CHRONIC TREATMENT WITH THC DURING ADOLESCENCE INDUCES LONG LASTING NEUROBIOLOGICAL CHANGES IN ADULTHOOD: BEHAVIORAL AND NEUROCHEMICAL CORRELATES

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There are little and often contradictory studies on the long-term neurobiological consequences of cannabinoid consumption in adolescents. The endocannabinoid system plays an important role during the different development stages of the brain as cannabinoids modulate the release and the action of different neurotransmitter and promote neurogenesis.
This work studied the long-term consequences of adolescent assumption of delta-9 tetrahydrocannabinol (THC) on mood and cognitive parameters, through behavioural and neurochemical assays. Adolescent male and female rats (35-45 PND) have been treated with increasing doses of THC for 11 days and left undisturbed until their adulthood (75 PND) when the behavioural and neurochemical assays were performed.
Adolescence THC exposure produced different effects on male and female rats in adulthood. CB1 receptor level and functionality were significantly reduced in the amygdala, ventral tegmental area and nucleus accumbens (NAc) of female rats whereas in males significant alterations were determined in the amygdala and hippocampus. Neither female nor male rats showed alteration in anxiety responses (elevated plus maze and open field tests) but a significant "behavioural despair" (forced swim test) paralleled by anhedonia (sucrose preference) was present in females. In contrast, male rats did not present behavioural despair but exhibited anhedonia. This different behavioural picture was supported by biochemical parameters of depression, namely CREB alteration. In fact female rats exhibited decreased CREB activity in the hippocampus and prefrontal cortex and increased CREB activity in the NAc paralleled by increased dynorphin expression.
Finally adolescence exposure to THC did not alter short term memory but reduced spatial memory (radial maze) in both genders. In contrast long term memory (passive avoidance) was impaired only in males. In line with this picture, altered synaptic markers were found in the prefrontal cortex and hippocampus of pre-treated rats.
The present results suggest that cannabis consumption during adolescence may induce long term behavioural effects coupled with stable alteration in neurochemical marker and synaptic plasticity.

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