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Long-term Neurochemical Effects of Adolescent Nicotine Self-administration on Dopamine Dynamics in the Nucleus Accumbens Core

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Adolescence is a transitional period characterized by changes in reward seeking, novelty seeking, and risk taking. While these behavioral changes are necessary for the transition to adulthood, they also increase the risk of developing a range of psychiatric disorders, including substance use disorders. Smoking in adolescence is a strong predictor of perpetuated nicotine use that can lead to long-term modifications of the dopamine system in adulthood. Acetylcholine (ACh) from local cholinergic interneurons (CINs) is a potent modulator of dopamine (DA) release in the nucleus accumbens (NAc) core via nicotinic acetylcholine receptors (nAChRs) on DA varicosities. However, it is unclear the mechanistic role that CIN ACh plays during the transitioning period of the mesolimbic DA system both in naïve animals, and following nicotine exposure in adolescence. Here, we utilized ex vivo fast scan cyclic voltammetry (FSCV) in a rat model of adult and adolescent nicotine (0.03mg/kg/infusion) or saline self-administration (SA) to examine the long-term differences in regulation of NAc DA release in adulthood. We found that adolescent rats self-administer similar levels of nicotine as adult rats. Importantly, adolescent SA of either saline or nicotine, but not adult nicotine SA, decreased DA release as compared to adult saline SA. FSCV was performed in adulthood for all groups, suggesting this effect is due to adolescent exposure to nicotine and not age-related differences in testing. Moreover, α-conotoxin, an α6 nAChR subunit selective antagonist, decreased DA release in rats exposed to adolescent nicotine SA as compared to adult nicotine and saline controls. Further blockade of β2-containing nAChRs revealed an additive decrease in NAc DA release in adolescent nicotine SA rats as compared to adult nicotine and saline controls. This work provides a potential mechanistic avenue for greater nAChR control over NAc DA release in adolescence involving α6β2-containing nAChRs which, in turn, may provide a therapeutic target or potential biomarker for brain related changes that lead to smoking relapse and vulnerability to greater motivation for intake of other drugs of abuse.

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