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BRAIN CORTICOSTEROID AND NEUROSTEROID RECEPTORS AND EMOTIONAL STRESS

B. Bohus[1], S. M. Korte[1,2], H. J. A. Beldhuis[1], B. Roozendaal[1,3], S. F. de Boer[1], and B. Buwalda[1]
[1]*Department of Animal Physiology, University of Groningen, Haren, The Netherlands,* [2]*DLO Institute for Animal Science and Health, Lelystad, The Netherlands,* [3]*CNLM, University of California, Irvine, USA*

Corticosteroids are hormonal messengers of emotional stress. In the brain, intracellular mineralocorticoid (MR or Type I) and glucocorticoid (GR or Type II) receptors are the targets of corticosteroids. Recently, it also appeared that stress affects the formation of neurosteroids which influence brain functions via membrane-bound GABA-A/BDZ or glutaminergic NMDA receptors. Our findings indicate the role of both cortico- and neurosteroid receptor-bound processes in the expression of emotional stress-induced behavior. It is concluded that the involvement of brain MRs and GRs is situation specific. Neurosteroid effects on emotional behavior are related to their agonistic or antagonistic characteristics on the GABA/BDZ or NMDA receptor. The findings with genetic, molecular biological and pharmacological manipulation of the receptors point to their involvement in the pathomechanism of emotional disturbances such as fear, anxiety panic, depression.

STRESS TRIGGERED ACTIVATION OF NEUROTRANSMITTER GENE EXPRESSION

E. Sabban, B. Nankova, L. Serova, R. Kvetnanksy and E. Danailov
Department of Biochemistry & Molecular Biology, New York Medical College, Valhalla, New York, USA and Institute of Experimental Endocrinolgy, Slovakia

Prolonged stress is a major contributor to various pathological situations, such as cardiovascular diseases and mental illness. Some of these effects result from alterations in neurotransmitter gene expression. We examined the effect of single and repeated immobilization (IMO) stress on expression of a number of neurotransmitter (catecholamines, NPY, proenkephalin) related genes in several stress-responsive tissues in periphery (adrenal medulla (AM), sympathetic ganglia), and in the major noradrenergic and dopaminergic neurons in CNS. Northern blot analysis and run-on assays revealed that the inductions in gene expression are at least partially transcriptionaly mediated. Important tissue specific differences in molecular mechanisms of induction were found. The time of induction differed. For example, in AM and locus coeruleus, induction of tyrosine hydroxylase (TH) gene expression is maximal with single IMO for 30 min., while in superior cervical ganglia (SCG) and some dopaminergic regions of CNS, repeated IMO is required. Differences were observed in role of HPA axis. Thus, ACTH administration activates TH gene expression as much as IMO stress in SCG while attenuating the effect of stress in the AM. Moreover, infusion of nicotine was found to modulate the stress-elicited activation of neurotransmitter gene expression in a tissue specific fashion. The signaling pathways that may mediate these tissue specific differences will be discussed.

INVOLVEMENT OF REACTIVE OXYGEN SPECIES IN EMOTIONAL STRESS AND PREVENTION OF STRESS-INDUCED OXIDATIVE DAMAGE BY NATURAL SOURCE ANTIOXIDANTS

A. Mori, J. Liu* and S. Matsuura**
*Okayama University Medical School, Okayama, Japan, *Department of Molecular and Cell Biology, University of California, Berkeley, and ***Manda Fermentation Co., Ltd., Shigei-cho, Innoshima-city, Hiroshima, Japan*

Immobilization stress induces stomach bleeding in rats. We found that oxidative damages to lipid, protein, and DNA were induced in rats by immobilization-induced emotional stress. Glutathione was effective to protect oxidative damages. These findings suggest that oxidants are involved in emotional stress, and that the oxidative damages by emotional stress is a major contributor to aging acceleration and degenerative diseases associate with aging such as cardiovascular disease and brain dysfunction. In many epidemiologic studies, the consumption of fruits and vegetables is associated with low incidence and low mortalities of these diseases. MANDA, a natural product made by yeast fermentation of many fruits and black sugar, has an antioxidant activity. We administered MANDA, as an example of healthy food antioxidant, by a canula into the stomach of rats from the start of the emotional stress experiment. The control rats all showed congestion and some degree of bleeding in the mucosa of the stomach. However the rats treated with MANDA showed only congestion and did not show erosion or hemorrhage.

CHARACTERISTICS OF THE RESPONSES TO VASOACTIVE AGENTS IN THE CORONARY AND BASILAR ARTERIES OF STROKE-PRONE SHR (SHRSP)

A. Suzuki, H. Yamanishi, H. Higashino, Y. Nishimura
Department of Pharmacology, Kinki University School of Medicine, Osaka, Japan.

Hypertension induces stroke or cardiac infarction. Thus, it is important to study the function of coronary and cerebral arteries under hypertension. We studied the responses to vasoactive agents in the coronary and basilar arteries of SHRSP. The ring preparations of coronary and basilar arteries of SHRSP and Wistar-Kyoto rats (WKY) at 6 months of age were used. Serotonin (5-HT) and angiotensin II induced contractions in both arteries. Noradrenaline (NA) did only the relaxation. Phenylephrine did not contraction or relaxation. The contractions by angiotensin II and the relaxations by NA were not different between SHRSP and WKY in both arteries. The contractions by 5-HT at lower doses in both arteries were greater in SHRSP than in WKY. The 5-HT-induced contractions were inhibited by 5-HT_1 and 5-HT_2 antagonist. Although the effects of 5-HT_2 agonist were not different between SHRSP and WKY, the effects of 5-HT_1 agonist were greater in basilar and coronary arteries of SHRSP than in those of WKY. These results suggest the followings: (1) There is no alpha receptor in both arteries. (2) There exist 5-HT_1 and 5-HT_2 receptors in both arteries. (3) In the basilar and coronary arteries of SHRSP, 5-HT induced contractions accelerates, which is due to the increased responses to 5-HT_1 receptor.