Original Article

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Adolescent Rats Find Repeated Δ9-THC Less Aversive Than Adult Rats but Display Greater Residual Cognitive Deficits and Changes in Hippocampal Protein Expression Following Exposure

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Abstract

The current study examined whether adolescent rats are more vulnerable than adult rats to the lasting adverse effects of cannabinoid exposure on brain and behavior. Male Wistar rats were repeatedly exposed to Δ-9-tetrahydrocannabinol (Δ9-THC, 5 mg/kg i.p.) in a place-conditioning paradigm during either the adolescent (post-natal day 28+) or adult (post-natal day 60+) developmental stages. Adult rats avoided a Δ9-THC-paired environment after either four or eight pairings and this avoidance persisted for at least 16 days following the final Δ9-THC injection. In contrast, adolescent rats showed no significant place aversion. Adult Δ9-THC-treated rats produced more vocalizations than adolescent rats when handled during

the intoxicated state, also suggesting greater drug-induced aversion. After a 10–15 day washout, both adult and adolescent Δ9-THC pretreated rats showed decreased social interaction, while only Δ9-THC pretreated adolescent rats showed significantly impaired object recognition memory. Seventeen days following their last Δ9-THC injection, rats were euthanased and hippocampal tissue processed using two-dimensional gel electrophoresis proteomics. There was no evidence of residual Δ9-THC being present in blood at this time. Proteomic analysis uncovered 27 proteins, many involved in regulating oxidative stress/mitochondrial functioning and cytoarchitecture, which were differentially expressed in adolescent Δ9-THC pretreated rats relative to adolescent controls. In adults, only 10 hippocampal proteins were differentially expressed in Δ9-THC compared to vehicle-pretreated controls. Overall these findings suggest that adolescent rats find repeated Δ9-THC exposure less aversive than adults, but that cannabinoid exposure causes greater lasting memory deficits and hippocampal alterations in adolescent than adult rats.

Keywords: adolescent, hippocampus, memory, aversion, cannabinoid, proteomics

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