ALTERED NEUROGENESIS OF HIPPOCAMPAL NEURONS IS ASSOCIATED TO NEUROFUNCTIONAL DEFICITS OBSERVED IN ADULT RATS PRENATALLY EXPOSED TO CANNABINOIDS

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Marijuana is the most widely used illegal drug among women at reproductive age. Reports dealing with the effects of prenatal exposure to this substance of abuse are still controversial.
We have recently shown that subtle neurofunctional alterations can be observed in the offspring of rats exposed to the synthetic CB1 agonist WIN 55,212-2 (WIN) (0.5mg/kg) during pregnancy (1,2). The dose used is equivalent to a moderate or low exposure to marijuana in humans and has no overt toxic effects. WIN treatment with did not affect, indeed, gestational and reproduction parameters and WIN-exposed pups did not show any malformation or sign of malnutrition. However, a deeper investigation revealed that prenatal treatment with WIN altered pup performance in homing behavior and produced a decrease in the rate of separation-induced ultrasonic vocalizations. Behavioral deficits resulted long-lasting, since prenatal WIN exposure caused a disruption of memory retention in both young and adult offspring subjected either to a passive or an active avoidance task.
Cannabinoids have been shown to stimulate neural progenitor proliferation and regulate neuritogenesis, axonal growth and synaptogenesis (3). In agreement with these observations, we found an altered dendritic morphology of hippocampal CA1 pyramids was detected in young rats prenatally exposed to WIN. In particular, prenatally WIN-exposed rats exibited a significant increase in estimated total dendritic length and a highly significant increase in branching in the middle-third of the dendritic tree. These findings suggest that moderate exposure to cannabinoids during crucial periods of brain development can cause dysmorphic maturation of the hippocampus. Such subtle morphological alterations would be, in turn, a factor underlying the behavioral deficits observed both in early and late postnatal life.

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