

# Chronic cannabinoid exposure during adolescence leads to long-term structural and functional changes in the prefrontal cortex

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## Abstract

In many species, adolescence is a critical phase in which the endocannabinoid system can regulate the maturation of important neuronal networks that underlie cognitive function. Therefore, adolescents may be more susceptible to the neural consequences of chronic cannabis abuse. We reported previously that chronically exposing adolescent rats to the synthetic cannabinoid agonist CP55,940 leads to impaired performances in adulthood i.e. long-lasting deficits in both visual and spatial short-term working memories. Here, we examined the synaptic structure and function in the prefrontal cortex (PFC) of adult rats that were chronically treated with CP55,940 during adolescence. We found that chronic cannabinoid exposure during adolescence induces long-lasting changes, including (1) significantly altered dendritic arborization of pyramidal neurons in layer II/III in the medial PFC (2) impaired hippocampal input-induced synaptic plasticity in the PFC and (3) significant changes in the expression of PSD95 (but not synaptophysin or VGLUT3) in the medial PFC. These changes in synaptic structure and function in the PFC provide key insight into the structural, functional and molecular underpinnings of long-term cognitive deficits induced by adolescent cannabinoid exposure. They suggest that cannabinoids may impede the structural maturation of neuronal circuits in the PFC, thus leading to impaired cognitive function in adulthood.

## Keywords:

Cannabinoid, Adolescence, Prefrontal structure, Dendrites, Synaptic plasticity, Synaptic markers

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