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Title: Dopamine D2R assessment during cocaine self-administration maintenance, extinction, and abstinence

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Dopamine D2-like receptors are known to be especially important in mediating the abuse-related effects of cocaine and there appears to be an inverse relationship between D2R availability and vulnerability to the reinforcing effects of cocaine. (Volkow et al, 1993; Caine et al, 2002; Nader & Czoty, 2005). It has been previously shown that D2R decrease after chronic cocaine abuse in humans (Volkow et al, 1997). Chronic cocaine exposure in primates produces decreases in D2R binding, which may contribute to further drug use (Nader and Czoty, 2005). Environmental variables can alter D2R binding, and the resulting changes in D2R function can impact the vulnerability to cocaine abuse.

The aim of this study was to evaluate the time-course changes of D2R in c57 mice with a different history of cocaine self-administration, using in vitro digital β-imager autoradiography (ARG). 4 week old male mice were trained, in operant chambers equipped with two levers, to self-administer cocaine (1 mg/kg/infusion) under FR1 schedule of reinforcement and 11 different groups were examined: (1) Sham, (2) 2d of cocaine self-administration (SA), (3) 10d of cocaine SA, (4) 15d of cocaine SA, (5) 15d of cocaine SA + 7d extinction, (6) 15d of cocaine SA + 40d of extinction, (7) 15d cocaine SA + 7d extinction without cues, (8) 15d cocaine SA + 40d extinction without cues, (9) 15d cocaine SA + 7d abstinence, (10) 15d cocaine SA+ 40d abstinence and (11) 15d cocaine SA + with and without cues + cue induced relapse. Only mice that achieved the acquisition criteria (80% of stable responses during 3 consecutive days, 75% of discrimination between the active and the inactive lever and a minimum of 5 infusions per session) were included in the study. After the behavior experiment, animals were sacrificed their brains were harvested and sectioned for ARG. Sections were washed for endogenous dopamine and incubated in the D2R ligand [^{3}H] spiperone. ARG qualitative and quantitative analysis will be reported in terms of specific / non specific binding and the cerebellum will be used for non-specific binding as it is deficient in D2R.

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