Besides, the anxiety estimation have been carried out before and after the treatment by non-medication method of forming and activation of artificial stable functional connections of the human brain (method ASFC), based upon the photostimulations with fixed frequency. The method ASFC mechanism of action is concerned with the optimization of intracerebral regulation of the brain. The course of treatment by the method ASFC has consisted of 10 sessions each of which has presented 6 pulses of photostimulations with fixed frequency and 10 seconds duration. **RESULTS AND DISCUSSION:** In patient with MS, the averaged index in Taylor test was $25,2 \pm 9,6$, at the same time the increased level of anxiety was revealed in 35% of the

patients (16 persons) and the high level of anxiety – in 29% of the patients (13 persons). In the group of patients with OCN the averaged index by this test was $30,9 \pm 8,5$ while in 70% of the cases (21 persons) the anxiety was very high. Yet the high level of unconscious anxiety by the “Lusher test” has been observed only in 16% of the cases (8 persons) in patients with MS and in 28% of the cases (8 persons) in the group OCN. By the drawing tests adjectives both groups of patients significantly differed from the control group of healthy people by the highest anxiety ($p < .05$) in all the attitudes (to themselves, to their family, to the people of other sex, to social environment), in other words all the patients suffered from the disorder of the attitudes system that pointed out the instability of their emotional state. Thus the levels of conscious and unconscious anxiety have been appeared to be high in all the patients and the most distinctly these rises have been revealed in the personality attitudes system. After the course of treatment by the method ASFC the reliable reduction ($p < .01$) of all the types of anxiety was reported in the group of patient with OCN whereas in the group with MS the reduction ($p < .05$) touched upon only the unconscious anxiety in the attitude toward the social environment. It should be emphasized, that in patients with OCN the most evident positive dynamics by the drawing tests adjectives have been observed in the attitude toward themselves and the social environment and varied depending on the initial level of anxiety by the data of the “Taylor test”. Thus under the same modes of impulses during the course of treatment by the method ASFC the levels of various types of anxiety have reduced differently in the patients with organic and functional CNS pathology that could suggest of the distinction of the anxiety mechanisms in these groups of patients. Also the results of our investigation demonstrate the opportunities of emotional state optimization by the psychophysiological way that can be effectively used in rehabilitation in psychotherapy.

CONCLUSIONS: The levels of conscious and unconscious anxiety are high in the patients with obsessive-compulsive neurosis and multiple sclerosis and the most distinctly these rises are revealed in the personality attitudes system. Under the treatment by the method ASFC the levels of various types of anxiety have reduced differently in the patients with obsessive-compulsive neurosis and multiple sclerosis that could suggest of the distinction of the anxiety mechanisms in these groups of patients. The treatment by the psychophysiological method ASFC allows us to optimize the emotional state of the patients with obsessive-compulsive neurosis and multiple sclerosis.

EFFECT OF NEUROPEPTIDE DRUG SEMAX ON INTRACELLULAR PH OF CULTURED CEREBELLAR GRANULE CELLS. AV Odgaeva, VB Turovetsky, AA Kamensky. Department of Human and Animal Physiology, Moscow State University, Moscow, Russia

INTRODUCTION: The drug Semax Met-Glu-His-Phe-Pro-Gly-Pro (ACTH₄₋₇-Pro-Gly-Pro), a synthetic analogue of the N-terminal fragment (4-10) of adrenocorticotrophic hormone, has been developed in the Institute of Molecular Genetics of Russian Academy of Sciences (Moscow). This nootropic peptide is successfully used in treatment of patients with injuries of the central nervous system. Semax has nootropic effects, stimulating attention, memory's consolidation, increasing learning ability and resistance to hypobaric, vascular hypoxia and behavior stress. In vitro, this peptide significantly prolongs the life-time of neurons in culture and also increases survival of rat pheocromocytoma cells (nervous cell's analogue) during oxidative stress. However, the cellular and molecular mechanisms of its neuroprotective action upon the cell are far from clear yet. In view of the foregoing, the aim of the present research is to investigate the effects of neuropeptide drug semax and its inactive analogue (Gly-Met-Glu-His-Phe-Pro-Gly-Pro) on intracellular pH of cultured cerebellar granule neurons. It is well known that this parametr is involved in different aspects of cell functions, is closely connected with other regulatory systems, and, in the opinion of some scientists, may claim to be the crucial system of cell regulation. **METHODS:** Here we used 7-day culture medium of cultured cerebellar granule neurons of male Wistar rats, which were obtained from brain by method of fermentative mechanical dissociation. The culture medium developed in CO₂- incubator at temperature 35,5°C and relative humidity 98%. Neuropeptide drug semax and its inactive analogue were added to culture medium in final concentration 10 µg/ml. The intracellular pH of cultured cerebellar granule neurons was obtained by incubating cells with fluorescein diacetate in final concentration of 5 µg/ml for 15 min. After the unbound indicators had been wash out. The cover slips were placed in chamber with Hanks solution containing 10 mM HEPES (pH 7,2). The intensity of fluorescence of individual cells was measured during 20 min at wavelengths 520 and 570 nm with LUMAM-I3 luminiscent microscope. The intracellular pH was determined with the use of calibration curves. The results were statistically processed by programm Statistica 6.0. **RESULTS:** Application of neuropeptide drug semax (10µg/ml) to culture medium of cerebellar granule neurons significantly ($p < .05$) decreased their intracellular pH (by .24 unit of pH). **CONCLUSIONS:** Semax leads to phasic changes in intracellular pH during the

time that indicates a participation of pH-regulatory system in processing of observed cellular effect. More information is needed to understand the cellular and molecular pathways involved in the neuroprotective action of peptide semax on the cells of central nervous system.

CHRONIC VIRAL NEUROINFECTIONS AND SCHIZOPHRENIA-RELATED SYNDROME. VF Grycik, Yul Ilyuk, GM Zilberblat, EA Erschova, IG Vasilyeva, NG Chopic, OI Tsyubko, ES Galanta, NP Olexenko, AN Makarenko. Kyiv Regional Psychiatric Center, Glevacha, Romodanov Kyiv Institute of Neurosurgery, Kyiv, Ukraine

INTRODUCTION: The frequency of neuroviral disease in Ukraine has increased during the last ten years. It is caused by reduced immunity, incorrect use of antibiotics and drugs with immunosuppressive activity and possible mutation of viruses towards the biggest virulence. It is known that chronic brain disturbances, caused by persistent viruses, can be a reason of psychoneurological diseases. **METHODS:** We have studied 12 patients (4 females and 8 males) 16-28 years old. Nine of them have been treated in hospital for mental diseases with diagnosis "Schizophrenia" or "Acute psychotic disorder with schizophrenic symptoms". Three of them were hospitalized with hallucination-paranoid symptoms first. MRI and CT allowed to detect such pathological changes as single and multiple foci of density's decrease in paraventricular areas (2 cases), cystic changes in medial regions of temporal lobes (2 cases), intracerebral cyst in frontal lobe (1 case) spiculolike affection of occipital and parietal lobes (2 cases). In other cases we found unequal dilation of subarachnoid space. Lumbar puncture was taken from each patient. Polymerase chain reaction and immunological assay were used to detect an infection in cerebrospinal fluid. **RESULTS AND DISCUSSION:** Increased level of IgG to viruses was found in 6 cases. PCR analysis showed a presence a DNA of HSV1/2 (3 cases), EBV (3 cases), HSV1/2 and HHV-6 (1 case) EBV and HHV-7 (2 cases), HHV-7 (2 cases). After treatment with antiviral and immunomodulation therapy, based on virostatics, interferons and immunoglobulins, 9 of patients demonstrated reduction psychopathological symptomatology. 3 patients with cystic disorders had no improvement. Resistance and intolerability to different neuroleptic medications that had all of them were stopped. Follow-up study was from 1 to 5 years. 7 patients returned to their usual life and there was no need to continue a neuroleptic treatment. 2 patients sometimes accepted small doses of medications. There was only one relapse that caused a repeated course. **CONCLUSIONS:** The study shows that chronic viral infection of brain can be one of reasons for hallucination-paranoid psychopathological symptomatology. Its early diagnostic and treatment can save patients from such serious diagnosis like schizophrenia.

RAT IMMUNOREACTIVITY IN EXPERIMENTAL MODELING OF ACUTE AUTOHEMORRHAGIC STROKE WITH CYCLOPHOSPHANINDUCED IMMUNOSUPPRESSION (CHERNOBYL CONDITIONS) BY STAPHYLOCOCCUS INFECTION. AN Makarenko, YuN Mironyuk, OS Molozhavaya, VK Pozur, IG Vasilyeva, ES Galanta. Romodanov Kyiv Institute of Neurosurgery, Taras Shevchenko Kiyv National University, Kiyv, Ukraine

INTRODUCTION: Hemorrhagic stroke affects many people all over the world. Functional and biochemical disorders are often complicated by immunosuppression and infection. Therefore we created a novel experimental model of hemorrhagic stroke with staphylococcal infections with cyclophosphaninduced immunosuppression and studied rat immunoreactivity in these conditions. **METHODS:** The study has been carried out on white random bred male rats. Experimental modeling of hemorrhagic stroke (HS) was performed according to (Makarenko at al, 2002). Staphylococcal infection was induced via standard method (Aphonin at al, 1990). Cyclophosphaninduced suppression has been created via single injection of cyclophosphane in amount 50 mg/ml/kg (Arkadiev at al, 2003). Intact animals, infected animals with cyclophosphaninduced immunosuppression and rats with modeled HS on the background of cyclophosphaninduced immunosuppression and Staphylococcus aureus infection where the groups of comparison. Functional activity of neutrophiles (spontaneous and induced nitroblue tetrasolium reduction test (NST-test)), level of circulating immune complexes in serum, level of antibrain antibodies (ABA), proliferative activity of the lymphoid cells were detected. **RESULTS AND DISCUSSION:** Antibacterial activity of neutrophils of peripheral blood was significantly higher in rats with Staphylococcal aureus infection and immunosuppression without HS and reliably higher in rats with HS Staphylococcal aureus infections with cyclophosphaninduced immunosuppression groups in comparison to intact animals. The level of immune complexes in serum of rats with HS Staphylococcal aureus infections with cyclophosphaninduced immunosuppression was lower than in group without HS and significantly lower than in intact animals. The level of antibrain antibodies was significantly elevated in both experimental groups in comparison to intact animals.

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Proliferative activity of the main populations of lymphoid cells was strongly depressed in rats with and without HS infection and immune suppression, compared to control. Positive preliminary results were obtained by using drug "Cerebrolysin" (Ebewe, Austria) for correction of experimental condition. **CONCLUSIONS:** These data show the development of second immunodeficiency state under conditions of modeling hemorrhagic stroke, complicated with cyclophosphaninduced immunosuppression and Staphylococcal infection.

Our future meetings

- 11th "Stress and Behavior" Conference – 1st ISBS Congress (May 16-20, 2008, St. Petersburg, Russia)
- 1st ISBS Summer School on behavioral neuroscience (May 9-15, 2008, St. Petersburg, Russia)
- 12th "Stress and Behavior" Conference – 2nd ISBS Congress (May 16-20, 2009, St. Petersburg, Russia)
- 2nd ISBS Summer School on behavioral neuroscience (May 22-27, 2009, Riga, Latvia)

For notes

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