Long-lasting alterations of hippocampal GABAergic neurotransmission in adult rats following perinatal Δ9-THC exposure.

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Abstract

The long-lasting effects of gestational cannabinoids exposure on the adult brain of the offspring are still controversial. It has already been shown that pre- or perinatal cannabinoids exposure induces learning and memory disruption in rat adult offspring, associated with permanent alterations of cortical glutamatergic neurotransmission and cognitive deficits. In the present study, the risk of long-term consequences induced by perinatal exposure to cannabinoids on rat hippocampal GABAergic system of the offspring, has been explored. To this purpose, pregnant rats were treated daily with Delta⁹-tetrahydrocannabinol (Δ⁹-THC; 5mg/kg) or its vehicle. Perinatal exposure to Δ⁹-THC induced a significant reduction (p<0.05) in basal and K⁺-evoked [³H]-GABA outflow of 90-day-old rat hippocampal slices. These effects were associated with a reduction of hippocampal [³H]-GABA uptake compared to vehicle exposed group. Perinatal exposure to Δ⁹-THC induced a significant reduction of CB1 receptor binding (B_max) in the hippocampus of 90-day-old rats. However, a pharmacological challenge with either Δ⁹-THC (0.1μM) or WIN55,212-2 (2μM), similarly reduced K⁺-evoked [³H]-GABA outflow in both experimental groups. These reductions were significantly blocked by adding the selective CB1 receptor antagonist SR141716A. These findings suggest that maternal exposure to cannabinoids induces long-term alterations of hippocampal GABAergic system. Interestingly, previous behavioral studies demonstrated that, under the same experimental conditions as in the present study, perinatal cannabinoids exposure induced cognitive impairments in adult rats, thus resembling some effects observed in humans. Although it is difficult and sometimes misleading to extrapolate findings obtained from animal models to humans, the possibility that an alteration of hippocampus aminoacidergic transmission might underlie, at least in part, some of the cognitive deficits affecting the offspring of marijuana users, is supported.

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KEYWORDS:

CB1 receptor binding; GABA outflow; Maternal marijuana consumption; SR141716A; Slices; WIN55,212-2

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