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Mechanisms of prenatal effects of caffeine in rats: role of nitric oxide

Key words: caffeine, nitric oxide, neurophysiological prenatal effects

Caffeine is the most widely consumed psychoactive compound worldwide. It is mostly found in coffee, tea, energizing drinks and in some drugs. In recent years, caffeinated energy drinks are increasingly popular among adolescents. The number of women, who use psychotropic substances during pregnancy, including caffeine, also increases from year to year. It was showed that the prenatal effect of psychostimulants could lead to a delay in development and behavioral disorders in their offspring [3]. However, mechanisms by which caffeine could influence the brain development are still not well established. It was found that ability to bind to adenosine receptors of the brain plays a key role in the neurochemical mechanisms of the stimulating effect of caffeine [2]. At the same time, its possible interaction with other neurotransmitter systems has not been studied enough. Results of our group and other have led to hypothesis that neurophysiological effects of psychostimulant drugs are mediated by free radicals [1]. The aim of the work was to investigate a role of neuronal messenger nitric oxide (NO) in the neurophysiological prenatal effects of caffeine.

Experiments were performed using male Wistar rats, originating from pregnant female rats. Pregnant dams received solution of caffeine (1g/L) or water as the sole source of fluid during all their gestation period. NO content in brain structures was determined using the direct quantitative method of electron paramagnetic resonance. No major difference in physiological characteristics of juvenile male rats admitted prenatally by caffeine or water was observed. In the first four postnatal days NO generation in the brain of rats of both studied groups was significantly reduced in comparison with the values of NO in the brain of adult rats. However, NO content was lower in the brain of juvenile male rats received caffeine on postnatal day 2 and 3 but not 4, as compared with control animals. It was found that prolonged intake of caffeine by female rats during pregnancy led to increase in locomotor activity, as well as hypoalgesia in their offspring at the age of 1 month. Preliminary administration of NO synthase inhibitor induced analgesic and anxiolytic effects in rats treated prenatally, both caffeine and water. It was shown that rats from mothers who received caffeine during pregnancy found the underwater platform in the water maze faster than control group. This fact might indicate that the spatial memory of the experimental group is better developing than in the control group of animals. It was found that the administration of inhibitor of NO-synthase before the first training session in the water maze significantly increased the latency period in both studied groups of animals. Although, it should be noted that rats treated with NO-synthase inhibitors and caffeine reached the platform more quickly than those received prenatally water. It was found that NO content

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in rat hippocampus was significantly increased in the group of rats receiving prenatal caffeine compared to the control rats before testing in the water-maze. Preliminary administration of NO-synthase inhibitor has led to significant decrease in NO generation in the hippocampus of rat treated by caffeine and water prenatally. In summary, we can conclude that the nitrergic system of the brain is involved in prenatal effects of caffeine in rats.

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