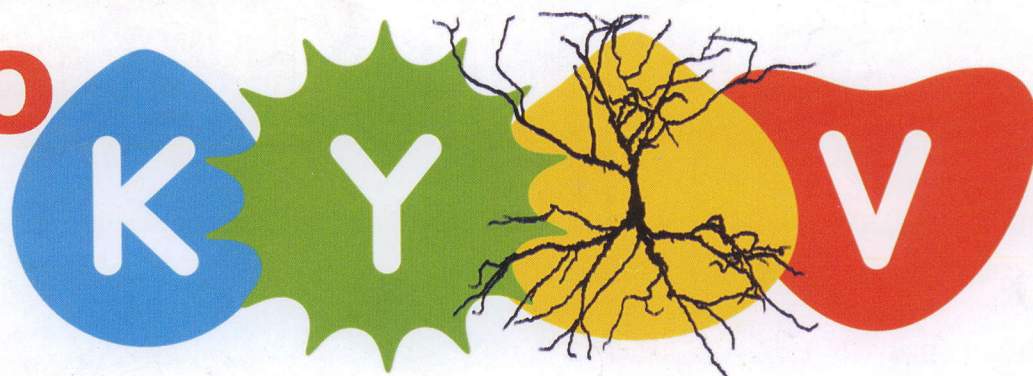


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INHIBITION OF PROTEASE-ACTIVATED RECEPTOR 1 AFTER STATUS EPILEPTICUS MODULATES EMOTIONALLY DRIVEN BEHAVIORAL RESPONSES OF EPILEPTIC RAT

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Protease-activated receptor 1 (PAR1) is an important contributor to the pathogenesis of a variety of brain disorders associated with a risk of epilepsy development. We recently showed that inhibition of PAR1 results in decreases of post-SE animal mortality, SE-induced cell loss, and the likelihood of the occurrence of interictal-spikes and spontaneous seizures. As PAR1 is expressed in the CNS regions of importance for the processing emotional reactions, including amygdala and hippocampus, and TLE is frequently associated with a chronic alteration of the functions of these regions, we tested the hypothesis that PAR1 inhibition could modulate emotionally driven behavioral responses of rats experiencing SE. We show that SE induces a chronic decrease in the animals' anxiety-related behavior and an increase of locomotor activity. PAR1 inhibition after SE abolished the alteration of the anxiety level but does not affect the increase of locomotor activity in the open field and elevated plus maze tests. Moreover, while PAR1 inhibition produces an impairment of memory recall in the context fear conditioning paradigm in the control group, it substantially improves contextual and cued fear learning in rats experiencing SE. These data suggest that PAR1-dependent signaling is involved in the mechanisms underlying emotional disorders in epilepsy.

Keywords: PAR1; temporal lobe epilepsy; lithium-pilocarpine model; anxiety; con-textual and cued fear learning

EFFECTS OF N-STEAROYLETHANOLAMINE ON BEHAVIOR OF RATS WITH CHRONIC SOCIAL STRESS

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Chronic stress is the cause of many violations of the normal functioning of various body systems, including the brain activity that may be associated with the development of depressive anxiety disorders, cognitive disorders and addictive behavior (drug addiction). Modulation of endocannabinoid system with the exogenous endocannabinoid substances influence is a new way of treatment diseases which caused by stress. Treatment with N-stearoylethanolamine (NSE) which is a member of the family of bioactive compounds N-acylethanolamines (NAE) could be promising pharmacological tool for modulation of activity of endocannabinoid system. The aim of this study was to estimate the effects of NSE on behavior of rats with chronic social stress. The study was carry out on 74 mature outbred white male rats (weight: 185±17 g

at the beginning of the experiment). Stress was induced by daily antagonistic interaction between animals (intruder and domestic) during 14 day by putting intruders into home cage of domestic for agonistic interaction for 10 min. After the last stress-inducing interaction, NSE was administrated intragastrically to 2 groups of animals daily during 14 days at a dose of 50 mg/kg of body weight. Another group of animals without NSE treatment received equal volume of distilled water by the same administration method. Behavior responses of rats of all groups were tested in the Novel Object Recognition behavioral test. It was revealed that chronic social stress during two weeks reduced investigative behavior, memory state and level of recognition of a new object. Animals which were exposed to chronic stress were exploring novel objects in the test phase $25,4 \pm 7,6$ s, whereas in rats that received NSE after stress this parameters was $39,9 \pm 19,1$ s ($p < 0.05$). Moreover, in rats that received NSE after stress the discrimination index was higher compare with rats, which were exposed only to stress ($p < 0.01$) that may indicate of improvement of memory level. Thus, we can conclude that the introduction of NSE after chronic social stress increases investigative behavior and memory state which impairs after stress. Publications are based on the research provided by the grant support of the State Fund For Fundamental Research (F64/28-2016).

Keywords: endocannabinoids, N-stearoylethanolamine, chronic social stress, rats, behavior, memory, learning

EEG-BEHAVIORAL PHENOTYPING OF NRXN-1 KNOCK-OUT MICE

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Synapses are a highly important part for normal functioning of nervous system. More than 100 neurological and psychiatric deceases are believed to be caused by abnormal work of synapses - synaptopathies. We used neurexin (NRXN1) knock-out mice to assess the possible effect of this gene on changes in brain's functional activity at the behavioral and system levels. This gene codes the presynaptic protein that participates in forming the cells contact between neurons. In humans mutations in it are associated with the autism and other cognitive disorders. We have recorded the EEG from prefrontal and parietal (close to the hippocampus) electrodes using small wireless recording device Neurologger (NewBehavior AG) in freely behaving mice (controls and NRXN1 mutants) during several standard behavioral tests: open field, novel object exploration, social interaction. Animal's movements were tracked with the EthoVision software and then synchronized with the EEG. The records were split into short 2s epochs, each of them was classified according to behavioral state (still, moving, exploring, etc). Wavelet-based EEG spectra for every epoch were calculated using the EEGLab software. We revealed that NRXN1 mutants had greater amplitudes of high-frequency bands (>20 Hz) during all tests, which may indicate greater arousal associated with the exploration of novel territory or objects. This between-group difference reduced with the habituation of the animals to experimental conditions in long (30-60 min tests). Presentation of non-social novel objects lead to the increasing of the frequency of dominant theta activity in controls but not in mutants. This may indicate the lack of hippocampal activation related to the exploration of new objects in NRXN1