

to chronic isolation stress for a period of 21 days, as a model system for depression, sole or in combination with 2h of acute stress immobilization or cold (4°C). Results have shown that hypothalamic-pituitary-adrenal axis activity was compromised by chronic isolation stress and could not be resumed after subsequent acute stressors. Both acute stressors led to increase of nNOS protein level while iNOS was unchanged. Chronic isolation stress increased cytosolic nNOS and iNOS protein levels as well as caspase-3 activation. Given that activities of mitochondrial Mn- and cytosolic CuZn-superoxide dismutase were reduced after chronic isolation stress and combined stress (isolation followed by acute stress), it can be concluded that chronic-induced stress is probably a consequence of increased iNOS, causing the activation of caspase-3 and apoptosis. The significance of these findings is to clarify the factors involved in the progression of neurotoxicity as well as to identify potential therapeutic targets for stress-related diseases, such as depression.

Increase of nNOS protein expression has no influence on redox balance in the hippocampus of chronically isolated rats

Zlatkovic J, Filipovic D

Laboratory of Molecular Biology and Endocrinology, "Vinca" Institute, University of Belgrade, Serbia

Exposure to stressors may lead to overproduction of reactive oxygen and nitrogen species. Nitric oxide (NO), although necessary for proper function of nervous system, if present in higher concentrations may cause cellular damage through a phenomenon known as nitrosative stress. Since NO production can occur as a result of activity of either inducible nitric oxide synthase (iNOS) or neuronal nitric oxide (nNOS), we examined whether 21 daily isolation as chronic stressor, sole or in combination with 2h of acute stress immobilization or cold (4°C), could alter iNOS/nNOS protein expression in cytosolic fraction of rat hippocampus. A protein expression of inducible form of heat shock protein 70 (Hsp70i), as protective molecule, was investigated. Also, concentration of serum corticosterone (CORT) was measured, as a marker of stress response. Significant increase in the level of nNOS following all types of stress was found. Chronic isolation, which is characterized by unchanged levels of CORT, led to increased expression of Hsp70i protein level, which was remained after exposure of animals to both additional acute stressors. Decreased expression of iNOS protein level was detected in chronic isolation stress and combined isolation followed by immobilization stress, while elevated levels of this protein was found in isolation followed by cold stress. Although elevated, expression of nNOS protein level does not imply a state of nitrosative stress since the activity of cytosolic CuZnSOD and mitochondrial MnSOD was not changed. Increased levels of Hsp70i may have a protective effect, probably by reducing the expression of iNOS protein level, which explains the absence of apoptosis in hippocampus. These results indicate the ability of neurons to maintain homeostasis (redox balance) in hippocampus after exposure of animals to chronic isolation stress.

Possible hypothalamic laterality in the central regulation of GnRH release: thoughts that might lead to a novel approach in hypothalamic studies

Zsarnovszky A, Tóth I, Johnson TS, Somogyi V, Kiss DS, Gyórfy A, Goszleth A, Bartha T, Frenyó LV
SzIE, Állatorvos-tudományi Kar, Élettani és Biokémiai Tan-szék, Budapest

The midcycle E2 surge induces a synaptic reorganization in the mediobasal hypothalamus (MBH), thus increasing the ratio of stimulatory/inhibitory synapses. This synaptic reorganization disinhibits GnRH neurons and leads to an LH surge. Synaptic functions are energy dependent and require mitochondrial ATP production. Ectonucleoside triphosphate diphosphohydrolase 3 (NTPDase3) may play a crucial role in the regulation of mitochondrial ATP levels in stimulatory MBH neurons. The positive gonadotrophin feedback involves the generation and function of large numbers of hypothalamic stimulatory synapses, thus, it might be associated with increased mitochondrial ATP production and increased mitochondrial respiration (mr). Anatomically, there are paired brain areas in the two hemispheres and unpaired structures along the anatomical midline. Distinct sides of paired brain areas usually regulate distinct physiological processes, rather than sharing roles to regulate the exact same functions. However, there are certain brain regions with no known functional differences between the two sides. One such brain area is the MBH, which has always been investigated as an unpaired midline structure despite its clearly symmetric anatomical characteristics. Investigation of mr in MBH synaptosomal fractions in our laboratory has indicated that besides ipsilateral intrahypothalamic differences (i.e., differences between the lateral and medial regions of the MBH on the same side) a functional laterality may exist between homologous areas of symmetric hypothalamic structures. Therefore, we have investigated mr rates, with special regard to ADP-dependent state 3 mr, in the MBH with isolated left and right sides. Our initial results imply that the MBH regulation of the E2-induced gonadotrophin surge is unilateral, and that there is an urging need for a technical solution to identify in vivo the dominant hypothalamic side that enters into the positive gonadotrophin phase of the estrous cycle.

Using small animal MRI in measurement of peripheral effects of anorexic agents

Zsedrovitsné Gőcze K¹, Kocsis P¹, Gajári D¹, Pápay G¹, Deli L¹, Terlezky P¹, Kovács P², Varga B², Tihanyi K¹
¹Preclinical Imaging and Biomarker Center, Gedeon Richter plc., ²Neurophysiology, Gedeon Richter plc., Budapest

Obesity and its related comorbidities such as non-alcoholic fatty liver disease (NAFLD), type-2 diabetes and dyslipidemia are very serious health issues in the developed countries. Their pharmacological treatments are not solved; in part due to the lack of adequate animal models and the poor predictability of the used ones, which make the animal-human translation of the rodent data more difficult. This poster makes a review of using MRI in obesity studies. MRI measurements were taken of body fat, visceral fat and liver fat in the diet-induced obese (DIO) C57BL/6 mouse with imaging and spectroscopy methods. T1-weighted images and spectroscopy data were acquired, both on a 9.4 Tesla Varian scanner. The spectroscopic measurement was performed on the whole body of mouse. The 1H spectrum is a two-peak-curve, one represents hydrogen of the water and the other represents hydrogen in fat. Similar spectroscopic measurement was performed on a voxel in the liver. The ratio of areas under the curve (AUCs) of the peaks shows the ratio of the fat and water in the body and in the liver. The results showed interesting issues. The whole body fat content shows sigmoid correlation with the body mass and in the same way with the visceral fat, while the content of the liver fat shows linear correlation with the body mass. A big advantage of the imaging method is the measurement of visceral and subcutaneous part of the body fat. However, we