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Neuropharmacology. 2019 Mar 1;146:212-221. doi: 10.1016/j.neuropharm.2018.11.035. Epub 2018 Nov 26.

Peripubertal cannabidiol treatment rescues behavioral and neurochemical abnormalities in the MAM model of schizophrenia.

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Abstract

In agreement with the neurodevelopmental hypothesis of schizophrenia, prenatal exposure of rats to the antimetabolic agent methylazoxymethanol acetate (MAM) at gestational day 17 produced long-lasting behavioral alterations such as social withdrawal and cognitive impairment in the social interaction test and in the novel object recognition test, respectively. At the molecular level, an increased cannabinoid receptor type-1 (CB1) mRNA and protein expression, which might be due to reduction in DNA methylation at the gene promoter in the prefrontal cortex (PFC), coincided with deficits in the social interaction test and in the novel object recognition test in MAM rats. Both the schizophrenia-like phenotype and altered transcriptional regulation of CB1 receptors were reversed by peripubertal treatment (from PND 19 to PND 39) with the non-psychotropic phytocannabinoid cannabidiol (30 mg/kg/day), or, in part, by treatment with the cannabinoid CB1 receptor antagonist/inverse agonist AM251 (0.5 mg/kg/day), but not with haloperidol (0.6 mg/kg/day). These results suggest that early treatment with cannabidiol may prevent both the appearance of schizophrenia-like deficits as well as CB1 alterations in the PFC at adulthood, supporting that peripubertal cannabidiol treatment might be protective against MAM insult.

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KEYWORDS: Cannabidiol; Cannabinoid CB1 receptor; MAM model; Schizophrenia

PMID: 30496751 DOI: [10.1016/j.neuropharm.2018.11.035](https://doi.org/10.1016/j.neuropharm.2018.11.035)

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