Preclinical study of therapeutic potential of cannabidiol on cocaine and caffeine-induced sensitization and neuroinflammation in mice

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Cannabidiol (CBD), a non-psychotomimetic cannabinoid from the plant *Cannabis sativa*, has been proposed as a potential candidate for the treatment of cocaine use disorders; however contradictory data exist. Our previous studies, have shown that street-seized smoked cocaine samples were frequently adulterated with caffeine. We demonstrated that caffeine accelerates and enhances the cocaine-induced locomotor sensitization in rodents. Pretreatment of CBD attenuated this effect, supporting its therapeutic potential. It is well-known that the expression of psychostimulant-induced locomotor sensitization is associated with neuroinflammatory processes, involving the microglial reactivity. Regarding the CBD anti-inflammatory property, we hypothesized that CBD prevents the cocaine and caffeine-induced neuroinflammatory process and helps to attenuate the sensitization. Male adult mice were treated with CBD (20 mg/kg/i.p.) and CocCaf (5:2.5 mg/kg) or its respective vehicles for 5 days. Locomotor activity was recorded in an open field by the video-tracking software EthoVision XT 17.0. Microglial reactivity in the nucleus accumbens (NAc) was evaluated by anti-Iba1 immunofluorescence (microglial marker). As expected, CocCaf-induced locomotor sensitization was accompanied by an increase in Iba-1 immunoreactivity in the NAc. However, CBD did not attenuate the behavioral effects. It remains to be tested whether CBD attenuates the neuroinflammation associated with behavioral sensitization.

Key words: Cannabidiol, Cocaine, caffeine, sensitization, drug-addiction