

Involvement of cholinergic system in the induction of some early genes in hippocampal cells after stress depends on the novelty of stress context

Dobryakova Y.V.*, Deryabina A.K., Fedulova A.A., Koryagina A.A., Bolshakov A.P.

Institute of Higher Nervous Activity and Neurophysiology, RAS, Moscow, Russia

* julkadobr@gmail.com

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Motivation and Aim: The stress response is a universal response of the body to various changes in the external environment. The stress response includes many components, among which are nonspecific components such as the activation of the sympatho-adrenal axis and the hypothalamic-pituitary-adrenal axis, As well as specific components that involve the activation of various brain regions and signaling systems depending on the characteristics of the stressor. Changes in the expression of a number of genes are often considered as a result of the activation of cells in a particular brain region, including early genes such as *egr1*, *fos*, *npas4*, and others. The induction of early gene expression is a complex process, and the involvement of various signaling systems in the induction of diverse genes remains a poorly researched area.

Studies have shown that stress activates various signaling systems in the brain, including the noradrenergic, serotonergic, cholinergic, and other systems. It has been demonstrated that the expression of a number of early genes depends on the release of noradrenaline. The involvement of the cholinergic system in regulating the transcriptional response during the development of the stress response remains virtually unexplored, so the aim of our work was to analyze the involvement of metabotropic muscarinic receptors in the regulation of gene transcription in the acute period after brief unavoidable swimming stress.

Methods and Algorithms: Our study included two series. In the first series, Wistar rats were handled and then subjected to unavoidable swimming stress in a cylinder for the Porsolt test for 15 minutes. This series included 4 groups of animals. (1) Control animals injected with saline; (2) control animals injected with scopolamine (antagonist of muscarinic receptors); (3) animals injected with saline and then subjected to swimming; (4) animals injected with scopolamine and then subjected to swimming. Each group contained 7–8 animals.

In second series, Wistar rats were handled and then, for 4 days, daily were subjected to swimming stress for 5 min. On the fifth day, some animals were subjected to swimming for 15 min as in the first series. The animal groups in this series were as follows: (1) intact animals not subjected to training for 4 days; (2) control animals injected with saline on the fifth day; (3) animals injected with scopolamine on the fifth day; (4) animals injected with saline and then to swimming on the fifth day; (5) animals injected with scopolamine and then to swimming on the fifth day.

In both series, the animals were decapitated 45 min after the onset of stress, the brain was extracted, and the dorsal and ventral hippocampi were isolated for subsequent analysis of gene expression using quantitative PCR.

Results: We found that, in the first series of experiments, swimming induced an increase in the expression of fos and npas4 genes in both hippocampal parts and egr1 only in the ventral hippocampus. Scopolamine suppressed stress-induced increase in the expression of npas4 and egr1 but not fos gene.

In the second series of experiments, stress caused by swimming on the fifth day also induced an increase in fos expression in both hippocampal parts and an increase in egr1 expression in the ventral hippocampus. Like in the first series, scopolamine did not affect fos expression after stress; however, in contrast to the first series, scopolamine has no effect on egr1 expression in the ventral hippocampus.

Conclusion: The acute unavoidable stress induces expression of early genes in both dorsal and ventral hippocampi; however, inhibition muscarinic receptors suppressed stress-induced changes in the gene expression only in the case of presentation of novel stress context. Presumably, involvement of cholinergic system in the induction of stress-associated changes in the gene expression is determined by novelty of stress context.

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