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EFFECT OF NOS INHIBITOR ON FORCED SWIM TEST AND NEUROTRANSMITTERS TURNOVER IN THE MOUSE BRAIN

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The previous experiments have demonstrated that NMDA receptor antagonists and nitric oxide synthase (NOS) inhibitors have antidepressant- and anxiolytic-like activities in rodents. Moreover, chronic treatments with these agents result in down-regulation of β-adrenoceptors in the brain cortex with a magnitude comparable to clinically effective antidepressants. However, still little is known about the effect of NOS inhibitors on the regulation of neurotransmitter utilization *in vivo*. The aim of present study was to elucidate the effect of NOS inhibitor at doses active in forced swim test (FST) on dopamine and serotonin turnover in the mouse brain structures. Mice were treated with imipramine (15 mg/kg *ip*), electroconvulsive shock (ECS) and NOS inhibitor, N^G-nitro-L-arginine (L-NA) acutely (at doses of 1, 3, 10 mg/kg *ip*) and chronically (0.3, 1, 3 mg/kg *ip*). Experiments were carried out 1 h after single and 3 h after chronic (21 days) administration. Metabolism of dopamine and serotonin was investigated using high pressure liquid chromatography (HPLC) with electrochemical detection. The metabolism rate was calculated as a ratio of a metabolite to the parent amine. FST was performed using protocol described previously by Porsolt et al. Now we report that L-NA decreases the level of immobility with potency similar to imipramine. The effect of L-NA was reversed by NOS substrate, L-arginine. L-NA given acutely at doses active in FST did not change the dopamine metabolism rate but it did decrease the serotonin turnover rate in the frontal cortex in a manner similar to imipramine. Thus, it appears that under basal conditions endogenous NO may influence the serotonin turnover, and the acute inhibition of NOS can mimic the effect of imipramine what may result in the antidepressant-like effect in FST. Imipramine given acutely produced massive increase in the level of serotonin in the frontal cortex as well as in the hypothalamus (by 40%, $p < 0.01$) what was reflected in significant decreases in the metabolism rate. Contrary to acute effect, chronic treatment of L-NA (the most effective dose was 1 mg/kg) produced increase in the dopamine metabolism rate within all investigated structures. In the present study, we demonstrated for the first time that L-NA may alter the neurotransmitter utilization *in vivo* and the observed effect may be due to adaptational changes in neuronal function.

Key words*: mice, forced swim test, dopamine, serotonin, N^G-nitro-L-arginine, L-arginine, imipramine, ECS, frontal cortex, hypothalamus, striatum*

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