Chronic THC exposure during adolescence increases stress-induced reinstatement of heroin seeking-behaviour in adulthood: a preclinical study

S. Stopponi[1], L. Soverchia[1], M. Ubaldi[1], G. de Guglielmo[1], G. Serpelloni[2], R. Ciccocioppo[1]

[1]School of Pharmacy (Pharmacology Unit)., University of Camerino, Camerino Italy
[2]Dipartimento Politiche Antidroga, Presidenza del Consiglio dei Ministri

The developing brain of adolescents is particularly vulnerable to exposure to drugs of abuse. Cannabis derivatives are considered the mostly widely used illicit substances among adolescents and its exposure in the early stage of life may increase the vulnerability to neuropsychiatric disorders. While the addictive potential of delta-9-tetrahydrocannabinol (THC), the major active ingredient of cannabis has been well documented less is known about the consequence of THC exposure during adolescence on the development of addiction in adulthood. The aim of this study is to investigate the long term effects of delta-9-tetrahydrocannabinol exposure during adolescence on subsequent vulnerability to develop heroin addictive behaviors in adulthood. Adolescent male rats from postnatal day (PND) 35 to PND-46 were treated with increasing daily doses of THC (2.5-10 mg/kg). One week after intoxication, the rats were tested for anxiety-like behavior in the elevated plus maze (EPM) test. One month later (starting from PND 75), rats were trained to self-administer heroin intravenously. Acquisition and maintenance of heroin-related operant responding were assessed. Finally, following extinction phase, reinstatement of lever pressing elicited by the pharmacological stressor, yohimbine (1.25 mg/kg) was evaluated. Results revealed that in comparison to controls, animals treated with chronic THC during adolescence showed a higher level of anxiety-like behavior. When tested for heroin self-administration (20 µg per infusion) no differences in either the acquisition of operant responding or in heroin intake at baseline were observed. Noteworthy, following extinction phase, administration of yohimbine elicited a significantly higher level of heroin seeking in rats previously exposed to THC. Altogether these findings demonstrate that chronic exposure to THC during adolescence is responsible for heightened anxiety and increased vulnerability to drug relapse in adulthood.