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**Title:** The effect of chronic THC exposure on cocaine self-administration in adolescent rats

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Individuals between the ages of 12 and 25 with a history of marijuana use were estimated to be 15 times more likely to abuse cocaine than those without (Wagner and Anthony, 2002). The psychoactive constituent  $\Delta^9$ -tetrahydrocannabinol (THC) that is found in marijuana activates the mesolimbic dopamine (DA) system by increasing DA in the nucleus accumbens (NAc; Gardner, 2005). Cocaine has been shown to activate the same DA pathway (Ferrari et al 1999, Arnold et al 1998). Previously it has been shown that rats treated twice daily with THC (5mg/kg, i.p.) for 2 weeks, resulted in a 44% increase in the firing rate of DA neurons in the ventral tegmental area. This area is well described as involved in the brain reward circuit (Wu and French, 2000). The present study investigated the hypothesis that chronic exposure to THC would impact the reward circuit in a manner that would change cocaine self-administration behavior. We used three groups of 4 week old Sprague Dawley rats treated i.p. daily for 3 weeks with either: 1) vehicle (saline), 2) low dose of THC (0.75 mg/kg) or 3) high dose of THC (2 mg/kg). Following this, all rats were trained to self-administer food (45 mg pellets) under a Fixed Ratio 1 (FR1) schedule in operant conditioning chambers. Once rats achieved a stable lever-pressing criteria they were implanted with a jugular vein catheter and started on daily cocaine self-administration sessions (90 minutes/day) for 15 days. For the first 8 days animals were presented with a 0.75 mg/kg/infusion of cocaine. During the last 7 days and for the purpose of looking at the sensitivity in the dose response rate for all treatment groups, the dose was halved to a 0.375 mg/kg/infusion of cocaine. These findings will help gain insight into the potential impact of early cannabinoid exposure on later risk for cocaine seeking and self-administration behavior.

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