Addictive-like behaviour for Acetaldehyde: involvement of D2 receptors

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Acetaldehyde (ACD), ethanol's first metabolite, is centrally active and shows rewarding and motivational properties. It is able to activate mesolimbic dopamine system, since it enhances neuronal firing of dopamine cells in ventral tegmental area and exerts dopamine release in the nucleus accumbens (Foddai et al., 2004; Melis et al., 2007; Deehan et al., 2013). ACD motivational properties are demonstrated by self-administration studies in rodents (Rodd et al., 2005), particularly behavioural evidence suggests that ACD could produce positive reinforcing effects in operant-conflict paradigms (Cacace et al., 2012).
In order to shed light on neurobiological substrate underpinning ACD-related behaviours, the present study aims at investigating D2-receptor role in the different phases of an operant self-administration paradigm, able to mirror core feature of addictive phenotype.
Male Wistar rats underwent ACD (3.2%) oral self-administration, in an operant paradigm which includes Training, Extinction, and repeated cycle of forced abstinence and relapse, as a simple reinstatement model.
The effect of two different D2-receptor agonists was evaluated. Quinpirole (0.03 mg/kg, i.p.) was administered during Extinction and Relapse phases. Ropinirole (0.03; 0.05 mg/kg, i.p.) was injected daily during abstinence.
Our results show that ACD is able to induce and maintain a drug-taking behaviour, which involves D2-receptor neurotransmission. In particular, Quinpirole administration can decrease the number of lever presses for ACD during Extinction and Relapse phases; Ropinirole daily administration during abstinence, at both dosages, is able to reduce the number of lever presses and ACD intake in the relapse phase. ACD has its own motivational properties, which involve dopamine neurotransmission. Activation of D2-autoreceptors by Quinpirole negatively affects operant behaviour for ACD, likely decreasing ACD-induced dopamine release. The activation of post-synaptical D2-receptor, by Ropinirole treatment during abstinence, could restore dopaminergic tone during withdrawal, leading to a decrease in the motivation to subsequent relapse. These data further strengthen the evidence that ACD may play a crucial role in ethanol's central effects.

Foddai et al. (2004). Neuropsychopharmacology 29:530–536.
Melis et al. (2007). European Journal of Neuroscience 26: 2824–2833
Deehan et al. (2013) Alcohol Clin Exp Res. 37(5):722-9.
Rodd et al. (2005). Neuropsychopharmacology 30:330–338.
Cacace et al. (2012). Alcohol Clin Exp Res. 36(7):1278-87.