Centre for Physiology and Biochemical Research (CPBR)
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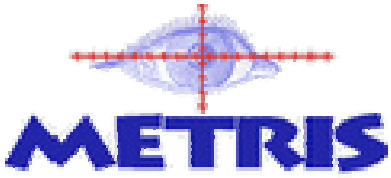
Proceedings

17th Multidisciplinary International Conference on Neuroscience and Biological Psychiatry
"Stress and Behavior"
ISBS Conference

St-Petersburg, Russia
May 16-19, 2012

IN PARTNERSHIP WITH:



Day 1. Wed, May 16, 2012

Oktiabrskaya Hotel, Grand hall (2nd floor), 10 Ligovsky Prospect, St-Petersburg, Russia

13.00-18.00 Conference registration

14.30-14.45 OPENING CEREMONY, WELCOMING ADDRESSES
A Kalueff (Conference Chair), V Klimenko (Program Committee Chair)

14.45-18.00 SPECIAL LECTURES (45 min)

DOPAMINE AGONIST MODELING OF SCHIZOPHRENIA INCREASES ETHANOL INTAKE IN RATS. AY Egorov, EO Kutcher, NA Chernikova, EV Filatova, Behavioral Neurophysiology and Pathology Laboratory, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia

INTRODUCTION: Comorbid substance abuse disorders have emerged as one of the greatest obstacles to the effective treatment of persons with schizophrenia. Animal models may help researchers and clinicians determine the mechanisms of alcoholism and co-occurring psychiatric disorders (i.e., schizophrenia.) The first possible model of dual diagnosis included neonatal ventral hippocampal lesion as a rat model of schizophrenia together with subsequent alcoholization. The aim of this study was to elaborate a new model of experimental psychosis (positive symptom schizophrenia) induced by dopamine agonist (Levodopa+Carbidopa) and to examine the alcohol preference in rats with experimental psychosis compared to intact animals. **METHODS**: In the first experiment (aiming to develop a new model of experimental psychosis), the study was carried out on 60 adult male Wistar rats ages, 10-11 weeks, with weight 180-200 grams were administered antiparkinsonic dopamine agonist Nacom© (Levodopa+Carbidopa) 300/50 mg/kg p.o.. In the second experiment 45 adult Wistar male rats were administered Levodopa+Carbidopa for 5 days every month of the four month experiment. 30 control animals were drug-free. In all animals we used the model of forced intermittent alcoholization. Every two weeks the level of alcohol preference was assessed in the «two bottle» test. The behavior activity in both experiments was evaluated in the "Open field" test. The animal responses to an auditory stimulus were also elucidated. **RESULTS AND DISCUSSION**: The analysis of behavior parameters (locomotor activity, peeping, defecation and tone reaction) in rats that were administered Levodopa+Carbidopa has shown the validity of the introduced dopamine pharmacological model of schizophrenia. Animal modeling of positive symptom schizophrenia leads to a significantly greater ethanol consumption for experimental rats on the early stages of chronic alcoholization. It can be assumed that high dopamine level is one of the reasons for the alcohol consumption in patients with schizophrenia. Accelerated ethanol preference forming was observed only after the period of forced alcoholization together with dopamine agonist administration, suggesting the model of common dopaminergic mechanisms of addiction and schizophrenia.

THE NEED FOR MULTI-MODAL AND MULTI-FUNCTIONAL MEASUREMENT SYSTEMS IN LABORATORY ANIMAL RESEARCH AND MATRIX ANALYSIS. L Bachdasarian, R Bulthuis, E Molenwijk, S Zhuchkov, Metris B.V., NG Hoofddorp, Kruisweg, Netherlands; University of Orel, Orel, Russia

Current trends in the Pharmaceutical industry are not only requiring shorter lead times but also better quality of pre-clinical test results. To achieve this animal experiments will have to collect data from different domains at the same time, (i.e. animal behavior, animal physiology and animal vocalizations.) To make this practically possibly, the automation and integration of different

measurement technologies is becoming crucial in preclinical research. Animal behavior is an interpretation of internal and external factors (stimulus). Behavior = Function {Dynamic Internal Stimulus/Drugs effects}; if external factors /stimulus = constant}. A constant environment is essential to build reliable behavioral study and analysis. To enhance the quality of the study and have better statistical probability, it is important to analyze many parameters from the same behavior (i.e. group of parameters or matrix). Matrix method for Behavior Analysis: Proper analysis and statistics of data is very important for in-vivo experiments. Therefore, the use of many independent parameters in the automated recognition of a behavior of the animal is crucial. To recognize a behavior automatically, LABORAS applies the 'Matrix Method' involving the analysis of several parameters that are derived from the measurement system. Your specific behavior = matrix / X1, X2, X3 - - -- - Xn; Y1, Y 2, Y 3 - - - - - Y n; E1, E2, E3 - - - - - En/ The above matrix shows an example of the different parameters for a specific behavior. Where X1, X2, X3 - - - - - - Xn, E1, E2, E3 - - - - - - En are functions from the specific behavior (e.g. amplitude, frequency, total energy, locomotion energy, locomotion energy / oscillation energy, etc.). Measuring matrix parameters and all kinetic energy during in-vivo experiments is very important to obtain a full ethogram of all behaviors shown by the laboratory animal. Traditional methods, based on observation or video analysis, offer only limited information. The Metris Laboras system enables measurement of all types of kinetic/movement energy while other non-invasive automated systems for behavior detection can only measure the locomotion component of the kinetic energy (e.g. locomotion energy $mv^2/2$). In addition, the matrix method and technology used in Laboras provides a way to measure more behaviors and to recognize them automatically and more precisely than ever before. By combining parameters from different systems the matrix will get better and further improve the quality of the research results. Experiment Results= function {Behavior (matrix), Physiology(matrix), Ultrasounds(matrix); External(matrix)=Constant}. Please contact levon@metris.nl (www.metris.nl) for more information.

NOVEL EXPERIMENTAL MODELS OF HALLUCINOGENIC DRUG ACTION, ANXIETY AND DEPRESSION – FROM FISH TO HUMANS. AV Kalueff, E Kyzar, J Cachat, S Gaikwad, J Green, A Roth, C Collins, M El-Ounsi, M Pham, A Davis, S Landsman, Department of Pharmacology and Neuroscience Program, Tulane Medical School, New Orleans, LA, USA

INTRODUCTION: In recent years, adult zebrafish models have been increasingly utilized in the fields of neuroscience and biological psychiatry. Adult zebrafish possess a fully characterized genome and a complex behavioral repertoire, and they represent an important bridge between model organisms. Although early publications were critical of the potential usefulness of this model, research by our group has shown that zebrafish behavioral and physiological domains are sensitive to a variety of pharmacological manipulations. **RESULTS AND DISCUSSION:** Adult zebrafish display robust geotaxis (bottom preference) in response to novelty – an anxiety-related behavior which is enhanced by anxiogenic drugs and reversed by anxiolytic compounds. Apart from anxiety, chronic doses of reserpine induced marked hypolocomotion and increases in whole-body cortisol in absence of top-bottom preference, resembling depressive-like states observed in rodents and humans. We have recently tested hallucinogenic compounds of various classes (e.g., LSD, MDMA, mescaline, ketamine, phencyclidine, salvinorin A and ibogaine) on adult zebrafish, revealing significant alterations in locomotion, geotaxis, melanophore aggregation, and endocrine function. Importantly, testing these drugs using standardized methods permits comparison of their various efficacies in aquatic models, thereby facilitating an evolutionary prospective in psychopharmacology. This model has also proven sensitive to pharmacologically-induced seizures, providing an alternative to rodents for anticonvulsant drug screening. Behavioral analysis is rapidly advancing in complement with high-throughput video-tracking techniquesand currently allows for the dissection of zebrafish behavior in both spatial and temporal dimensions. Our lab has explored the spatiotemporal dynamics of zebrafish novelty exploration, revealing conserved and patterned exploration that is distinct from anxiety-related states. Physiological parameters, such as whole-body cortisol and brain *c-fos* expression, are easily quantified in zebrafish and provide additional

biological correlates of drug-induced states. Taken together, our results indicate that zebrafish models will prove invaluable for the field of biological psychiatry in the near future. Their low cost of maintenance, robust behavioral responses and easily-manipulated genetic structure provide researchers with an effective tool for multifaceted, yet inexpensive investigations. **RESEARCH SUPPORT:** NIDA SOAR R03, CELT, Tulane Synergy and LA BoR OPT-IN grants to AVK.

ANXIETY IN GENERAL PRACTICE. E Akarachkova, Sechenov First Moscow State Medical University, Moscow, Russia

INTRODUCTION: Anxiety is the body's natural response to stress. It is physiological anxiety that allows the body to adjust itself under the influence of stressors. It is related to a specific dangerous situation. It increases in proportion to the level of danger and is associated with external factors. Its duration depends on the period of exposure to a traumatic factor. **METHODS:** In case of general practice, patients' anxiety disorders can manifest themselves as phobias. This anxiety is linked to certain situations (situational anxiety that appears as a response to the exposure to a specific irritator) and is accompanied by avoidance behavior. In Russia patients with anxiety disorders seek assistance from physicians and neurologists. The range of the patients' complaints arebroad and includes physical pain. A whole system of how practicing doctors should attend to the needs of such patients has been recently developed and upgraded. Anxiety provides favorable conditions for depression at an older age with high risks of such diseases as cerebrovascular pathology, metabolic syndrome or cancer. **RESULTS AND DISCUSSION**: If all anxiety disorders among 12-24 year-old individuals are successfully treated, 43% of all occurrences of depression at the beginning of adult life can be prevented. The optimum treatment tactics and therapy duration are determined at the next stage. The management of anxiety cases consists of two stages. The first stage is the reduction of anxiety and priority is currently given to psychotropic medications. At the second stage it is necessary to activate natural anti-anxiety mechanisms and increase stress resistance through the methods of traditional and non-traditional medicine. Taking into consideration the fact that psychovegetative syndrome is a frequent occurrence of chronic anxiety, which is caused by the imbalance of certain neuromediators (serotonin, noradrenaline, GABA and others) psychotropic medications need to be prescribed. Dual-action and tricyclic antidepressants are the most effective medications. In recent years magnesium-containing medications have started to be widely used because of the important role of NMDA-receptors of glutamate in the manifestation of not only psychic, but also physical occurrences of anxiety.

Day 2. Thur, May 17, 2012

Oktiabrskaya Hotel, Grand hall (2nd floor), 10 Ligovsky Prospect, St-Petersburg, Russia

Morning session

9.15-10.00 SPECIAL LECTURE (45 min)

THE PHENOWORLD CONCEPT – A MULTI-DIMENSIONAL APPROACH IN MULTI-ARENA HOME CAGE PHENOTYPING. E Wenzler, J Fehmer, TSE Systems GmbH, Bad Homburg, Germany

A thorough characterization of animal models of human diseases often faces issues of data quality due to non-standardized procedures and equipment, experimenter interference and animal stress. In recent years, TSE Systems has pioneered a home cage based research approach to increase animal welfare, reduce experimenter interference and increase throughput. The participation in international projects such as PhenoScale has resulted in a number of standardized operating procedures for phenotyping applications. Despite the flexibility of complex home-cage phenotyping instrumentation such as PhenoMaster or IntelliCage, there are still paradigms that could not be performed with these systems. Therefore, TSE Systems has developed the PhenoWorld concept of a multi-arena experimental environment architecture. In the PhenoWorld, we use hardware and software components from diverse TSE Systems product families to create a new dimension of experimental flexibility and comprehensiveness. Basic modules such as PhenoMaster for behavioral and metabolic phenotyping of single animals, IntelliCage by NewBehavior for cognitive analysis of group-housed animals, or modules of the Multi Conditioning System can now be combined to create highly customized solutions. The use of the AnimalGate as a central connector allows the access of individual animals to specific arenas for detailed analysis of any animal within the group. With this approach, additional paradigms such as maze systems can be implemented. Depending on the combinatorial options chosen, experimental setups for research areas such as addiction, cognition, neurodegeneration, aging, circadian, obesity/diabetes and many more could be envisaged or have been implemented. In conclusion, this unified, yet diverse approach opens new horizons for a large variety of high-quality in-vivo research approaches in biomedical and preclinical science.

10.00-13.00 SYMPOSIUM I: UNDERSTANDING DOPAMINE NEUROTRANSMISSION
Chair: R Gainetdinov (Italy)

TARGETING NETWORKS, AKT/GSK3 SIGNALING IN THE ACTIONS OF PSYCHIATRIC DRUGS. JM Beaulieu, Departments of Psychiatry and Neuroscience, Faculty of Medicine, Universite Laval-CRULRG, Quebec, Quebec, Canada

Psychotropic drugs acting on monoamine neurotransmission remain the principal form of pharmacological treatments for neuropsychiatric conditions such as schizophrenia, depression, ADHD and bipolar disorder. Several lines of research involving behavioral and biochemical approaches in normal and/or genetically modified mice provide evidence for the involvement of the protein kinases glycogen synthase kinase-3 (GSK3) and Akt in the behavioral functions of dopamine and serotonin (5-HT). These kinases have also received attention for their role in the actions of psychoactive drugs including lithium, antidepressants and antipsychotics. Furthermore, investigations of the mechanism by which D2 dopamine receptors regulate Akt/GSK3 signaling strongly support the physiological relevance of a new modality of G protein-coupled receptor

(GPCR) signaling involving the multifunctional scaffolding protein beta-arrestin 2. Here we provide an overview of how this dual function of components of the GPCR desensitization machinery relates to the mechanism of action of several psychoactive drugs and summarize recent insights into the relevance of the Akt-GSK-3 signaling cascade for the expression of monoamine-associated behaviors.

NEUROPLASTIC CHANGES FOLLOWING REPEATED EXPOSURE TO COCAINE DURING ADOLESCENCE. G Giannotti, L Caffino, G Racagni, F Fumagalli, Department of Pharmacological Sciences, University of Milan, Milan, Italy

INTRODUCTION: Single or repeated exposure to cocaine causes long-lasting functional and structural modifications in various brain regions that participate in different aspects of cocaine abuse and contributes to addiction, which can be considered a form of drug-induced neural plasticity. Recent data have implicated neurotrophic factors (namely FGF-2, GDNF, BDNF) in the action of acute or long-term cocaine exposure suggesting that they may contribute to the mechanisms that lead to cocaine addiction. Interestingly, the effect of exposure to cocaine during adolescence has not been widely explored. To this end, the major aim of our work was to investigate the expression of adolescent exposure to cocaine on neurotrophic factors at different time points (i.e. early after adolescence and at adulthood).

METHODS: Rats were treated with cocaine (20 mg/kg) during adolescence, i.e. from post-natal day (PND) 28 to PND 42. Some of the animals were then exposed to an acute stress on PND 45 whereas another group grew adult and was then exposed to stress on PND 90. Animals were then killed 15 min after the end of stress, either at PND 45 or PND 90, and the brain regions of interest were rapidly removed and put on dry ice. We focused our analysis on basic Fibroblast Growth factor (FGF-2) by means of Real Time PCR. **RESULTS AND DISCUSSION:** We found that 1) adolescent cocaine exposure increased FGF-2 mRNA levels in the prefrontal cortex of PND 90 rats with no effects in nucleus accumbens and striatum and 2) adolescent exposure to cocaine altered the subsequent trophic response to stress in adulthood in rat prefrontal cortex. These results indicate that the administration of cocaine during adolescence causes a long-lasting effect on trophic factor expression and that such changes are not only permanent but also dynamic since they influence the subsequent response to stress. **CONCLUSION:** Repeated exposure to cocaine during adolescence alters FGF-2 mRNA levels and it distorts or impairs the mechanisms responsible for FGF-2 regulation under acute challenging situations. The inability to mount a homeostatic trophic response to subsequent stress at adulthood may impair the normal responses of the cell to challenging situations pointing to specific mechanisms underlying lifelong susceptibility to adverse environmental conditions.

MANIPULATING BRAIN DOPAMINE TRANSMISSION THROUGH OPTOGENETICS. EA Budygin, Wake Forest School of Medicine, Winston-Salem, North Carolina, USA

INTRODUCTION: Optogenetics is an exciting technique based on light-sensitive ion channels called opsins. Although relatively new, optogenetics has already proven to be extremely powerful, particularly since opsins can be targeted to specific neuronal subtypes, and the resultant millisecond timescale control over neuronal firing can be used to mimic natural firing patterns. **METHODS:** Lately, our group has successfully employed optogenetics, combined with fast-scan cyclic voltammetry (FSCV), to manipulate dopamine (DA) release in the rat striatum. We used a viral vector to deliver the channelrhodopsin2 (ChR2) gene to the ventral tegmental area (VTA) and substantia nigra (SN) and implanted a fiber optic – which is coupled to a blue laser – into these regions. The light-driven stimulation of cell body DA neurons in the VTA and SN was used to mimic real neurochemical events that take place in the terminal field. **RESULTS AND DISCUSSION:** In the first set of experiments, changes in the sub-second DA release in the striatum of freely moving rats were detected with FSCV during the presentation of different rewarding and stressful stimuli. As expected, abused drugs (nicotine and cocaine) induced marked increase in sub-second DA release in striatal sub-regions. The classical aversive stimuli, including a tail pinch, resulted in a

unique DA signal patterns characterized by a significant increase in accumbal DA release that was time locked with the painful stimulus and which gradually declines after the stimulus was discontinued. In the second set of experiments, by combining the tight spatial and temporal resolution of both optogenetics and FSCV we have determined the parameters of optical stimulation necessary to mimic observed DA release patterns. We were able to repeatedly evoke concentrations of DA release as small as a single DA transient (50 nM). A U-shaped frequency response curve was found with maximal stimulation inducing DA effluxes (>500 nM) that approach therapeutic levels. This unique frequency dependence is likely based on the biological properties of the ChR2 proteins. Furthermore a lack of change in extracellular pH indicated that optical stimulation does not alter blood flow. **CONCLUSION:** According to our results, striatal DA is very responsive to optogenetic manipulation of frequency, pulse (flash) duration, number of flashes and light pulse power. Therefore, light-driven stimulation of brain DA neurons can be used to mimic divergent patterns of striatal DA dynamics that are observed in different behavioral situations. These tools will be essential in understanding the neural microcircuitry underlying brain DA neurotransmission. **RESEARCH SUPPORT:** NIH Grant DA021634.

THE ROLE OF G PROTEIN-COUPLED RECEPTOR KINASE 6 (GRK6) IN ANIMAL MODELS OF PARKINSON'S DISEASE AND L-DOPA TREATMENT. F Manago, S Espinoza, A Salahpour, TD Sotnikova, MG Caron, RT Premont and RR Gainetdinov, Department of Neuroscience and Brain Technologies, Italian Institute of Technology, Genoa, Italy; Department of Cell Biology, Duke University, Durham, NC, USA

INTRODUCTION: G protein-coupled Receptor Kinase 6 (GRK6) belongs to a family of kinases that can phosphorylate different G Protein-Coupled Receptors (GPCRs) upon their activation by agonist. Phosphorylation leads to rapid receptor desensitization by blocking the activation of G proteins. It has been reported that animal models of Parkinson's Disease (PD) and PD patients have an increased levels of GRK6 in the striatum. Moreover, mice lacking GRK6 (GRK6-KO mice) have been demonstrated to be supersensitive to several dopaminergic agonists, including cocaine and amphetamine. This study was undertaken to understand how GRK6 can affect the behavioral manifestations of dopamine deficiency and responses to L-DOPA in mouse models of PD. **METHODS:** For this purpose we used three approaches to model PD in GRK6-KO mice: 1) the cataleptic response to D2 dopamine receptor antagonist haloperidol; 2) crossing these mutants to dopamine transporter knockout mice and developing an acute model of absolute dopamine deficiency, DDD mice; 3) hemiparkinsonian 6-OHDA mouse model developed in GRK6-KO mice. To further clarify the role of GRK6-mediated regulation in dopamine-stimulated β-Arrestin2/AKT/GSK3β and MAPK signaling, we analyzed the pattern of phosphorylation of AKT/GSK3β and ERK1/2. **RESULTS AND DISCUSSION:** The results confirmed that GRK6 is important for the modulation of dopaminergic responses. GRK6 deficiency reduced cataleptic behavior, potentiated the acute effect of L-DOPA in DDD mice, reduced rotational behavior in hemi-parkinsonian mice, and reduced abnormal involuntary movements (AIMs) induced by chronic L-DOPA. **CONCLUSION:** These data suggest that pharmacological approaches to regulate GRK6 activity could be useful in modulating both therapeutic and side-effects of L-DOPA.

ROLE OF TRACE AMINE ASSOCIATED RECEPTOR 1 (TAAR1) IN D2 DOPAMINE RECEPTOR-RELATED BEHAVIOR AND SIGNALING. S Espinoza, F Manago, M Messa, TD Sotnikova, M Caron, RR Gainetdinov, Department of Neuroscience and Brain Technologies, Istituto Italiano di Tecnologia, Italy

INTRODUCTION: Mammalian Trace Amine Associated Receptor 1 (TAAR1) is a G protein-coupled receptor (GPCR) that is mainly expressed in limbic regions and monoaminergic nuclei, such as ventral tegmental area, dorsal raphe and nucleus coeruleus. TAAR1 can be activated by several members of a class of endogenous biogenic amines called "trace amines" (TAs) that includes β-phenylethylamine (β-PEA), p-tyramine, octopamine, and tryptamine as well as by several compounds known to target monoaminergic transmission such as amphetamine and some of its

derivatives. There is evidence indicating that TAAR1 is involved in the modulation of dopaminergic system. In mice lacking TAAR1 (TAAR1-KO mice), amphetamine induces more pronounced locomotor stimulation and dopamine release. Moreover, it has been reported that D2 receptor function is altered in TAAR1-KO mice. Dopamine system is involved in many physiological functions and has been implicated in various pathological states such as schizophrenia and Parkinson's disease. **METHODS**: By analyzing effects of several doses of haloperidol at different time points we found that haloperidol-induced catalepsy is significantly reduced in TAAR1-KO animals with the strongest effect at 4 hours. In order to investigate the intracellular signaling events that might be involved in TAAR1-mediated modulation of dopaminergic function, we analyzed D2 receptor-related signaling events in the striatum of mutant mice. **RESULTS AND DISCUSSION**: Haloperidol-induced c-Fos expression in the striatum was reduced in TAAR1-KO mice and western blot experiments revealed a significant reduction in AKT and GSK-3 phosphorylation with no difference in phosphorylation of DARPP32, ERK and CREB between WT and TAAR1-KO mice. We also studied β-arrestin2 recruitment to D2R using BRET technique and its role in vivo in striatum of TAAR1-KO mice. Since AKT/GSK3 signaling cascade is known to be linked to D2 receptor-mediated behaviors and β-arrestin2 dependent signaling, we hypothesize that these signaling events are important in the modulation of D2 receptor functions by TAAR1.

Afternoon session

14.00-16.00 SYMPOSIUM II. NEUROSCIENTIFIC APPROACHES TO THE STUDY OF HUMAN FEAR AND ANXIETY
Chair: D Mobbs (UK)

FEAR, SURVIVAL INTELLIGENCE AND THE NERVOUS SYSTEM. D Mobbs, MRC-Cognition and Brain Sciences Unit, Cambridge, UK
I will talk about a series of brain imaging experiments showing that higher-cortical areas, such as the ventromedial prefrontal cortex, control behaviour when the degree of threat is appraised as non-life endangering and guides the organism to choose the most effective strategy for avoidance. At extreme levels of threat, the periaqueductal gray may in turn inhibit more complex processes when a fast response is required, preparing the organism for tissue damage and survival through active (e.g. flight) and passive (e.g. freezing) coping (Mobbs et al., Science 2007).

THE NEURAL MECHANISMS OF EMOTIONAL CONTROL AND FLEXIBILITY. D Schiller, Mount Sinai School of Medicine, New York, US
My talk will focus on the neural mechanisms underlying emotional control. Because the environment we live in is constantly changing, our learned emotional responses need to be continuously updated to appropriately reflect current circumstances. Understanding the neural mechanisms that make such emotional flexibility may shed light on the impairments leading to anxiety disorders and may also promote new forms of treatment (Schiller et al, Nature, 2010).

MOLECULAR IMAGING OF EMOTIONAL DECISION MAKING IN HUMAN. H Takahashi, Kyoto University Graduate School of Medicine, Kyoto, Japan
We sometimes make decisions which are not accounted for by normative economic theories (e.g. expected utility theory). These decisions are highly influenced by emotions, such as fear. I will talk about a series of positron emission tomography studies investigating the role of neurotransmitters in emotional and bounded rational decision-making in human (Takahashi et al., Molecular Psychiatry, in press).

GENETIC AND PHARMACOLOGICAL APPROACHES TO HUMAN FEAR. A Perkins, Institute of Psychiatry, University of London, London, UK
My research is aimed at investigating the possibility that anxiety and fear stem from evolved defensive reactions. I explore state and trait forms of these phenomena. I have developed a human translation of a runway task previously used to measure the defensive reactions of rodents. I am now extending the use of this task to measure activity in the brain during human defense as well as examining the effects on human defensive reactions of psychiatric drugs and genetic risk factors for psychiatric illness (Perkins et al., Molecular Psychiatry, 2011).

16.20-17.35 CONFERENCE TALKS (25 min)

TECNIPLAST iSPAWN, ZEBTEC: ZEBRAFISH HOUSING AND HUSBANDRY NEEDS - TOWARDS A COMMON SET OF RULES. H Lehtinen, Techiplast, Italy
Brachydanio rerio (commonly known as zebrafish) is a well-known petshop fish since. Only during the 1970s zebrafish started swimming in research laboratories, when George Streisinger began his scientific work utilizing this new small teleost fish. Although his pioneering application was the beginning of everything, this alone would have not been sufficient. It is with contribution of Christiane Nusslein-Volhard in the second half of 1980s, that zebrafish was acknowledged as an animal model. The introduction of a new aquatic animal into the scientific community raised the need for a new housing environment. In order for zebrafish to be maintained properly, a basic understanding of water systems must be taken into consideration. At the beginning, standard aquaria were the preferred (or obliged) choice for new facilities. But while the programs were growing and the research expanded, professional systems started to appear, providing clear housing benefits and evident ergonomics advantages. Plastic was introduced as the main material for housing tanks, gradually replacing glued glass pet aquaria. Static solutions (where water is manually discharged by hand over a certain period of time) are now far back in our memories, as well-engineered recirculating systems are currently holding zebrafish almost everywhere in the world. The theory behind these RAS (Recirculating Aquaculture Systems) has been well applied to the zebrafish housing technology, and now is globally the preferred choice. All over the world, zebrafish is now swimming in stand-alone systems, normally the best option for small research facilities or as quarantine piece of equipment, as well as in large or “oceanic” multilinked racks systems, all controlled by a single or multiple redundant CLSs (Centralized Life Supports). In both cases, the housing system is not the only element that needs to be taken into consideration: the environment around it needs to be prepared to accommodate it. Once everything is set up, populating the system with animal is one of the most critical steps and it is not rare to make important mistakes during this phase. Now animals are swimming into multiple tanks and proper husbandry is the next challenge. It must be said that even if there are common efforts to define standards at this level, commonly accepted housing rules are not established yet. During this talk, we will be able to discuss the most used ones… - let’s start diving together.

THE PEPTIDE COMPENSATION OF THE POSTSTRESSOR COGNITIVE AND BEHAVIOUR DISTURBANCES OF THE MAMMALS. TN Sollertinskaja, MV Shorokhov, IM Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia
The problem of the neuropeptide compensation of disturbed cognitive functions and behaviour reactions, including negative being at the basis for the development of the emotional and posttraumatic stress is one of the most critical problems of the modern neurophysiology and medicine. It’s known that the leading role in emotional and motivated conditions belongs to the limbic structures such as hypothalamus (Hyp), hippocampus (Hipp) and amygdala (AM). Moreover significant role in the memory processes at the lower stages of the mammalian phylogenesis (the insectivores, rodents) belongs to the Hipp. However the peculiarities neuropeptide compensation of the cognitive and emotional disturbances in the different levels development of the mammals due to

the by influence the Hyp, Hipp and AM structures have not studied yet. The role of these structures in their mediated influence on the new cortex activity is practically absent. The aim of present work is the comparative studying of the synthetic peptides drugs, such as Semax (Sem) and Selank (Sel), in compensation for the cognitive and emotional (neurotizied) disturbances and the studying of the role Hyp, Hipp and AM in the mediation their effects on the neocortex activity in the ascending row of mammals. The experimental models of food conditioned reflexes (CR), delayed conditional reflexes (DCR) and motor interhemispheric relations (the choice the reactions of the side reinforcement), were used in the present study. The computer registration of the objective (EEG, vegetative and motor) components and analysis of EEG indices were applied. The Sem and Sel drugs were induced intranasaly, intramusculary as 0.1-5.0 and 30-100 mg/kg, accordingly. It has been established, that in insectivores, the effects of Sem and Sel are more expressed at the inherent forms of behaviour. In fact, they are wholly uniform in hedgehogs with neurosis: the food motivation restored, the emotional disturbances disappeared, and the motor activity increased. It was established that the of Sem and Sel compensatory effects on the disturbance memory processed in hedgehogs lasted for a short time (1-3 days). They had nonspecific facilatatory character. In comparison with hedgehogs, in rats the role of Sem and Sel in the compensation of the disturbance behaviour reactions, memory processes and various homeostatic functions have a different features. It was shown that Sel leads to the vivid changes of the rats on the «profile of behaviour» and handing. It has been established that the conditioned reflexes in animals with the Hipp and AM destruction after Sel administration are being restored and formed faster. For all that, the degree capacity for work in the Sel background increased. It was shown that the compensatory effects of the drugs were especially significant at the early stages of the limbic structures destruction. It has been established that in neurotic monkeys, the antiamnestetic and cerebroprotective effects Sem and Sel are different of the disturbance behaviour reactions and various types of memory processes. The Sel compensatory effects were especially significant and prolonged. Our new data have been received about the antiepileptic Sel activity of two forms of epilepsy: «frontal» induce by the application of stressor stimuli and the electrical stimulation of ventral Hipp. The wide computer analysis of the EEG disturbances revealed the dynamic of the Sel compensatory effects. It was shown that on the Sel background the full normalization of the EEG parameters (on the amplitude-frequency spectrum) and capacity for work obtained on the 2-3 days after drug application. Overall, our data reveal a potential neurophysiological underpinning for the application Sel in neurological clinics.

EFFECTS OF STRESS ON THE ACTIVITY OF A NEUROPEPTIDASE NEPRILYSIN IN RAT BRAIN STRUCTURES. DI Bagrova, NN Nalivaeva, NM Dubrovskaya, SA Plesneva, AJ Turner, IA Zhuravin, IM Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia; Institute of Molecular and Cellular Biology, University of Leeds, Leeds, UK

INTRODUCTION: It is well known that any stressor induces changes in the central nervous system at the level of neurotransmitters and enzymes participating in their degradation. In this study, we analyzed the effects of various types of stress on a neuropeptidase neprilysin (NEP). NEP can cleave a wide range of biological substrates, and as such participates in various processes in the brain, such as synaptic plasticity, memory, motor functions, stress response, etc. As we have shown previously, NEP activity in the cortex (Cx) and hippocampus (Hip) of rats reduces with age, and is even more decreased in animals subjected to such stress as prenatal hypoxia (PH). These animals have also demonstrated significant memory loss similar to the effects induced in adult rats by i.c. injections of NEP inhibitors (phosphoramidon and thiorphan). The aim of this study was to analyze the effect of another type of stress, immobilization stress (IS), on NEP activity in the Cx and Hip of adult naïve rats and PH rats. We have also analyzed the effects of such therapeutic agents as valproic acid (VA) and epigallocatechin gallate (EGCG) on NEP activity in rats subjected to PH.

METHODS: The study was conducted in four groups of adult (4 months old) Wistar male rats: 1) rats exposed to PH on E14 (7% O2, 3 h); 2) naïve rats exposed to IS in a narrow transparent box (5 minutes per day, during 10 days); 3) rats subjected to PH and IS; 4) control group. NEP activity was

measured in the membrane fractions from the Cx and Hip by a fluorescence assay with a fluorigenic synthetic NEP substrate. Some rats have been treated orally with VA (200mg/kg of body weight per day) or EGCG (5 mg/kg per day) for 10 days. **RESULTS AND DISCUSSION:** NEP activity in the Cx and Hip of adult PH rats was found to be lower by 16 and 13%, respectively, compared to the values in control rats (3.10±0.11 and 3.66±0.04 nmol/mg per min, respectively, in the Cx and Hip). IS has also resulted in a significant decrease of NEP activity (by 78 and 63%, respectively) in the Cx and Hip of adult naïve rats compared to control. Thus, both types of stress at various stages of ontogenesis (embryos or adult animals) led to a reduction of NEP activity in the brain. Surprisingly, when PH rats were exposed to IS stress, NEP activity in both brain structures was significantly increased (61 and 38%) compared to controls. It might be explained by the fact that in PH animals the mechanisms responsible for adaptation to stress have already been modified by the previous stressor and the newly applied stress led to activation of NEP. In fact, in animals preconditioned to mild hypoxia before PH on E14 levels of NEP expression in the brain on P30 were higher compared to non-preconditioned animals. It is known that NEP can be activated by a histone deacetylase inhibitor VA or an antioxidant EGCG. Administration of VA to adult PH rats with reduced NEP activity resulted in its activation.Similar results were obtained when PH rats were treated with EGCG. Thus, various stressors and their combination have different effects on brain NEP activity while such therapeutic agents as VA and EGGC can attenuate its decrease caused by PH. **RESEARCH SUPPORT**: RAS “Fundamental Sciences to Medicine”, RFBR N10-04-01156.

Day 3. Fri, May 18, 2012

Oktiabrskaya Hotel, Grand hall (2nd floor), 10 Ligovsky Prospect, St-Petersburg, Russia

Morning session

9.30-10.00 CONFERENCE TALK (30 min)

SPADIN, A SORTILIN-DERIVED PEPTIDE: A NEW CONCEPT IN THE ANTIDEPRESSANT DRUG DESIGN. M Borsotto, H. Moha ou Maati, J. Veyssiere, O. Petrault, G. Lucas, C. Widman, C. Gandin, J. Mazella, C.Heurteaux, CNRS-UNSA, Valbonne, France

INTRODUCTION: Current antidepressant treatments require several weeks of administration before therapeutic effects can be observed, but remain inadequate for many individuals. Improving the treatment and the prevention of depression is challenging. The two pore-domain potassium channel, TREK-1 has been identified as a new target in depression and it has been hypothesized that TREK-1 antagonists might be effective antidepressants. We validated the antidepressant effects of spadin, a peptide derived from the maturation of the N-terminus part of the neurotensin receptor 3 (NTSR3 /Sortilin) that specifically blocks TREK-1 channel. **METHODS**: Spadin efficacy was studied through five different animal behavioral models, namely the Porsolt forced swim, the tail suspension, the conditioned suppression of motility, the learned helplessness and the novelty-suppressed feeding test. Spadin specificity on different potassium channel was tested by using electrophysiological patch-clamp technique. **RESULTS AND DISCUSSION:** Spadin blocks the TREK-1 activity in COS-7 transfected cells and CA3 hippocampal neurons. These effects are absent in TREK-1-/- mice. Spadin does not affect the activity of four other K2P channels. Spadin increases the efficacy of serotoninergic neurotransmission. Similarly to that observed in TREK-1-/- mice, spadin induces a resistance to depression in the five behavioral models. Spadin appears to be specific for the depression because it had no effect in three anxiety animal tests: the elevated plus maze, the stair case and the white-dark box. More importantly, a spadin intravenous 4-day treatment induced a strong antidepressant effect and also enhanced hippocampal phosphorylation of CREB protein and neurogenesis, considered to be key markers of antidepressant action after chronic treatment with selective serotonin reuptake inhibitors. Spadin does not affect other functions of TREK-1 like pain or epilepsy. Spadin has no effects on cardiac function because it does modify neither the systolic pressure nor cardiac pulse number. Our data, together with the Alpha Screen dosing method, that we developed, indicated that Spadin could be used as an antidepressant molecule and as a biomarker for depression disease. Spadin can be considered as a putative endogenous antidepressant of new generation with a rapid onset of action. **RESEARCH SUPPORT**: Centre National de la Recherche Scientifique (CNRS) and the Agence National de la Recherche -Maladies NeuroPsychiatriques (ANR-2009-MNPS-026.01).

10.00-15.00 SYMPOSIUM III: ZOFIA ZUKOWSKA SYMPOSIUM ON EXPERIMENTAL MODELS IN BRAIN RESEARCH
Chairs: I Ekimova (Russia), A Kalueff (USA), presentations 20 min

PROFESSOR ZOFIA ZUKOWSKA (1948-2012) AV Kalueff (USA)

Professor Zofia Zukowska received her MD and PhD and was trained in cardiovascular medicine at the Warsaw Medical Academy in Poland. She then pursued post-doctoral training at the NIH, where she worked with such renowned scientists as Irwin I. Kopin, Scientific Director of NINDS, and Julie Axelrod, Nobel Laureate. It was during this research period when her interest in stress and neuropeptides became galvanized. For the last 25 years, she was a professor and, recently, a Chair of the Department of Physiology and Biophysics at Georgetown University, before moving to the University of Minnesota. The overall topic of her research has been to determine how stress affects cardiovascular and metabolic health and diseases, and the role of peptides, in particular neuropeptide Y (NPY), a sympathetic neurotransmitter and a stress mediator. She was the first to determine that NPY mediates stress-induced prolonged vasoconstriction and vascular mitogenic and pro-atherosclerotic effects (via Y1 receptors) and potent angiogenic actions (via Y2 receptors), establishing the role ofNPY in ischemia, retinopathy, tumors and recently, also in obesity *(Nat Med, '07)*. Also, recent finding of other non-neuronal sources of NPY in megakayocytes and platelets in some strains of mice started a new line of lab's research on the role of this platelet-derived factor into vascular remodeling in restenosis and acceleration of atherosclerosis. Finally, her lab is developing a novel model of stress-induced adipogenesis/obesity in the zebrafish. Zofia was a remarkable person, a talented scientist, an enthusiastic colleague, a supportive collaborator, a great mentor, and a good friend. She was an active participant of several of our "Stress and Behavior" conferences, and is sorely missed by all who knew her.

INCREASED CONTEXT-DEPENDENT SENSITIZATION TO AMPHETAMINE IN TAAR1-KO MICE. I Sukhanov, TD Sotnikova, L Cervo, RR Gainetdinov, Department of Neuroscience and Brain Technology, Istituto Italiano di Tecnologia, Genova; Department of Experimental Psychopharmacology, 'Mario Negri' Institute for Pharmacological Research, Milan, Italy
INTRODUCTION: It has been recently recognized that amphetamine derivatives may act also as direct agonists of the G protein-coupled trace amine associated receptor 1 (TAAR1). Thus, TAAR1 might be important for reinforcing and addictive properties of amphetamines. The present study aimed to investigate the role of TAAR1 in psychostimulant actions by analyzing context-dependent sensitization to d-amphetamine in TAAR1-KO mice. **METHODS**: After assessing baseline activity animals were divided on 3 groups: control (WT N=13; KO N=10); paired (WT N=10; KO N=14); unpaired (WT N=14; KO N=9). Immediately before being placed in the activity cages, the Paired group was injected with 2 mg/kg amphetamine i.p. while the Unpaired and Control groups were injected with saline i.p. Locomotor activity was recorded for 60 min and the mice were then returned to their home cages. One hour after return to the home cage, mice in the paired and control groups were injected with saline, mice in the unpaired group were given 2 mg/kg i.p. amphetamine. Sensitization phase included 7 daily conditioned sessions. Mice were tested for conditioned amphetamine activity 24 h after the final conditioning day. All animals were given i.p. saline immediately before being exposed to the activity cages for 60 min. Next day testing was repeated, but all mice were injected with amphetamine (2 mg/kg). **RESULTS AND DISCUSSION:** Under present conditions no differences between KO and WT mice was observed in baseline activity. Both

WT and KO mice of paired group developed significant context-dependent sensitization. However, in amphetamine test paired KO mice were more active than WT paired mice. Additionally, in saline test paired KO mice exhibited more increased level of horizontal activity than paired WT mice. In conclusions, our data suggest that activation TAAR1 receptors may play an inhibitory role in the modulation of psychomotor and addictive properties of amphetamine.

THE RELATIONSHIP BETWEEN THE UBIQUITIN-PROTEASOME SYSTEM AND EXPRESSION OF HSP70 IN NIGRAL NEURONS. IV Ekimova, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia

INTRODUCTION: In the cytosol and nucleus, the major proteolytic pathway used by eukaryotic cells for disposing of misfolded or damaged proteins is the ubiquitin-proteasome system (UPS). In mammalian cells, it is estimated that 80–90% of protein degradation is carried out by the UPS [Lee, Goldberg, 1998]. The function of the UPS can be impaired by many factors including the aging process, leading to the formation of ubiquitin protein aggregates detected in non-pathologic aging as well as in neurodegenerative disorders. A loss of proteasome activity with age is supported by decreased subunit expression, alterations and/or replacement of proteasome subunits and formation of inhibitory cross-linked proteins [Keller et al., 2002]. Increasing evidence indicates that UPS dysfunction may represent the principal molecular pathway that commonly underlies the pathogenesis of Parkinson's (PD) disease [Moore et al., 2005]. PD is characterized mainly by progressive and selective loss of dopaminergic (DA) neurons in the substantia nigra pars compacta (SNpC), with subsequent dopamine decline in the nigrostriatal pathway, and by the presence of intracytoplasmic fibrillar *α*-Syn protein aggregates (Lewy Bodies) in the remaining nigral neurons. It has been demonstrated that heat shock protein 70 kDa (Hsp70) overexpression reduced *α*-Syn accumulation and toxicity in both mouse and Drosophila models of PD [Auluck et al., 2002; Klucken et al., 2004]. However, expression of Hsp70 decreases with age and PD [Moore et al., 2008]. The relationship between the ubiquitin-proteasome system and expression of Hsp70i in DA neurons of SNpC is unknown. In this study we employed an immunocytochemical approach to examine the expression levels of Hsp70 in DA neurons of SNpC under moderate and deep suppression of UPS function in Wistar rats**. RESULTS AND DISCUSSION:** It was found that 77% DA neurons in SNpC contain Hsp70i under normal basal conditions. 14 days after two-fold injections of inhibitor of UPS lactacystin (LC, 1 mM) into the SNpC decreased a number of DA neurons containing Hsp70i (15%). At the same time, Hsp70i content in survived nigral neurons (62%) increases. This may enhance their resistance to LC action and preserve them from degeneration. Injections of LC in higher concentration (10 mM) revealed a more considerable decrease in a number of DA neurons expressing Hsp70i (42%) and drop in the Hsp70i level in the remaining (40%) nigral neurons. The similar difference in Hsp70i changes were elicited in the tissue of SNpC by immunoblotting assay. **CONCLUSION:** The present data provide new evidence a significant association between Hsp70i level and the degree of suppression of UPS function. There is a good reason to think about a rising interest in the Hsp70 as a pharmacological target to prevent/treat neurodegeneration. This study was supported by the Russian Foundation for Basic Research grant 11-04-01588.

SLEEP-DEPRIVATION STRESS AND VASOTOCINERGIC BRAIN SYSTEM IN FROGS. AE Hramenkova, DM Surzenko, AE Aristakesyan, VV Kuzik, Sechenov Institute of Evolutionary Physiology and Biochemistry, RAS, St. Petersburg, Russia

INTRODUCTION: Vasotocin (vasopressin in mammals) is a neurohormone that is synthesized in hypothalamus and plays an active role in homeostasis regulation. Recently it has been shown that vasotocin plays in active role in stress regulating processes, in different behavior reactions and in mammals it has a day rhythm secretion. The aim of our study was the investigation of vasotocinergic cells functional activity under sleep-deprivation stress in frogs. **METHODS**: The experiments were carried out on frogs (Rana temporaria). Sleep deprivation was made for 6 hours. There were three groups of animals: control, after 6 hours of sleep deprivation, during post deprivation sleep. Paraffin brain slices(6 μm) containing preoptical area were analyzed through

polyclonal rabbit anti-vasopressin antibodies (Sigma) , diluted 1:2000, goat anti-rabbit biotinilated secondary antibodies (Sigma), diluted 1:300 the immunohistochemical on vasotocin reaction was made and streptavidin-peroxidase method. **RESULTS AND DISCUSSION**: It was shown the medium level of immunoreactive material (IRM) in vasotocin cells and fibers in preoptical area in the control group. After 6 hours of sleep deprivation the level of IRM in cells decreased, but in fibers the level of IRM markedly increased. So sleep deprivation activates processes of release more than synthesis. During post deprivation sleep the level of IRM enhanced in cells more than in fibers, so synthesis processes activates. Thus vasotocinergic system takes an active part in stress reaction regulation during sleep deprivation and post deprivation sleep.

BEHAVIORAL EFFECTS OF SINGLE INTRACEREBROVENTRICULAR ADMINISTRATION OF AMYLOID-BETA PEPTIDE FRAGMENT 25-35 IN RATS. V Mukhin, I Abdurasulova, K Abdurasulova, V Klimenko, Institute of Experimental Medicine RAMS, St. Petersburg, Russia
INTRODUCTION: Amyloid-beta peptide plays a physiological role as a neurotrophic factor. On the other hand, accumulation of this peptide in the form of the soluble oligomers is the principal link of Alzheimer disease pathogenesis. It is known that portion 25-35 is the functional domain of this peptide which showed the same neurotrophic and neurotoxic effect as the amyloid beta 1-40. For this reason central injection of this fragment could be considered as animal model of Alzheimer disease. Besides morphological and neurochemical changes such injections cause some cognitive impairment of behavior. This disturbance is usually treated as impairment of learning and memory. But our research experience has shown that behavioral changes are not so simple. The aim of this study was to investigate behavioral changes due to icv administration of amyloid-beta protein fragment 25-35. **METHODS:** Four groups of Wistar rats (285 ± 12 g) were in study. In the experimental group water solution of fragment 25-35 of amyloid-beta peptide was injected into the right brain ventricle (5 or 1.2 µl/min). The other three groups were used as controls as follows: 1) the group of central administration of saline solution, 2) the sham operated and 3) the intact rats groups. After a fortnight the rats were exposed to behavioral testing: open field test, novel object recognition test, passive avoidance test and learning of operant food-getting behavior in the TSE PhenoMaster system. **RESULTS AND DISCUSSION:** The rats of the experimental group had complex behavioral impairment including amnesia, neophobia, and reduction in exploratory and locomotor activity. So we have seen not only syndrome of cognitive impairment but also some depression-like signs of affective disorder. It seems not surprising because it is well known that depression and neophobia may often be the early syndromes of Alzheimer disease. Depression-like affective component has also been seen in transgenic models of Alzheimer disease. **CONCLUSION:** Single administration of the amyloid-beta peptide fragment 25-35 is valid not only as a model of amnesia but also as a model of the complex of neuropsychiatric symptoms of the early stage of Alzheimer disease. Because of neophobia and impaired exploratory behavior behavioral learning and memory tests based on natural exploratory activity are irrelevant for this model.

THE EFFECT OF VALPROIC ACID ON NEURODEVELOPMENT MICE DURING GESTATION. J Podgorac, S Sekulic, I Capo, Lj Martac, G Kekovic, Institut Za Bioloska Istrazivanja Sinisa Stankovic, University of Belgrade, Belgrade, Serbia
INTRODUCTION: Medications, which are being taken during pregnancy, is common despite that most drugs cross the placenta, even prenatal subtoxic exposure, may lead to neurobehavioral impairments in the offspring. Valproic acid (VPA) is known as human teratogen. VPA exposition during pregnancy is associated with congenital malformation and neurodevelopmental disorders. In experimental research, behavioral models widely used are hot plate test, as condition learned test and the elevated plus maze as behavioral assay, used to asses states of anxiety/depression-like behavior. The hot plate is a test that is very susceptible to learning phenomena, which results in a progressive shortening of the reaction time, if testing is being continuously repeated. Our aim was to investigate influence of low VPA doses on neurobehavioral development. **METHODS:** Three

groups were included in our study, two experimental and control group. Adult female NK mice were treated with subcutaneous injection of 50mg/kg VPA (n=6) or 100mg/kg (n=6) and control group (n=5) were treated with saline, during breeding and gestation. Body weight was measured daily and concentration of VAP, which was administered, was adjusted. Hot plate test was performed at 25 and at 32 postnatal days. Elevated plus maze test was conducted on postnatal day 35. **RESULTS AND DISCUSSION:** Between groups of pups, which mothers were treated with 50 mg/kg and 100 mg/kg VPA, the controls did not significantly differ in activity in the repeated hot plate test, whereas the elevated plus maze test showed significant differences ($p<0.001$) between the two experimental groups, and between control group and experimental group of mothers treated with 100mg/kg, in time spent and number of entries in the open arms. Age of offspring, which underwent behavioral testing, corresponded to adolescent period of mice. Prenatal VPA administration is related to less quality of behavioral development, regarded to anxiety/depression-like behavior at non-malforming doses. **RESEARCH SUPPORT:** Ministry of Science and Technological Development of Republic of Serbia (Project 175006).

THE POLYMORPHISM IN LIMK1 GENE AND STRESS EFFECTS ON COURTSHIP BEHAVIOR AND MEMORY FORMATION IN *D. MELANOGASTER*. EV Savvateeva-Popova, EA Nikitina, AV Medvedeva, AN Kaminskaya, YuF Dolgaya, AV Zhuravlev, GA Zakharov, TL Payalina, Pavlov Institute of Physiology RAS, St. Petersburg State University, Institute of Evolutional Physiology and Biochemistry RAS, St. Petersburg, Russia
INTRODUCTION: LIMK1 – is the key enzyme of actin remodeling which controls dendritic spine morphology necessary for synaptic plasticity during learning and memory formation. LIMK1 phosphorylates cofilin at Ser3 and thereby affects actin filament dynamics leading to axon reorganization. The LIMK1 isoforms D and C are characterized by different length due to the presence or absence of two LIM- and one PDZ-domains. **METHODS:** Conditioned courtship suppression paradigm and a set-up for communicative sound production during courtship were used to asses learning acquisition and memory formation in four Drosophila strains polymorphic for the limk1 gene harbored by the agnostic locus: the wild type strains Canton-S (CS), Berlin, Oregon-R (Or-R) and the mutant agnts3. The ratio of the two LIMK1 isoforms in these strains was investigated using Western blot analysis. **RESULTS AND DISCUSSION:** We have shown that a different ratio of LIMK1 D and C isoforms in the heads of Drosophila males in wild type strains Berlin, Or-R and CS was accompanied by a similar total content of LIMK1, while the agnts3mutant had high activities of the both isoforms. After heat shock (HS) the content of the both LIMK1 isoforms increased in CS and decreased in agnts3, but did not change in Berlin and Or-R. Behavioral analysis demonstrated that the main parameters of courtship behavior of intact males and males that have experienced HS did not change in agnts3 but a decrease in their sexual activity and an increase in duration of sound trains in the songs were evident. Deviation of D and C isoforms ratio in Berlin and Or-R correlated with changes in singing index and percent of distorted impulses. The performance indices showed a negative correlation with the D-isoform content and D/C isoform ratio. The conditioned courtship suppression paradigm revealed dramatic impairments in learning and memory in Or-R and agnts3 which were completely alleviated following HS. As to CS and agnts3, the more the content of the short and active D-isoform of LIMK1 increases, the more the learning ability in conditioned courtship paradigm lowers. The higher resistance of characteristics of their behavior to HS was in agreement with the fact that the extremely high LIMK1 and p-cofilin concentrations in their cells dropped down to normal values after HS. At the same time the amyloid aggregations disappeared and defective learning and memory restored. **RESEARCH SUPPORT:** RFBR Grant 09-04-01208, RAS Program “Biodiversity and Genofonds”, Contract with the Ministry of Science and Education P-316.

COMPARATIVE EFFECTS OF DIFFERENT COMPOUNDS ON STRESS-INDUCED BEHAVIOURAL RESPONSES. Z Dzirkale, R Svarcbahs, B Jansone, N Karajeva, M Vanina, L

Adlere, E Berzina, J Rumaks, S Svirskis, A Plotniece, E Bisenieks, G Duburs, V.Klusa, Faculty of Medicine, University of Latvia, Latvian Institute of Organic Synthesis, Riga, Latvia

INTRODUCTION: Severe stress is widely accepted as a contributor to neuronal vulnerability which triggers to cognitive impairment. Therefore a search for the novel type of stress protectors and memory enhancers is still available. The aim of present work was to study two novel 1,4-dihydropyridine (DHP) derivatives containing propargyl (D3-69) or adamantyl group (AV-6-93). Propargyl and adamantyl groups are regarded as essential for neuroprotective action in the case of rasagiline/selegiline and amantadine, respectively (Volbracht et al., 2006; Binda et al., 2011; Gerlach et al, 1996). Comparative behavioral studies of the novel compounds, and amantadine and rasagiline (as the reference drugs) in stress-conditions were carried out. Additionally, mildronate, previously found as neuroprotective (Klusa et al., 2010; Pupure et al., 2010), was also tested. **METHODS**: Male Wistar rats were pre-treated with amantadine, AV-6-93, rasagiline, D3-69 (all in dose 1 mg/kg, ip; saline for control) and mildronate (50 mg/kg, i.p.) for two weeks. On the first experimental day passive avoidance (PAR) test in Shuttle box apparatus was performed. On the second day Forced swimming (mild stress), Open field and PAR retention (24h) tests were carried out. On the third experimental day animals received 2h-immobilization stress (severe stress) followed by repeated PAR retention (48h) test. **RESULTS AND DISCUSSION:** The obtained results showed that neither mild stress nor tested drugs influenced animals' behavior in open field and PAR tests. In the severe stress conditions (immobilization), was observed impairment of PAR-task performance. According to acquired results rasagiline and amantadine, as well as novel DHP derivatives did not improve this behavior, suggesting that propargyl and adamantyl moieties cannot be considered as crucial to design memory-improving drugs for the protection of stress induced cognitive impairments. However, mildronate significantly improved learning/memory responses, suggesting its molecule as optimal for the regulation of cell processes even in severe stress conditions. **RESEARCH SUPPORT**: ESF project 2009/0217/1DP/1.1.1.2.0/09/APIA/VIAA/031; Latvian Council Grants 09.1025 and 10.0030.

PRECONDITIONING TO PRENATAL STRESS HAS DIFFERENT BEHAVIORAL CONSEQUENCES DURING POSTNATAL ONTOGENESIS. NM Dubrovskaya, DS Vasilev, NL Tumanova, NN Nalivaeva, OS Alexeeva, IA Zhuravin, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia

INTRODUCTION: The phenomenon of preconditioning to stress is widely investigated and has clinical implications. The molecular mechanisms of preconditioning by mild repeated stress which increases tolerance to more severe insults, involve modulation of ion transport, receptor signaling and gene regulation. However there are very few data about the effects of preconditioning in prenatal period although it is well known that prenatal stress results in the changes in animal behavior which last during all lifespan. The present research has been undertaken for studying the effects of prenatal preconditioning to severe hypoxia on rat behavior during postnatal ontogenesis.

METHODS: Wistar rats were subjected to severe prenatal hypoxia (SPH, 7 % O2, 3 h, E14) with or without preconditioning by mild hypoxia (PPH, 15 % O2, 2 hours, daily on E11, E12 and E13). Development of motor behavior in the pups during the first month of postnatal life was investigated using a standard battery of tests (Dubrovskaya, Zhuravin, 2010) and cognitive functions of males rats when they reached adulthood (3-4 months) have been analyzed using the two-level radial maze and «novel object recognition» tests. After the behavioral tests animals were sacrificed and their brains were analyzed by morphological methods. **RESULTS AND DISCUSSION:** The analysis of the influence of SPH and PPH on behavior of rat pups in postnatal ontogenesis has revealed that, in contrast with the SPH group, during the first month of postnatal life the rats subjected to PPH had the dynamics of their motor activity similar to those registered in control rats by the majority of the tests (general motor activity, placing reactions, geotropism, body rotation and locomotion). According to the similar tests the pups subjected to SPH only had a delay in the development of motor reactions ($p<0,01$). Although these animals at older age did not differ in their

motor reactions from the control group, they had significant memory deficit. Therefore we have undertaken an analysis of the effect of PPH on the performance of cognitive tasks which revealed that rats from both SPH and PPH had similar disruption of short- and long-term memory. They also had a decrease in the number of labile sinaptopodin-positive spines in the cortex and hippocampus. Thus, PPH eliminated disturbances in development of motor behavior in young rats subjected to SHP but did not recover the cognitive deficit in adult SHP rats. This is, most likely, because PPH can prevent the disturbance of brain maturation rate and development of general motor reactions in early ontogenesis, but at the same time cannot prevent the disruption of neuronal mechanisms underlying neuronal plasticity required for cognitive functions. **RESEARCH SUPPORT:** RAS Fundamental Sciences to Medicine, RFBR N10-04-01156.

ULTRASOUND VOCALIZATION AND INDEPENDENT INGESTIVE ACTIVITY DURING SOCIAL ISOLATION IN PREWEANLING RAT. AP Kozlov, ME Nizhnikov, NE Spear, Pavlov Physiological Department, Institute of Experimental Medicine RAMS, St. Petersburg, Russia; Center for Development and Behavioral Neuroscience, Binghamton University, Binghamton, NY, USA
I**NTRODUCTION:** Social isolation (SI) represents ecologically natural stressful experience for preweanling rat. The immediate response of infant rat to isolation from the dam and peers is emission of ultrasound vocalization (USV) accompanied by motor activation. Whereas factors affecting USV production were extensively studied as animal models of anxiety-like behavior or early communication disorders (Scattoni et al., 2009; Winslow, 2009), there were no works specifically designed to assess USV in pups engaged in ingestive activity during SI. A remarkable plasticity of USV response to various conditions of SI has been also demonstrated (Shair, 2007). However the sources of variation of this measure of infant rat reactivity to SI still not well understood. The objective of the present experiments was two-fold: 1) to analyze how USV of isolated pup interacted with independent ingestive activity- free consumption of palatable fluid; 2) to assess whether association of novel taste stimulus with sensory attributes of suckling or attachment to dam could affect USV to subsequent SI when the same taste stimulation was presented during SI episode. **METHODS:** Preweanling 9 and 10-day-old Sprague-Dawley rats were maternally separated and deprived from food for 4.5-5.0 hours before start of experiment. The experiment included two phases – pre-exposure to novel gustatory stimulus while pups were in contact with anesthetized dam for 10 minutes and re-exposure to the same stimulus during short-term (duration 15 minutes) SI. Pups with no taste stimulation prior to SI were set as controls. At test phase we performed combined assessment of voluntary intake and stress reactivity to SI. Pups were infused with 0.1% saccharin or water through intraoral cannula during attachment to dam while their voluntary intake of saccharin was subsequently evaluated in three 1.5 minutes periods of free accessibility to saccharin. These feeding episodes occurred during exposure to SI that followed contact with anesthetized dam. The rate of USV in frequency range of 32-40 kHz, locomotion and rearing activity were used as measures of stress reaction to SI. **RESULTS AND DISCUSSION:** We found that brief taste stimulation and associated drinking activity did not stop emission of USV in pups that were not pre-exposed to the same stimulus during dam attachment. Interestingly, that USV calls were emitted relatively close in time to licks: the lag time of peaks of cross-correlation between USV and fluid drops (“licks”) ranged between 1-2 s with time resolution of single lick measurement of 100 ms. In contrast, a reduction or even block of USV calls has been found during ingestion of saccharin in pups who experienced the same taste stimulus previously, in association with attachment to dam. However, the strength of USV reduction varied as function of several variables (background level of USV and time from preceding exposure to dam were among them). The results of experiments indicate that emission of USV did not interfere with execution of independent ingestive activity in preweanling rat. However, a concurrent block of USV by drinking could emerge from previous association of taste stimulus triggering drinking with sensory experience of attachment to the dam. **RESEARCH SUPPORT:** NIH grants R01AA015992; R21AA018164 and RO1AA13098 to NE Spear.

MODELING OF PRECLINICAL STAGE OF PARKINSON'S DESEASE IN RODENTS. KV Lapshina, YuF Pastukhov, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia

INTRODUCTION: Parkinson's disease (PD) is characterized by dramatic motor disorders such as bradykinesia, tremor and rigidity. The progressive degradation of dopaminergic nigrostriatal pathways plays a pivotal role in pathogenesis of this illness. The first motor symptoms can appear only 20-30 years after the beginning of the nigral neurodegeneration. The current therapeutical methods are not very effective at that stage because at least 50-60% of nigral cells are lost and medical treatment can only help to improve the dopaminergic neurotransmission [Ugrumov, 2010]. Thus it is very important to find the early markers of PD and to design the strategy of the preclinical diagnostics and neuroprotective therapy. But firstly, it is necessary to create an appropriate preclinical animal model, especially in rodents as in the most wide-spread laboratory object. **METHODS:** To induce PD model in animals a wide range of pharmacological approaches can be used. The most common models are classical 6-hydroxydopamine (6-OHDA) rat and 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) models, pesticide model (rotenone, paraquat), inflammogen (lipopolysaccharide, LPS) and other. The biggest part of these investigations are focused on late stage of PD whereas a only a few studies are devoted to preclinical stage of PD [Truong et al., 2005; Ugrumov et al., 2011]. **RESULTS AND DISCUSSION:** It was shown that neurotoxins, such as 6-OHDA, MPTP and other induce the mitochondrial dysfunction, oxidative stress and inhibit the ubiquitin-proteasome system (UPS) activity. UPS is responsible for the degradation of damaged proteins. It protects cells from the accumulation of these toxic proteins and the disturbances of cellular functions. It seems that the decrease in UPS activity can be one of the main reasons of the development of PD and this system appears to be a common target of neurotoxins (MPTP and 6-OHDA) and proteasome inhibitors, such as lactacystine. Pastukhov and colleagues developed the lactacystine preclinical model of PD which is not accompanied by motor disturbances but leads to the increase in the total time of rapid-eye-movement sleep (REM) and to 28% loss of nigral neurons [Pastukhov et al., 2010]. The effects of lactacystine also involved the increase in the level of key enzyme of dopamine synthesis tyrosine hydroxylase and in the content of the inducible form of heat shock protein 70 kDa in survived nigral neurons [Pastukhov et al., 2011]. These data support the hypothesis that the increase in the duration of REM can be a non-motor symptom of PD and reflect the reservation of compensatory potential in the nigrostriatal system. We suggest that preservation of the compensatory capacity and maintaining of the high neuroprotective potential of chaperones using the known and new inductors and different kinds of preconditioning can be a base for the development of new therapeutic strategies to slow or stop the neurodegeneration in preclinical phase of PD. **RESEARCH SUPPORT:** RAS Program "Fundamental Sciences for Medicine".

15.20-17.00 MODERATED POSTER SESSION

Posters are on display for the whole day; presenters should be available for questions during the poster session

ZEBRAFISH AS A MODEL FOR STUDYING PARKINSON'S DISEASE. RS Soares, HV Linde, R Willensen, T Outeiro, S Sousa, N Afonso, AD Correia, Instituto de Medicina Molecular, Instituto de Fisiologia, Faculdade de Medicina da Universidade de Lisboa, Lisboa, Portugal; Department of Clinical Genetics, Erasmus Medical Center, Rotterdam, Netherlands; Department of NeuroDegeneration and Restorative Research, University Medizin Goettingen, Goettingen, Germany; TechnoPhage, SA, Portugal

INTRODUCTION: Parkinson's disease (PD) is the second most common neurodegenerative disease. Several in-vivo models have been generated to unveil the mechanisms associated with this pathology; however, they do not fully recapitulate the key features of the disease. Zebrafish (Danio rerio) has recently emerged as an important model to study different aspects of

neurodegeneration. Specifically, it presents a basic organization of the central nervous system, and specialized neuronal populations, including the dopaminergic system that appears to be well conserved among vertebrates. Thus, we are generating several transgenic lines expressing selected wild type and mutant PD-associated genes. **METHODS:** We are using the tyrosine hydroxylase promoter to drive expression of the selected genes specifically in dopaminergic neurons in an attempt to model the motor symptoms characteristic of PD. The constructs were injected in the one-cell stage of zebrafish development using the Tol2 transposase technique which guarantees a single-copy mode insertion. **RESULTS AND DISCUSSION:** Currently, we are in the process of validating these models by immunohistochemistry, western blot analysis and behavior analysis. The generation of a zebrafish transgenic model of PD will afford the possibility to study the role of several genes in the pathogenesis of PD. The transgenic lines will also to be used as in vivo screening tools to discover and test novel disease-modifying strategies. **RESEARCH SUPPORT:** EUROSTARS sponsored by EUREKA/EU (Project 5553, PARK), EMBO Installation Grant.

EFFECTS OF IMMOBILIZATION STRESS ON MEMORY AND NEURONAL PLASTICITY IN THE CORTICAL DIVISIONS OF RATS. DS Vasilev, NM Dubrovskaya, NL Tumanova, IA Zhuravin, Sechenov Institute of Evolutionary Physiology and Biochemistry RAS, St. Petersburg, Russia
INTRODUCTION: Acute stress is able to cause various changes in brain properties and functions, including neuronal plasticity, and animal behavior (e.g. cognitive dysfunction). On the other hand, repeated mild stress can lead to the adaptation of the organism to the stressor. The increase of expression of some synapse-associated proteins (e.g. actin-associated protein synaptopodin) after various types of stress has been described in the literature. Synaptopodin is a protein localized in the spine apparatus of dendritic spines and plays an important role in neural network plasticity via reorganization of the cytoskeleton of labile spines and changes in their size and shape. In normal rat aging, or after acute stress during embryogenesis, we have observed a decrease in the number of labile synaptopodin-positive spines in brain cortical divisions which correlated with the changes in brain functions including memory deficit. The present work was designed to analyze the changes in brain plasticity and memory after mild repeated immobilization stress, both in control rats and in rats subjected to prenatal hypoxia. **METHODS**: This study was performed using either naïve adult Wistar male rats or rats subjected to prenatal hypoxia (E14, 7% O2, 3 hours) at the age of 3 months. The 5 min immobilization stress was performed daily, during 10 days, in both groups of rats using a narrow transparent box. Rat short- and long-term memory was checked using the “novel object recognition” test. The morphology of the nervous tissue from various brain cortical divisions was investigated by light microscopy (the Nissl method). Distribution of synaptopodin in the brain was analyzed by the immunofluorescent method using antibody S9567 (Sigma) and confocal microscopy. **RESULTS AND DISCUSSION**: At the morphological level immobilization stress caused a decrease ($p < 0.05$) in the number of labile synaptopodin-positive spines in the CA1 field of the hippocampus as well as an increase in the number of labile spines in the molecular layer of the neocortex of adult naive rats compared to control. In the brain of animals, exposed to prenatal hypoxia on E14, Nissl staining has revealed changes in the morphology of some pyramidal neurons. In the “hypoxic” animals either subjected to the immobilization stress or not, there was a decrease ($p < 0.05$) in the number of labile spines both in the neocortex and CA1 of the hippocampus compared to the naive control rats. We have also observed memory deficit after repeated immobilization stress, both in naive rats and rats exposed to hypoxia on E14, which might be related to the decrease in the number of labile interneuron contacts in the hippocampus. The increase in the number of labile spines in the neocortex of adult rats after mild repeated stress might have a compensatory character although it has not been observed in animals subjected to prenatal hypoxia. **RESEARCH SUPPORT:** RAS “Fundamental Sciences to Medicine”, RFBR N10-04-01156.

COMPARATIVE ANALYSIS OF THE INFLUENCE OF EMOTIONALLY NEGATIVE AND NEUTRAL TV-NEWS PLOTS ON THE PSYCHO-PHYSIOLOGICAL CONDITION OF THEIR

VIEWERS (BASED ON THE EXPERIMENT). YD Havrylets, SV Tukaiev, VV Rizun, NE Makarchuk, Taras Shevchenko Kyiv National University, Kyiv, Ukraine

INTRODUCTION: The influence of TV news on humans and their level of aggression is an important direction of research. Particular interest induces the impact of content on the psycho-physiological and emotional condition of the viewer. Most studies of the impact of television violence are devoted to long-term changes in behavior. The purpose of this study was to identify immediate reactions and intensity of display of emotional distress arising from viewing emotionally-accented news stories. **METHODS**: 26 healthy volunteers (17-20 yo) participated in this experiment. Current study used two types of news pieces, divided by emotional stress - negative and neutral. To assess the impact on the mental state of volunteers, data of experimental tests were collected before and after the experiment. The following tests were used: WAM (Wellbeing Activity/Mood), State Anxiety Inventory by Spielberger-Hanin and diagnosis of internal aggression by Daihoff. At the end of the experiment we used Aggression Test by A. Assinger (assessment of aggressiveness in the relationship), and assessed each TV-news plots on the scales of "relaxing - activating" and "unpleasant-pleasant". Facial reactions observed while viewing the TV-plots, were recorded with video camera. Emotional activation is usually accompanied by shifts in the autonomic area of the body, the nature of which depends on the type of emotion. Registration of the electrocardiogram allowed estimating the degree of emotional activation, caused by news' effect. **RESULTS AND DISCUSSION**: TV-plots were evaluated on scale "unpleasant-pleasant" as follows: neutral stories were regarded as more pleasant, negative – more unpleasant, on a scale "relaxing-activating" negative stories make a more activating effect, neutral - more relaxing one. We indicated that negative news worsen mood more significantly than neutral ones. More than twice as much situational anxiety is felt because of the negative set of videos, than neutral ones. Overt aggression was not caused by the viewed TV-stories. Instead, the negative videos more often cause anger than neutral. Feeling worse was most impressive because of neutral scenes, though a mood worsened more of the negative (more than twice as much as in opposite collections of TV-plots). Instead, activity when viewing neutral videos (compared with negative) was a half less. During the experiment, we observed 140 volunteers' facial reactions (signs, confirming the experience of certain emotions). Of these reactions, towards negative TV-plots we counted 83 reactions (59.29%) towards neutral - 57 reactions (41.71%). Overall among emotional states, when viewing negative stories, fear, anger, abomination (eyes wide open (or vice versa squinted with stress), or intense eyebrows raised up or strained, or dropped down) often occurred. Among the neutral emotional states there usually dominates boredom (eyes relaxed, slightly covered, relaxed brows, looks beyond the monitor while viewing scenes), which sometimes passed into drowsiness. The most significant changes in ECG observed in pauses between viewing of the videos, when volunteers remembered what they just saw and heard and perceived updated information. So we can conclude clear short-term effect of negative and neutral news. Regarding all the parameters negative news stories exert a significant influence on the psycho-physiological condition of the volunteers.

ANXIOLYTIC EFFECTS OF 5-HT3 ANTAGONISTS. DS Yakovlev, NA Kolobrodova, AA Spasov, VA Anisimova, Volgograd State Medical University, Volgograd, Russia

INTRODUCTION: At present there are a lot of sometimes contradictory data about anxiolytic properties of 5-HT3 antagonists. Some data describe high effectiveness of these agents, others show the opposite action. Perhaps such differences are caused by dissimilar psychopharmacological profile, unequal selectivity and additional unknown receptor activity. Also possible mistakes during the investigations and their interpretation cannot be totally excluded. At present study we set a goal to reexamine anxiolytic profile of some 5-HT3 antagonists like Ondansetron and RU1276 in different models of angiogenesis and schemes of pretreatment and compare it with known anxiolytic Diazepam. **METHODS**: All experiments were carried out on Wistar male rats. At the first step the anxiolytic action of compounds were investigated in conflict anxiolytic test "Vogel" and exploratory anxiety models "Plus-maze" and "Light/dark box" in wide range on doses 0,1; 1 and 5 mg/kg after a single administration. The reference drug Diazepam was used in

the dose 1 mg/kg. At the second step all experiments were done after sub-chronic 10 days pretreatment of Ondansetron, RU1276 or Diazepam in the dose 1 mg/kg/day. And as well as in the first step both conflict (Vogel) and exploratory (Plus-maze) models were used. The obtained data were statistically analyzed with Kreskas-Wallis test. **RESULTS AND DISCUSSION:** The present study has shown that Ondansetron, as well as RU1276, increased time rats spend in open arms or light box in exploratory tests after a single administration in the dose 1 mg/kg. On conflict model, there were no differences comparatively with a control group of rats. Interestingly, after 10 days administration of Ondansetron or RU1276, no significantly differences comparatively to the control group were shown in all used tests. At the same time, Diazepam significantly increased as tame rats spend in open arms or light box as the number of electric shocks received in Vogel test in both situations: after the single or sub-chronic pretreatment. Thus, investigated 5-HT3 antagonists Ondansetron and RU1276 don't demonstrate statistically significant anxiolytic effect. During present investigation only insignificant anxiolytic trends were found on exploratory anxiety models, totally absent after sub-chronic pretreatment. **RESEARCH SUPPORT**: Volgograd State Medical University.

THE LEVEL OF OXIDATIVE STRESS AND THE CHARACTER OF BEHAVIOR DISORDERS IN LIMITING PHYSICAL ACTIVITY IN RATS WITH HIGH AND LOW TOLERANCE TO HYPOXIA.
DA Kozochkin, VE Tseylikman, DN Gimazutdinova, AD Semenova, RV Deev, AA Nikitina, Chelyabinsk State Medical Academy, Chelyabinsk, Russia
INTRODUCTION: During the analysis of the stressors mechanisms, it's reasonable to follow the conceptions about two types of the adaptation strategy; they are the resistant and the tolerant. The usage of this conception was productive for the presumptive analysis of the neuro-endocrinical, metabolic and immunological changes during the stress and unspecific immunopotentiation. The resistant strategy is characterized by the activation of the catabolic process and the considerable oxygen consumption, and that's actually during the hypoxia. The adapt effect of the tolerant strategy isn't reached by saving the homeostasis at any cost, but it's reached by yielding to the environmental conditions and minimization of the organism functions. The changes observed during the early and distant periods after the stress effect are connected with the free-radical oxidation processes (FRO). In addition, the reaction of the organism to the effect of the stressors depends on the initial reactivity of the organism. Therefore, the aim of our research is the analysis of the activity of pro- and antioxidant ferments in the conditions of the triple three hours hypokinetic stress that animals with the different stability to hypoxia have got. **METHODS**: Researches were performed on 55 outbred rats. The animals were divided into three groups: The low stable (LS), highly stable (HS) and with intermediate resistance to hypoxia (MDP) (Grek et al., 2007). The Immobilization stress was performed by placing animals in cages three times for three hours with intervals between exposures 24 hours. Assessment of the activity of pro-and antioxidant enzymes was performed 24 hours after the last episode of immobilization. Determination of xanthine oxidase activity was produced according to Hashimoto (1974). Spectrophotometrically at 292 nm BY the formation of uric acid from xanthine. Catalase activity was determined according to Korolyuk (1988). Myeloperoxidase activity of blood was determined using modification of Simakov. **RESULTS AND DISCUSSION:** We found that the activity of pro-and antioxidant enzymes for animals, not subjected to stress with different sensitivity to hypoxia, was not statistically different. The immobilization stress caused at/IN animals LS and HS opposite changes of the pro-and antioxidant systems as well as behavioral reactions, in particular, IT WAS founded that activity of XO of LS rats rises from 0.061 ± 0.019 to 0.08 ± 0.0096 mU/min/ ml with a simultaneous increase in myeloperoxidase activity. Three-time 3-h hypokinetic stress in a HS group led to decreasing in enzymatic activity of XO from 0.212 ± 0.121 to 0.183 ± 0.026 mU/min/gHb, while reducing the activity of glutathione transferase. **RESEARCH SUPPORT:** RFBR 10-04-96091 and RFBR 11-04-01378.

INVESTIGATION OF THE RELATIONSHIP OF INVOLUNTARY ATTENTION TO THE DEVELOPMENT OF CENTRAL FATIGUE. VM Knyazeva, TS Deinekina, St. Petersburg State University, St. Petersburg, Russia

INTRODUCTION: Muscle fatigue can be defined as a decrease in the ability of muscles to produce force caused by work. During the development of central fatigue comes the inevitable oppression of cognitive functions. As a result of this process, voluntary and involuntary attention is particularly affected. Attention is an important activating system, due to the signals of the reticular formation. Mismatch negativity is the correlate of involuntary attention activation. Thus, our goal is to study the effect of the involuntary attention system activation on the development of fatigue. **METHODS**: The experiment consisted of three parts: the «oddball paradigm», in which the activation of involuntary attention was observed, the «go no go paradigm», where the system of involuntary attention was not activated, but the subject was to choose between two stimuli and the «deviants only paradigm», which was also served as a control by the two previous paradigms. «The oddball paradigm» consisted of 83% of stimulus 1, with a frequency of 1000 Hz and 17% of stimulus 2, with a frequency of 1200 Hz. The «go no go paradigm» - 50% of stimulus 1 and 50% of stimulus 2. The «deviants only paradigm» consisted only of stimulus 2. While listening to acoustic stimuli the subject must squeeze the working part of the wrist dynamometer to each stimulus 2 so that the line on the screen reaches the target level. The target level is going to be the value of the maximal voluntary contraction (MVC), which is measured before the experiment. In addition, the MVC is to be measured for three times: after the first block of the experiment, after a 3-min break and after the second block. **RESULTS AND DISCUSSION:** The data analysis revealed significant differences in the dynamometer compression curves for «paradigm oddball» and «paradigm deviants only», as well as the values of the compression curves for a «paradigm go no go» and «paradigm deviants only». However, when comparing the «paradigm go no go» and «paradigm deviants only» no significant differences have been demonstrated. In addition, significant differences were found between the amplitudes of the MVC «paradigm oddball» and «paradigm deviants only», as well as between the «paradigm go no go» and «paradigm deviants only». Significant differences between the «paradigm go no go» and «paradigm oddball» were found. Thus, the results of the experiment showed greater subject's fatigue in the «paradigm of deviants only» compared to the «paradigm of oddball» and «paradigm go no go». **RESEARCH SUPPORT:** Federal Program "Scientific and scientific-pedagogical personnel of innovative Russia," SC 14.740.11.0232.

OVERALL MEMORY IMPAIRMENT IDENTIFICATION WITH MATHEMATICAL MODELING OF THE LEARNING CURVE IN PATIENTS WITH CEREBROVASCULAR DISEASES. SG Belokoskova, IT Stepanov, SG Tsikunov, Institute of the Experimental Medicine RAMS, St. Petersburg, Russia,

At present, many researches focus their attention on assessment of cognitive disorders, which include impaired memory and other higher brain functions. Mini Mental State Examination (MMSE) test is widely used for assessment of cognitive functions with brief mental status evaluation scale. However, this scale does not imply a gradation in the region of easy and mild cognitive impairment. A.R. Luria (1962) developed a verbal learning free recall test using ten semantically unrelated Russian words during 10 subsequent trials. However, use ten words leads to the "ceiling" effect because healthy people are able to learn 15–16 words. The "ceiling" effect prevents correct assessment of encoding information to long-term memory. Modification of this test (Stepanov I.I. et al., 2011) includes 1) use 16 words, taken from four semantic categories: vegetables, animals, ways of traveling, and furniture, 2) use six lists that allows avoiding "item-specific" practice during retesting of each patient, and 3) changing the order of word presentation for each trial, 4) modeling the learning curve with an exponential function B3*exp(-B2*(X-1))+B4*(1-exp(-B2*(X-1))), where X is the trial number and Y is the quantity of correctly recalled words without repetitions. The parameters are: B2 — the learning rate; B3 is an estimator of the general functional state of a participant before starting the test and is called "readiness to learn"; B4 is an estimator of general ability to learn and is called "ability to learn". The software SPSS and Mathematica were used for

modeling the learning curves. The purpose of this study was to assess overall memory impairment in patients with dyscirculatory encephalopathy (DE) stage I or II and in patients with stroke. 37 patients in age 47–66 years were examined. The control group included 8 participants without cerebrovascular diseases. The average over three consecutive tests learning curve had the follow parameters: B2 = 0.85, B3 = 9.30, B4 = 15.49. The group of patients with DE included 24 patients, their averaged learning curve having B2 = 0.52, B3 = 7.05, B4 = 12.92. Moderate, but significant impairment of readiness to learn (p = 0.0024) and ability to learn (p = 0.006) was found in the DE group in comparison with the control group. Five patients suffered ischemic strokes of different localization. The patients did not have evident speech disorders and neurological deficit. The averaged learning curve had the follow parameters: B2 = 0.89, B3 = 7.06, B4 = 12.41, B3 (p = 0,011) and B4 (p = 0,0023) were lower than in the control group. At that, the learning curve did not differ between the DE and the stroke group (p > 0,2) for each coefficient. These results might be due to several factors: 1) restricted single focal lesions of the brain in patients with stroke, 2) examination of majority of patients in remote period after stroke. Thus, the modified Luria's verbal learning test might be used for estimation effects of pharmacotherapy in the rehabilitation of patients with diseases of the CNS.

THE USE OF BIOACOUSTIC CORRECTION FOR THE TREATMENT OF DELAYED CONSEQUENCES OF CNS PRENATAL DAMAGE IN CHILDREN. VN Trushina, KV Konstantinov, NV Shcheglova, DB Miroshnikov, KK Konstantinova, VM Klimenko, Institute of Experimental Medicine RAMS, St. Petersburg, Russia

The effective non-drug treatment technologies for children with delayed consequences of perinatal damages of the CNS are developing. Among these technologies is a bioacoustics method of correction (BAC). Feature of the method of the BAC is involuntary self-regulation of the functional state of the CNS, which makes possible its use in cognitive and affective disorders. The method of BAC is based on acoustic-EEG dependent biofeedback that allows converting the current brain EEG to a sound of musical range, which is presented to the patient in real time. The study of children aged 5 to 15 years with a long-term consequences of perinatal CNS damage: 53 children diagnosed with ADHD and comorbid disorders (mean age 8 years), 12 children aged 5-15 years with a delay of psycho-speech development of residual-organic background in which the EEG was estimated the number of paroxysms and (or) epi-complexes, 32 children of preschool age with mental retardation who have immature cognitive and emotional-volitional combined with communication and social and behavioral disorders. We have shown the treatment sessions with BAC lead to the reorganization of the EEG of the brain, which is expressed in the normalization of the BEA of the brain: increase the index of the alpha rhythm, it becomes structured, significantly reduced the ratio of the theta rhythm of the beta rhythm in the frontal regions of the brain, reduced levels of interhemispheric asymmetry the average number of paroxysms and epi-complexes in proceedings BAC decreased from 16±7,8 to 5,7±5,6 (p <0,05). Reorganization of the EEG is accompanied by a significant decrease in the number of clinical signs (80% of patients had marked reduction of clinical symptoms of ADHD 2.7 times), optimizing the function of attention, improve memory. During the BAC procedure, in children with mental retardation, there was a significant reduction in assessment of disorders of emotional and volitional from 5 to 4 stars (according to the method A. Sokolov): improved background mood, positive mood of the background color has become more pronounced and stable; emotional displays are more appropriate (decreased affective reactions disappeared impulsive acts of aggression aimed at the people around them, close), also noted a decrease stereotypes. The findings suggest the efficiency bioacoustics correction in patients with long-term consequences of perinatal CNS damage, impaired volitional, reduced ability to concentrate attention.

THE EXPERT ESTIMATION BASED ANALYSIS OF THE EEG ACOUSTIC IMAGE IN BIOACOUSTIC CORRECTIONS. KV Konstantinov, MK Leonova, DB Miroshnikov, KK Konstantinova, TV Avaliani, Institute of Experimental Medicine RAMS, St. Petersburg University of

Humanities and Social Sciences, St. Petersburg, Russia

INTRODUCTION: In this work we continue researches of reflex self-control mechanisms of the CNS (central nervous system) functional status. The main feature was in using the bioacoustics correction method. Bioacoustic correction techniques are based on listening of the own electroencephalogram acoustic image, which is received by the original computer transformation from the brain current bioelectric activity to the heard frequency range. We have shown that in bioacoustics correction sessions, there is the growth of the subjective sounding estimation of the acoustic image of the brain bioelectric activity along with a normalization of the functional condition (decreasing of reactive uneasiness and the depression level, increasing of the alpha rhythm index in the electroencephalogram, expressiveness decrease of beta- and delta-ranges). The basic moment, connected with the researching of the recovery mechanisms of the central nervous system functional condition in the bioacoustics correction method, is the answer to the question about the objective dynamics of an esthetic estimation of the electroencephalogram sound image. The real sound improvement of the transferred electroencephalogram could give the evidence about the mechanism of that positive determination of the brain patterns which have the most pleasant acoustic reflection. The observed transformation of the electroencephalogram rhythmic structure in bioacoustics correction sessions (where the alfa-rhytm are caused in the most cases of the bioelectric brain activity) allows to make the assumption that the pattern electroencephalogram acoustic image sound with a dominated alpha-rhythm and suppressed a beta- and delta-rhythms, has more esthetic importance in comparison with other patterns. The Aim of this study is to perform an expert estimation of acoustic images of electroencephalogram fragments with a different ratio of basic rhythm levels. **METHODS:** Electroencephalogram fragments of the acoustic image were shown to experts for the estimation. These fragments were taken at the first and at the last session of the patient with the asthenic syndrome, who passed a course of bioacoustics correction procedures (11 sessions). During bioacoustics correction procedures the patient had the increase in the alpha-index from 29 to 59 % in bioelectric activity of the brain, decrease in the beta-index from 25 to 16 %, decrease in the delta-index from 10 to 1.5%, reduction of the interhemispheric asymmetry of distribution of the electroencephalogram fluctuation period from 14 to 8%. The uneasiness decrease (the Spilberger-Haninp test), the health state, activity and mood improvement (the HSAM test) were detected during psychological testing of the patient. Subjective sound estimation of the modified electroencephalogram increased from 4,0 to 6,0 points (the O3 test). The expert estimation of sound was executed by two groups of volunteers: professional musicians (20 persons) and persons without music education (20 persons). There were the individual auditions of acoustic images of electroencephalogram fragments of the first and the last bioacoustics correction sessions in each group. The fragment duration was 3 minutes, the presentation order was casual. The expert estimation of the acoustic image of an electroencephalogram fragment was calculated after every listening at 10 scales: pleasant – unpleasant, quiet – disturbing, harmonious – disharmonious, light – gloomy, rhythmical – spasmodic, ordered – chaotic, calming – irritating, interesting – boring, melodious – immelodious, good – bad. Every scale was estimated from 0 to 7 points. The low point corresponded to the negative estimation and the high point - to the positive. The reliability estimation was done by Statistika programm by the Mann-Whitney U-test. It was revealed that the O3 acoustic image of the electroencephalogram fragment from the first session has 4,60±1,17 points in the group without any music education. O3 of the last session has 3,99±0,88 points. An authentic difference hasn't been revealed. In group of musicians O3 of the first session was 4,08±1,10; at the last session - 4,79±0,87 ($p < 0,05$). **CONCLUSIONS:** Thus, authentic differences of the expert estimation of the electroencephalogram acoustic image were observed only in the musical group. It is necessary to notice that in the real bioacoustics correction sessions, the patients are usually people without music education. In this case the dynamics discrepancy of the sound subjective and expert estimation don't allow to do an unequivocal conclusion in favor of the come out assumption of the positive electroencephalogram patterns mechanism in sessions the bioacoustics correction. Interpreting the received results it is possible to assume that at the electroencephalogram acoustic image listening in real time along with the operant determine

mechanism, at the expense of a positive acoustic reinforcement, there are other mechanisms which have the increase in a positive estimation of the acoustic electroencephalogram image sounding determined by the restoration of the central nervous system functional condition.

EFFECTS OF BIDIRECTIONAL SELECTION FOR BEHAVIOR TOWARDS HUMAN ON THE BEHAVIOR OF POSTPARTUM FEMALE NORWAY RATS. MY Konoshenko, RV Kozhemyakina, IZ Plyusnina, Institute of Cytology and Genetics SB RAS, Novosibirsk, Russia
INTRODUCTION: It is known that early postnatal environment can affect defensive behavior, emotionality and stress-response of adult animals. It is supposed that these effects are mediated by maternal behavior. Gray rats selected for absence and enhancement of aggressiveness towards human differ in emotionality, anxiety, aggression and stress response. This work was aimed to study the behavior of lactate tame, aggressive and unselected females. **METHODS**: The undisturbed maternal behavior was studied using tame and aggressive rats. Automated video registration was carried out from 1 to 21 postnatal days during one hour 5 times a day (06.00, 09.00, 14.00, 18.00, 22.00). Furthermore, the maternal aggression in resident-intruder test, maternal motivation in pup retrieval test and the anxiety in the "light-dark box" and startle response test were studied using lactate tame, aggressive and unselected wild-type rats. **RESULTS AND DISCUSSION:** The frequency of "outside the nest" and passive type of nursing was increased, arched-back nursing and mother licking/grooming were decreased in tame compared to aggressive dams especially at the first week of nursing. The tame dams spent less time building the nest; they displayed more often "rest" and self-grooming. Clear circadian rhythm of the activity outside the nest was observed in tame females beginning from the first week of nursing, while the similar circadian changes were observed in aggressive dams only at the third week. Taken together, these results suggest that tame rats are characterized by attenuation of maternal care. By contrast, the behavior in maternal aggression test and pup retrieval test didn't significantly differ between tame and aggressive females. Furthermore, females of both selected lines exceeded unselected rats in maternal motivation and maternal aggression. Tame females showed reduced anxiety in both "light-dark box" and startle response test. The aggressive dams demonstrated intermediate level of anxiety in the "light-dark box" and the highest amplitude of startle response. Our data show that the differences in anxiety between selected females and rats from unselected population persisted during lactation. Our data suggests that decreased anxiety in the tame dams could provoke the attenuation of maternal care. **RESEARCH SUPPORT**: OPTEC company, grants 11-04-00653 and 12-04-00494 from the Russian Fund for Basic Research.

CELLULAR AND MOLECULAR MECHANISMS OF THE FORMATION OF DELAYED COGNITIVE DEFICIT CAUSED BY INCREASED LEVEL OF INTERLEUKIN-1B IN NEONATAL PERIOD. A Trofimov, A Schwarz, O Zubareva, Institute of Experimental Medicine RAMS, St. Petersburg, Russia
Perinatal pathologies (infections, injuries, hypoxia and ischemia) are important factors in the formation of cognitive deficiency (e.g. in attention deficit disorder). These pathologies increase the production of pro-inflammatory cytokine interleukin-1β (IL-1β) by the cells of the immune and nervous systems. High levels of IL-1β have been shown in *in vitro* investigations to impair the development of neural progenitor cells. However, the delayed behavioral abnormalities caused by increased neonatal IL-1β and their molecular and cellular mechanisms are not sufficiently studied. We have analyzed the injuries to different types of memory in mature male Wistar rats after administration of IL-1β in early ontogenesis and have examined the possible molecular and cellular mechanisms underlying such injuries. It was revealed that injection of IL-1β during the third week of postnatal life (which corresponds to human perinatal period) caused the dysfunction of spatial memory (in Morris water maze) and conditioning (in active and passive avoidance tasks) in mature animals. It should be noticed that in all tests the long-term but not short-term memory is damaged. The disorders of brain dopaminergic system and expression of involved in the neuroplasticity regulation genes *Timp1* and *Fgf2* in hippocampus were considered as possible mechanisms of

shown cognitive dysfunctions. The investigations were carried out using the methods of HPLC and quantitative RT-PCR. The experimental rats that have never experienced the cognitive task have a decreased level of dopamine and its metabolism (3,4-dihydroxyphenylacetic acid/dopamine – DOPAC/DA), while after the cognitive task the level of dopamine metabolism is increased in prefrontal cortex. In the active avoidance test the experimental rats have elevated expression of *D4*-dopamine receptor gene in hippocampus and prefrontal cortex. The expression of *D2S* and *D3*-receptor genes is increased only in hippocampus; and the *COMT* gene, only in the prefrontal cortex. The expression of these genes in striatum is not impaired. In active avoidance task the rats that were injected with IL-1β during the 3rd week of postnatal life have decreased expression of *Timp1* and *Fgf2* mRNA in hippocampus. However the level of mRNA of these genes in hippocampus of experimental rats that have never experienced the cognitive task is the same as in control rats. The described abnormalities are likely to be the mechanisms of cognitive dysfunctions of mature animals which were administered IL-1β during the 3rd week of life. The data obtained could be used in developing new approaches for prevention and treatment of cognitive impairments caused by different perinatal injuries of the central nervous system.

STRESS AND THE DANGERS OF CURING CHRONIC BENIGN DISEASES. MP Rambarun, Alpha Med Clinic, Mauritius, Ukraine

INTRODUCTION: Chronic Benign Diseases serve as 'buffers' to variations of the level of stress of patients. Curing them opens the door to potential malignant diseases. This study thus shows us that our chronic benign diseases protect us against the onset of malignant diseases. **METHODS**: Our study comprises 200 patients suffering from 4 different types of chronic benign diseases. Half of these patients (Group 1) have received deliberate 'negligent' treatment while the others (Group 2) have received effective curative treatment. They had an age range from 20 to 54 years old and were followed on a period of 8 years between 2002-2010. **RESULTS AND DISCUSSION:** From 2002 till 2010, none of the Group 1 patients suffered from any onset of associated chronic benign or malignant diseases. The negligent mode of treatment received by these patients helped in keeping the diseases chronic. This feature 'barred' the route to the onset of other diseases. The Group 2 patients received appropriate and effective curative treatments; and 92 of them were completely cured within a period of 3 months to 3 years from receiving their respective treatments, starting in May 2002. From then on, till 2010 (a) 14 of them contracted other similar or different chronic benign diseases, including, inter alia, obsessional neurosis, chronic skin diseases, intestinal ulcers and litiasis and (b) 12 of them developed malignant diseases, including, inter alia, brain/breast/skin malignancies, vascular accidents and Crohn disease (1 case). In our modern society, the general level of stress suffered by man in general has considerably increased since the last 20-30 years or so. Our subconscious mind has the duty to control that stress when this is overwhelming. To achieve this end, one of the best ways devised by the subconscious mind is to delegate some of the said stress to our body. In consequence, our body serving as a 'buffer' to the overwhelming stress develops, in most cases, chronic diseases, benign or malignant. **RESEARCH SUPPORT:** Alpha Med Clinic.

FUNCTIONAL SIGNIFICANCE OF THE 3'-UTR IN THE MRNA OF THE STRESS-INDUCIBLE PROTEIN CHOP. WT Lui, NS Wong, Department of Biochemistry, Faculty of Medicine, University of Hong Kong, China

INTRODUCTION: Previous studies have implicated the expression of the stress-inducible protein C/EBP homologous protein (CHOP) in the development of neurodegenerative diseases, for example, Parkinson's disease. Although the regulation of CHOP expression at the post-transcriptional level is best exemplified by the role played by the 5'-UTR of the CHOP mRNA, much less is known about the function of its 3'-UTR. Here we investigated if expression of CHOP is regulated by the 3'-UTR of CHOP mRNA. **METHODS**: A reporter plasmid (pEGFP-3UTRCHOP) was constructed such that it will express an EGFP mRNA with a 3'-UTR same as that of the CHOP mRNA. A series of 3'-UTR deletion mutants were made to identity the specific regulatory sequence

elements that may be present. EGFP expression from such mRNA species is quantified in transient transfection assays in terms of the mean fluorescence of the transfected cell population by FACS analysis. **RESULTS AND DISCUSSION**: EGFP expression from all of the mRNA species is spontaneous and the highest EGFP fluorescence is produced from an EGFP mRNA (Δ171CHOP) in which the first 171-bp of the 3'-UTR of the CHOP mRNA is deleted, producing EGFP fluorescence that is approximately three times as high as that produced by the EGFP mRNA bearing the full length CHOP 3'-UTR (3UTRCHOP). The replacement of the 5'-UTR of the EGFP mRNA species with that of the 5'-UTR of CHOP mRNA resulted in marked repression of spontaneous expression of EGFP. However, much less repressive effect was observed from mRNA-Δ171CHOP carrying the 5'-UTR of CHOP mRNA. Introduction of arsenite stress resulted in an almost complete relief of repression of EGFP expression. The mean EGFP fluorescence was higher in stressed cells carrying the 5UTRCHOP-mRNA-Δ171CHOP when compared to those carrying 5UTRCHOP-mRNA-3UTRCHOP. Comparable mRNA levels were found between the arsenite-treated and the control cells. These results demonstrate for the first time that the first 171 bases in the 3'-UTR of CHOP mRNA may have repressor function in mRNA translation. **RESEARCH SUPPORT:** GRF grant (HKU 7686/06M) and HKU CRCG Grants.

AN IN VITRO PREPARATION OF THE TURTLE TELECEPHALON FOR THE ELECTROPHYSIOLOGICAL STUDY OF CORTICOSTEROID MODULATION OF CORTICOLIMBIC PATHWAYS. AK Petko, E White, DM Senseman, The Institute for Neuroscience and Department of Biology, UTHSC SA, San Antonio, USA

INTRODUCTION: Corticosteroids play a prominent role in promoting adaptive behavioral responses to stress. In the freshwater turtle, Pseudemys scripta, elevated plasma corticosterone levels, caused either by stress or exogenous administration, increases locomotor activity. Since the stimulatory effects of corticosteroids on locomotion is widespread among mammalian and non-mammalian vertebrates, it is possible, if not probable, that corticosteroids exert their behavioral control through the modulation of homologous neural pathways using similar neurophysiologic mechanisms. To examine these modulatory effects, we have recently developed an in vitro preparation of the turtle telencephalon that preserves nearly all of the corticolimbic neural circuitry. Moreover, since the preparation approximates a flat sheet, it is especially amenable to combined electrophysiological analysis using whole-cell recording from individual cortical, hippocampal, septal and striatal neurons in combination with simultaneous monitoring of population activity in these structures using voltage-sensitive dye imaging (VSDI). **METHODS**: Morphologically, the turtle telencephalon approximates a hollow cylinder since it lacks the extensive subcortical white matter found in mammals. After serving its connection with the diencephalon, the complete telencephalon (olfactory bulb, cerebral cortex, limbic cortices, septum and striatum) can be unfolded to form a nearly flat sheet after creating a single rostral-caudal incision along lateral side. Using very fine pieces of tungsten wire, the telencephalon sheet can be pinned, with its ventricular side facing upward, to the Sylgard-coated bottom of a recording chamber. This process is facilitated by placing a small hemi-ball lens (4 mm dia) underneath the preparation to support the dorsomedial cortical area. By virtue of turtle's brain well-known resistance to anoxia, apparently normal neural responses can be recorded from this preparation for 2-3 days or longer. Because the lateral incision only passes through the olfactory bulb and lateral (olfactory) cortical area, the extensive synaptic connections within and between the visual cortical area (dorsal cortex), limbic cortical areas (dorsomedial and medial cortex), the septum and striatal areas are preserved. It therefore becomes possible to assess the acute modulatory effects of corticosteroids on various corticolimbic pathways using concurrent whole-cell recording and voltage-sensitive dye imaging. **RESULTS AND DISCUSSION**: We are currently using this preparation to assess the acute effects of dexamethasone on septal-hippocampal and cortical-hippocampal pathways. **RESEARCH SUPPORT**: NSF Undergraduate Biology and Mathematics Program (UBM) Grant 0634588.

Day 4. Sat, May 19, 2012

Oktiabrskaya Hotel, Grand hall (2nd floor), 10 Ligovsky Prospect, St-Petersburg, Russia

Morning session

10.00-13.00 SYMPOSIUM IV: STRESS AND HUMAN BEHAVIOR
Chair: V Klimenko (Russia)

OCCUPATIONAL STRESS AMONG ADMINISTRATIVE PERSONNEL IN MENTAL HEALTH HOSPITALS. G Hayredin, MM/HRM, Center for Mental Health, Rousse, Bulgaria
INTRODUCTION: Objectives: To evaluate levels of occupational stress in administrative personnel in mental health hospitals. According to NIOSH - The National Institute for Occupational Safety and Health - professional stress is a combination of negative physical and emotional reactions that occur in the mismatch between job requirements and capabilities, resources or needs of the worker. This stress may have health problems and even cause accidents. Clinical work in mental health may be considered stressful for a variety of reasons. Psychiatry has been considered as one of the most stressful medical specialties. Most of the studies in the literature consist of samples of nurses and physicians and, while comparative studies amongst these groups are scarce, research comparing mental health professionals and administrative staff are practically non-existent. The purpose of this study is identifying those work situations which are potentially powerful stressors, as well as the nature of their consequences for health. The design of the study should allow us to examine the potential specific differences among occupations. **METHODS:** Subjects – A sample of 100 administrative personnel was chosen from different state mental health care services. Design – A pilot postal questionnaire was drawn up from the most frequently-mentioned issues in the psychiatric domain. The questionnaire comprised following aspects: Conflict situations; Sociodemographic aspects; Health; Job dissatisfaction. Procedure – Questionnaires were mailed to the chosen professionals according to the already described criteria and were personally addressed to the workplace of every professional interviewed, with a letter asking for their cooperation and guaranteeing anonymity. **RESULTS AND DISCUSSION:** The response rate was 85 % (85/100). By occupation, the percentage of returned questionnaires was 52 % for administrative personnel, 38 % for psychiatrist and 10 % for internal staff. Pronounced differences were found between the respondents in the evaluation of potential stressors and the overall occupational stress score. The category of stressors with the highest mean severity of stress score was time-related stressors, falling behind schedule, constant time pressure. Two-third of all interviewed described moderate to severity high levels of emotional exhaustion. **CONCLUSION:** The results indicate that administrative personnel rank factors related to time management as major job stressor. Results from the study indicate that persons employed in the administration of psychiatric hospitals need additional training in time management. This can be made with specialized training in techniques, enabling them to cope with stress in daily work.

RESTRUCTURING ATEMPORAL MEMORIES (REMA), A NOVEL TECHNIQUE TO ELICIT VARIATIONS IN HUMAN BEHAVIOUR AND PERSONALITY PATTERNS. A Quaini-Citoler, U Diego-Ayala, Research on Human Behaviour Applied (REHUBA) Association in Barcelona, Spain
INTRODUCTION: A new technique, based on the concept that the dissociation of negative emotion from memories (called disturbing memories) effect significant changes in the personality and behavioural patterns of individuals, was developed. The REMA technique is suitable to efficiently work towards the modification of personality patterns, stress, anxiety, among others, suitable to be applied in personality disorders and mild psychiatric cases, producing satisfactory results in a reduced time frame. **METHODS:** 61 subjects have been treated, with 472:34 hours total. Ten of

those subjects participated in a study where The Millon Clinical Multiaxial Inventory-III (MCMI-III) was applied before starting the process and between two and six months later. The main personality problems were anxiety, borderline, sadism, depression, dependent and somatoform. The identification and dissociation of disturbance in memories was conducted in various REMA sessions in a one to one basis. No drugs of any kind are used. **RESULTS AND DISCUSSION:** Improvement in life of the subjects was found. Dramatic changes in personality disorders patterns were found. Examples of Average reduction: Anxiety 91 to 4.6; Borderline 74 to 15; Negativistic and sadistic 90 to 18; Results were expanded to psychical conditions: significant remission in muscular dystrophy and psoriasis were also reported as well as, according to a medical report, the total remission of a Queratosis Actinica. The results confirm that disturbing memories that are stored in our system continuously affect our perception, psychological and physical behaviour. The specific memories are identified to proceed with the dissociation of the emotional link of those memories. It has been seen that in a time length of weeks, dramatic modifications in personality patterns and behaviour can be produced. Although the required time varies for each person, between 5 and 10 hours of treatment might be sufficient to obtain tangible results. Further studies are required to expand the range of pathologies for applications.

BEHAVIOR AS A CONSEQUENCE TO FULLY DESCRIBE SHORT-TERM OCCUPATIONAL STRESS. P Fauquet-Alekhine, Nuclear Power Plant of Chinon, Management Department, Avoine, Laboratory of Research in Energy, Montagret, France
INTRODUCTION: The stress which we are interested in this study is a short term occupational stress, while men at work are asked to perform a task bounded in a short time interval (about several seconds to several hours). To characterize the stress, (macro)variables can be distributed among three to six dimensions (McLean, 1974; Palmer et al., 2003). Consequences due to stress are absent of the models. Our work aims to make the demonstration that the consequences (among which behavior) induced by the short term occupational stress are important to fully describe stress.
METHODS: In order to show the importance of behavior to characterize short term occupational stress, we have proceeded in two steps: the first one investigated whether stressful (resp. stressless) conditions gave mainly stressed (resp. non stressed) behavior analyzing performance versus stress, and the second one analyzed how apparent similar stressed subjects might give different consequences in terms of behavior. **RESULTS AND DISCUSSION:** Stress in test conditions: Resulting data fulfill the theoretical proposal of Yerkes and Dodson (1908), divided into three main parts: i) the central part reflects the transient state for the subject in terms of stress effects, ii) the left part is linked to the positive stress state or stable cognitive state, and iii) the right part concerns the negative stress state or the potential cognitive disorder state. They remind the concept of Human Functional States (HFS) defined by Leonova (2009). The results illustrate the impact on the subject's behavior. Stress in working situations: Observations and interviews with trainers and trainees trained on full scale simulators for risky professions have been done, highlighting how apparent similar stress states can lead to different behaviors. It shows that both the source factors of stress and consequences induced by the situation of stress can be useful for its characterization. The two 3-D space model of stress: The conclusion is that stress is fully defined by a two 3-D space concerning source and consequences. The source 3-D is: i) the context dimension, ii) the request or job demand dimension (excluding the context), iii) the subject\'s characteristics. The consequences 3-D is: i) the psychological symptoms, ii) the physiological symptoms, iii) the behavioral symptoms, or resulting actions. In each 3-D space, the stress is defined by variables on each axis which determines a volume of stress. The first volume finds its consistency through the dimensions interactions and produces the consistency of the consequences volume in which dimensions interact together as psychological symptoms usually produce physiological responses, both making possible or not behaviors. The two spaces interact together, as symptoms produce a feedback on the source. **RESEARCH SUPPORT:** Larsen and Edf, and with the contribution of Air France-KLM, Chu Bicctre, Ecole Nationale de la Marine du Havre.

THE USE OF HIGH FIDELITY SIMULATIONS TO ASSESS THE ASSOCIATION BETWEEN STRESS AND PERFORMANCE IN EMERGENCY RELATED OCCUPATIONS. C Regehr, V LeBlanc, University of Toronto, Toronto, Canada

INTRODUCTION: Research has increasingly identified alarming levels of traumatic stress and acute stress symptoms in individuals working in emergency services and other high stress jobs. Yet the impact of these symptoms on performance and hence public safety remains uncertain. This presentation discusses a program of research that has examined the effects of both post-traumatic symptoms and acute psychological and biological stress on the performance and decision making during a simulated event among police officers, emergency communicators, paramedics and child welfare workers. **METHODS**: Four studies using simulation methods involving video simulators, human-patient simulators, and/or standardized patients, examined the performance of emergency workers in typical workplace situations related to their individual profession. Exposure to critical incidents in the workplace and current level of traumatic stress symptoms were assessed prior to participation in the scenarios. Subjective psychological stress and physiological stress response were measured before, during and after participation in the scenarios. **RESULTS AND DISCUSSION:** In all four studies the simulated workplace situation resulted in both increased subjective stress and a biological stress response. Results regarding performance and decision making varied by occupational group. For instance, police performance was not affected by PTSD symptom levels, while the clinical judgment of child welfare workers was correlated with PTSD. Paramedics demonstrated poorer performance in high stress scenarios than low stress scenarios, while child welfare workers were not affected by the level of acuity of the scenario. The use of simulated real life situations provides an opportunity to determine the impact of PTSD on decision making and performance in emergency service situations. Results of this type of study can assist in clinical decisions and policy making with respect to the ability of a worker with PTSD to continue to provide services to the public. **RESEARCH SUPPORT:** Canadian Institutes of Health Research; the Social Sciences and Humanities Research Council of Canada.

MEDICAL STUDENTS' LONELINESS, HOPELESSNESS AND ANXIETY AGAINST THEIR SELF COMPASSION. N Karaoglu, O Coskun, II Budakoglu, Medical Education and Informatics Department, Konya University, Meram Faculty of Medicine, Konya, Turkey

INTRODUCTION: One of the meanings of compassion is having nonjudgmental understanding for people making mistakes. It is known that medicine as a profession via high demand of education and health care creates physicians who are always trying to be perfect. But on the other side as a human a physician is not a perfect one. The irony of being a healer and in some cases being not to be able to stop death is the main conflict putting a physician in stress. It is also known that stress, health concerns and emotional problems of a physician increase beginning from medical education. The aim of this cross sectional and descriptive study was to describe loneliness, state and trait anxiety and hopelessness levels of preclinical medical students and analyze the correlation of them with self-compassion. **METHODS**: In the second half of the academic year in 2011 with the permission of the faculty an anonymous questionnaire consisting of socio demographic questions and UCLA Loneliness Scale, State-Trait Anxiety Inventory (STAI-I-II), Beck Hopelessness Scale and Self Compassion Scale was applied to every one of the three student of Meram Faculty of Medicine, voluntarily. While the questionnaires with missing answers about the first part were not eliminated, the unfilled Scales were all eliminated. Categorical variables were expressed as numbers and percentages and the continuous variables expressed as means with standard deviations. The association of the dependent variables (UCLA, STAI-I, STAI-II, Hopelessness and Self compassion) with the independent variables was determined. Student t-test, One-way ANOVA, chi-square, Kruskal–Wallis tests and correlation analyses were made. $P < 0.05$ was considered significant. **RESULTS AND DISCUSSION:** At the end 192 fulfilled questionnaires analyzed for this study. One fourth of the group was first year students (n=48, 25.0%) and above the half were male

(n=100, 52.9%). The mean age of the students were 19.80±1.24 years (range: 17-25 years) and approximately half of them were living in a dormitory (n=94, 49.0%). Just 15.3% of them (n=29) were not satisfied with the city and just 3.1% of them (n=6) were not satisfied with the career they choose. The UCLA, STAI-I, STAI-II, BECK Hopelessness and Self Compassion Scale scores of the study group were 33.19±9.47, 38.77±9.31, 43.35±8.27, 4.32±3.94 and 75.47±12.38, respectively. State anxiety and hopelessness level of the second year students, loneliness and the hopelessness level of the men, loneliness, state anxiety and the hopelessness level of the students who were not satisfied with the city, and loneliness, state- trait anxiety and the hopelessness level of the students who were not satisfied with the career selection were significantly higher than the others ($p<0.05$). There was no significance in between self-compassion levels of the students in respect to academic year, gender or residency. While loneliness, state and trait anxiety and hopelessness were in a positive correlation, self-compassion was in a negative correlation with all of them. Psychological well-being needs social and psychological support. Coping with the stressors at various stages of the medical profession should begin with self-compassion before compassion to others. Helping others can to be realistic without helping own self.

CONFERENCE RESEARCH COMMUNICATIONS:

1. NON-NEUROLOGICAL SURGICAL STRESS AND CEREBROSPINAL FLUID BIOMARKERS FOR NEURAL AND ASTROGLIAL INTEGRITY. R Anckarsater, H Anckarsater, C Wass, K Blennow, H Zetterberg, Department of Anestesiology and Intensive Care Kungalv Hospital, Sweden
INTRODUCTION: In a recent report, Tang and co-workers showed that biomarkers for inflammation (interleukins, S100Beta and TNF-α) and Alzheimer pathology (total tau and phosphorylated tau) increased progressively in cerebrospinal fluid (CSF) after surgery for idiopathic nasal CSF leak correction. **METHODS**: We aimed to replicate these findings in non-neurological surgery. Among 35 patients undergoing knee arthroplastics with a spinal blockade and propofol sedation, three CSF biomarkers were analyzed before, three hours after and the morning after the interventions: total tau (T-tau) as a biomarker for cortical axonal integrity, neurofilament light (NFL) as a biomarker for the integrity of large caliber myelinated axons, and glial fibrillary acidic protein (GFAp) as a biomarker for astroglial cell integrity. **RESULTS AND DISCUSSION**: T-tau concentrations increased significantly during and after surgery. NFL remained unchanged during surgery, while mean GFAP concentrations increased to the day after with a large standard deviation, so that the difference was not significant by an overall ANOVA and therefore not further explored. Tau concentrations correlated with the administered doses of bupivacaine. Also surgery that does not directly involve the CNS leads to increased levels of biomarkers for damage to the neural tissue in the CSF. Bupivacaine may be involved in these reactions. **RESEARCH SUPPORT**: The Vastra Gotaland, the Swedish Medical Society, and the Goteborg Medical Society. The staff at the Department of Anaesthesiology at Kungalv Hospital assisted in the data collection.

2. GLUTAMIC ACID AND THE COEFFICIENT OF UREA/AMMONIA AS MARKERS OF STRESS CAUSED BY INTENSE MUSCLE EXERCISES. V Furdui, A Leorda, S Garaeva, P Pavaliuc, G Redcozubova, O Garaeva, G Postolati, E Pulbere, Institute of Physiology and Sanocreatology MAS, Chisinau, Moldova
INTRODUCTION: The search of the significant prognostic markers which can be used to control the functional state of the organism is necessary for the goals solution of maintenance of sanogene morphofunctional status of the organism. **METHODS**: Our studies were conducted during 2 weeks at healthy volunteers with age of 18-20, who were exposed to the complex of sparing exercises - exercises for the body in combination with a cycle ergometer (50 rev/min) during 30 minutes three times a week. There has been detected a decrease in anaerobic threshold under the intensification of the exercises (the speed of the cycle ergometry increased in two times), indicating the excessive

physical activity and the development of the stress. The value of heart rate (HR), during which the straight-line relationship between the increase of heart rate and intensity of physical activity disappeared, was lower by 20-30 beats than the maximum values of heart rate. The determination of free amino acids in the saliva was carried out on amino acid analyzer AAA T339M. **RESULTS AND DISCUSSION**: The usage of complexes composed with sparing and intense physical exercises revealed that the amino acids spectrum of saliva samples, taken on an empty stomach prior before exercises and the next morning after their completion, differed significantly. The total content of free amino acids in the saliva increased 1.5-fold after sparing physical exercises, and 5.4 times after intense physical exercises. The concentration of urea in saliva decreased twice after sparing exercises, and ammonia level;s rose 1.4 times. At the same time, the contents of both indicators in saliva after intense exercises increases 1.2 times (urea) and 5.0 times (ammonia), suggested intensified catabolic processes in the organism. Coefficient of urea/ammonia reduced from 34.1 to 12.5 after sparing exercises, and to 8.3 after intense physical exercises. The concentration of glutamic acid in saliva was significantly increased (3.7 fold) after intense exercises, and 1.5 fold after sparing exercises. The ratio of glutamic acid/glutamine was 1.01 under the sparing physical exercises, and decreased to 0.44 under the intense exercises. Thus, the coefficient of urea/ammonia and glutamic acid concentrations can be used as markers of stress caused by intense muscular exercises.

3. AGE-RELATED CHANGES OF THE CONTENTS OF GAMMA-AMINOBUTYRIC ACID AND TAURINE IN RAT BLOOD PLASMA UNDER ACUTE STRESS. AV Nevoia, VK Ciochina, TS Beshetea, ZB Gheorghiu, Institute of Physiology and Sanocreatology MAS, Chisinau, Moldova
INTRODUCTION: The stress-limiting system, one of the mechanisms of which is neuroinhibition, suppresses the distress manifestation and prevents the development of stress-induced diseases. The key element of neuroinhibition is the neuromediator gamma-aminobutyric acid (GABA), the concentration of which in plasma reflects the GABA-ergic activity of the brain. Taurine is another non-protein amino-acid involved in the brain's inhibitory processes and the processes of adaptation. **METHODS**: The blood plasma concentrations of GABA and taurine in rats of different ages (3 weeks, 12 months and 24 months) stressed by immobilization for 24 hours have been investigated by the method of liquid chromatography. **RESULTS AND DISCUSSION:** In the relatively comfortogenic conditions, any clear age-related differences of the contents of GABA and taurine in blood plasma of rats of all the groups have not been revealed. Immobilization stress significantly increased the contents of GABA and taurine in blood plasma of rats of all the groups. GABA concentration changes rose in adults 4.6 times, in old individuals 7.3 times, and in young rats in 8.3 times. Taurine concentrations rose thrice regardless of the age group. Our results link the rat organism's stress-limiting system activity enhancement and the hyperactivity of the GABA-ergic mechanisms of neuroinhibition in young and old vs. adult rats.

4. COMBINING ATOMIC FORCE AND OPTICAL MICROSCOPIES TO STUDY CALCIUM RESPONSE IN DORSAL ROOT GANGLION NEURONS TO A LOCALLY APPLIED MECHANICAL STIMULUS. L Ponce, A Berquand, A Holloschi, M Petersen, M Hafner, HochSchule Mannheim, Bruker Nano, Heidelberg University, Heidelberg, Germany
INTRODUCTION: Mechanical hypersensitivity in response to nerve injury represents a major clinical problem, and mechanosensitive ion channels play an important role in pain transmission pathways. To get better insight in the mechanism by which neuronal cells can sense a mechanical stress and respond to it, a first mandatory step is to develop an integrated technology that enables applying controlled mechanical forces and investigating the consequences at the subcellular level. During the last two decades, people succeeded in stimulating the somatic parts of neurons by using patch-clamping but in order to better understand this mechanism we need a more accurate technique which allows stimulation of endings and axons with precision. Atomic Force Microscopy can be used not only to image biological samples, but also to apply a vertical force on the surface and sense local differences in elasticity. More recently, the combination of most of commercial

AFMs with inverted optical microscopy (IOM) techniques, especially epifluorescence, confocal and TIRF, enables easy and straightforward navigation to the location of interest and also displaying both AFM and optical information simultaneously. The experimental approach described here will provide possibilities to study other dynamic signals involved in mechanotransduction and pain mediation. **METHODS**: In the present study, we used a colloidal AFM probe as a mechanical tool to locally stimulate living dorsal root ganglion neurons. Using and AFM/IOM fully integrated system allowed us recording the calcium response of the stimulated cells in real time. The AFM was a Bioscope Catalyst. AFM tips were functionalized with 10 micrometer polystyrene beads. Due to the discovery of a range of fluorescent calcium probes with diverse spectral properties that permit calcium imaging with high spatial and temporal resolution, optical probes can be used for recording cellular responses simultaneously to the controlled application of mechanical forces. Here, the fluorescence calcium indicator Fluo8/acetoxymethyl ester (AM) TM was used. Cells were first washed with physiological buffer (140 mM NaCl, 3.5 mM KCl, 2 mM CaCl2 x 6 H2O, 1 mM MgCl2 x 6 H2O, 20 mM d-glucose and 10 mM HEPES), followed by incubation in physiological buffer containing 2 µM Fluo8-AMTM (ABD Bioquest) for 30 minutes at room temperature. Then, cells were washed with buffer to remove the buffer containing calcium probe. To allow intracellular hydrolysis of the AMester, cells were incubated for a further 20 minutes at room temperature. Intracellular free calcium changes were visualized using an inverted epifluorescence microscope Axio Observer Z1 (Zeiss). A HB 100 mercury lamp was used to provide fluorescence excitation in combination with specific filter sets (excitation BP 488/10 nm, FT 500 and emission BP 525/50 nm). Image acquisition was done using the Axiovision software from Zeiss with an AxioCam MRm; 7 images were captured and digitalized per second for as long as desired. The fluorescence movies were processed by using Image J. **RESULTS AND DISCUSSION**: Our present study shows, for the first time, simultaneous indentation by AFM and calcium imaging in individual living DRG neurons and their neurite endings. The study aimed at stimulating single cells and even smaller structures like neurites, without disturbing neighboring cells, and proved that investigation of intercellular signaling by using a combined AFM-live cell imaging system is possible. Due to this combination it is feasible at the same time to stimulate neurons and record the calcium response in the cell culture in a near-physiological environment, which allows the diffusion of molecules secreted as a result of the response. Further information obtained by this study is that both somata and terminal endings are mechanosensitive and the response can be spread out to neurons in close vicinity. The required forces used to mechanically stimulate somata and neurites were found to be around 234 pN and 346 pN, respectively. Nevertheless, those forces were calculated by taking into account the hard contact portion of the force curves. As mentioned above, smooth contact was sometimes enough to induce stimulation. Hence, in all likelihood the real required forces to induce stimulation are probably smaller than the values mentioned above. This preliminary study will help to increase our understanding of how DRG neurons communicate in response to mechanically-induced stress. The experimental approach described here will provide possibilities to study other dynamic signals involved in mechanotransduction (e.g., membrane potential, sodium, pH). Together with the evaluation of sensitivity thresholds for mechanical responses in somata and their neurite endings, the combined experimental AFM/live cell imaging approach will contribute to unravel the underlying mechanisms of mechanotransduction in pain mediation.

5. UTILIZING THE ZEBRAFISH NEUROPHENOME PROJECT (ZNP) DATABASE FOR ANALYSES OF COMPLEX NEUROPHENOTYPES IN ZEBRAFISH MODELS. E Kyzar, J Green, S Gaikwad, M Pham, A Stewart, C Collins, J Cachat, A Kalueff. Department of Pharmacology and Neuroscience Program, Zebrafish Neuroscience Research Consortium (ZNRC), Tulane University Medical School, New Orleans, LA, USA

As the rate of biomedical discovery is rising exponentially, electronic databases have become particularly effective in organizing and sharing scientific knowledge. Due to a well-characterized genome, robust behavioral responses and physiological similarity to humans, the zebrafish (*Danio rerio*) has emerged as a useful species for neurobehavioral research. The growing utility of this

model organism requires the development of specialized databases of zebrafish neurophenotypes, such as the Zebrafish Neurophenome Project (ZNP) (www.tulane.edu/~znpindex/search). Representing a new bioinformatics-based tool, the ZNP interactive searchable database consolidates neurobehavioral and related physiological phenotypes obtained in various zebrafish models and tests. ZNP contributes to increased accessibility of current zebrafish neurobiological knowledge, and may be used for various research projects. **RESEARCH SUPPORT:** ZNRC.

6. MINDBOMB1 MEDIATES DELTA-D REGULATION THROUGH AUTOPHAGOSOMAL DEGRADATION PATHWAY IN ZEBRAFISH NEUROGENESIS. SH Lee, MJ Kim, Sookmyung Women's University, Seoul, Korea

INTRODUCTION: Notch signaling is classically well known for cell fate specification and differentiation during animal development. Recent studies reveal a novel role for the regulation of neuronal behavior, like sleep and stress in the adult nervous system and suggest that the selective regulation of Notch or Notch ligand expression may play a key role for neuronal behavior. This study was focused on the regulatory mechanism of deltaD and mib1 during zebrafish neurogenesis. Mib1 and deltaD are co-localized into autophagosome and deltaD cannot place on the autophagosome without mib1. These findings suggest that mib1 may mediate deltaD regulation by autophagy during zebrafish embryogenesis. **METHODS**: Zebrafish wild-type AB and mind bomb alleles were used. Autophagosomal-related gene, deltaD, mib1-related gene were cloned. Whole-mount immunohistochemistry; Cell culture, transfection and immunocytochemistry; Fluorescent imaging. **RESULTS AND DISCUSSION**: DeltaD is localized in the cytoplasmic puncta in the developing neuronal domain of wild type zebrafish embryos. DeltaD promotes internalization by mib1. Mib1 is localized in the autophagosomal vesicles in HEK 293T cells. DeltaD and Mib1 is co-localized in the autophagosomal membrane in zebrafish embryos. DeltaD may be degraded by mib1 through autophagy-dependent way. **RESEARCH SUPPORT**: Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science and Technology (2011-002739).

7. IMPACT OF STRESS ON ELECTROMAGNETIC FIELD-INDUCED CORTICOSTERONE, CYTOKINES AND GFAP RESPONSES. M Bouji, A Lecomte, Y Hode, R de Seze, AS Villegier, INERIS, France

INTRODUCTION: The widespread use of mobile phones raises the question of the effects of electromagnetic fields (EMF, 900 MHz) on the brain. Experimentally, local brain EMF exposures are performed in rats maintained in contention in Plexiglas rockets. Previous studies reported increased levels of cerebral glial fibrillary acidic protein (GFAP) after a single EMF exposure, suggesting a potential inflammatory process. However, these effects were not always reproduced, and the present study aims to test the contribution of protocol-induced stress in EMF-induced responses. **METHODS**: To do so, plasmatic levels of corticosterone, GFAP, interleukin (IL)-1β and IL-6 were measured 48h following a single, 15 min, (0 or 6 W/kg) EMF-exposure in rats subjected to fear conditioning and tests (group 1 and 2). Test of stress was performed by measuring the same biological responses 30 min, 5h and 24h following (group 3) daily handling, (groups 4 and 5) a single, 15 min, (0 or 6 W/kg) GSM-exposure, and (group 6) a single 15 min sham (0W/kg GSM)-exposure followed by a fear conditioning session. **RESULTS AND DISCUSSION:** Results showed that corticosterone increase was found only in groups 2 and 6, and no effect on IL-1β, IL-6 or GFAP was obtained. According to these data, stressful situation linked to fear conditioning procedure did not modify GFAP or IL responses. Moreover, according to corticosterone measure, acute 15 min contention did not appear as a stressful event in our study. The use of fear conditioning in our protocol and the demonstration that it increases corticosterone after 30 min must be highlighted as a possible interacting parameter. Identification of contention-linked side effects may allow a better understanding of mobile phone EMF effects on neurobiological parameters. **RESEARCH SUPPORT**: PR 190 of French Ministry of Ecology (MEDDTL).

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