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Animals with a schizophrenia-like phenotype are differentially sensitive to the motivational effects of cannabinoid agonists in conditioned place preference.

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Abstract

Cannabis is the most consumed illicit drug worldwide, but among patients with a diagnosis of schizophrenia, this consumption is higher suggesting that they are differentially sensitive to cannabis. We chose to study this problematic using a neurodevelopmental model of schizophrenia: neonatal ventral hippocampus lesions (NVHL). In a first study, we compared the locomotor response to novelty, a mild stress and two doses of amphetamine (0.75 and 1.5 mg/kg) in sham and NVHL rats at post-natal day 35 (PD35) or 56 (PD56). In a second study, we investigated the valence of the motivational effect of Delta-9-tetrahydrocannabinnol (THC, 0.5 mg/kg, i.p.) and the cannabinoid receptor agonist, WIN55,212-2 (WIN, 1 mg/kg, i.p.), using the conditioned place preference paradigm; we used a biased procedure that comprised 12 days of testing with 3 paired-conditioning. The effects of this dose of WIN were also measured on locomotor activity. Results confirmed that the adult NVHL animals displayed a stronger locomotor response to the two doses of amphetamine, but not to novelty and a mild stress. In adult NVHL, but not sham animals, WIN stimulated locomotor activity and produced a conditioned place aversion. At the dose tested, THC tended to produce an aversion in adult sham but not NVHL animals. Taken together these findings show that adult animals with a schizophrenia-like phenotype are differentially sensitive to the motivational effect of cannabinoids.

KEYWORDS: Amphetamine; Cannabinoid; Conditioned place preference; Neonatal ventral hippocampus lesion; Schizophrenia

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