The neurobiology of tobacco dependence: a preclinical perspective on the role of the dopamine projections to the nucleus accumbens [corrected].

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Erratum in

Abstract

It is now widely accepted that nicotine is the primary addictive component of tobacco smoke and that a majority of habitual smokers find it difficult to quit smoking because of their dependence upon this component of the smoke. However, although nicotine replacement therapy elicits a clinically valuable and significant improvement in the number of quit attempts that are ultimately successful, its efficacy remains disappointingly low. This review considers some of the reasons for this problem. It focuses on the hypothesis that stimulation of the dopamine (DA) projections to the medial shell and the core of the nucleus accumbens play complementary roles in the development of nicotine dependence. The hypothesis proposes that increased extra-synaptic DA in the medial shell of the accumbens confers hedonic properties on behaviors, such as smoking, which deliver nicotine, and thereby increase the probability that the response is learned. It also summarizes the evidence that the primary role of the increased DA overflow, observed in the accumbal core of nicotine-pretreated individuals, challenged with nicotine, is the attribution of incentive salience to cues associated with delivery of the drug and the transition to Pavlovian responding to these conditioned stimuli. The review argues that sensitization of the DA projections to the accumbal core, and the behaviors that depend upon this process, play a pivotal role in the maintenance of the tobacco smoking habit and that it is this component of the dependence that is inadequately addressed by nicotine replacement therapy.