In vivo effects of CB₁ receptor ligands on lipid peroxidation and antioxidant defense systems in the brain of healthy and ethanol-treated rats

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Abstract
In vivo experiments were conducted to study the effects of N-(piperidin-1-yl)-5-(4-chlorophenyl)-1-(2,4-cochlorophenyl)-4-methyl-1H-pyrazole-3-carboxamide (SR141716A; a potent and selective CB₁-receptor antagonist) and arachidonyl-2-chloroethylamide (ACEA; a selective CB₁-receptor agonist) on spontaneous lipid peroxidation, glutathione (GSH) level and activities of antioxidant enzymes in rat tissues. Single doses of SR141716A (3 mg/kg, ip) and ACEA (10 mg/kg, ip) had no effect on all indices, studied in the brain, except for a decrease in GSH level by 10 mg/kg of SR141716A. The effects of repeated administration of the CB₁-receptor ligands (3 mg/kg, ip, once daily for 2 days) on the above indices in the brain and liver of control and ethanol-treated animals were also studied. Two weeks after ethanol exposure, the rats lost weight (by 41%), which correlated with their decreased water and food consumption (by 52% and 33%, respectively). The time of ethanol action was not sufficient to change the biochemical parameters in the brain, except for the lipid peroxidation. However, a decrease in GSH level and superoxide dismutase activity, as well as an increase in lipid peroxidation and glucose-6-phosphate dehydrogenase activity were registered in the liver. The repeated administration of CB₁ receptor ligands restored some of ethanol-induced changes. The present results suggested lack of pro-oxidant activity and potential antioxidant ability of the studied CB₁ receptor ligands, which might contribute to their beneficial effects.

Key words:
SR141716A, lipid peroxidation, GSH-level, antioxidant enzymes