Adolescent nicotine treatment changes the response of acetylcholine systems to subsequent nicotine administration in adulthood.

Slotkin TA, Bodwell BE, Ryde IT, Seidler FJ.

Author information

1Department of Pharmacology and Cancer Biology, Duke University Medical Center, Durham, NC 27710, USA. t.slotkin@duke.edu

Abstract

Nicotine alters the developmental trajectory of acetylcholine (ACh) systems in the immature brain, with vulnerability extending from fetal stages through adolescence. We administered nicotine to adolescent rats (postnatal days PN30-47) and then examined the subsequent response to nicotine given in adulthood (PN90-107), simulating plasma levels in smokers, and performing evaluations during nicotine treatment (PN105) and withdrawal (PN110, PN120 and PN130), as well as assessing persistent changes at 6 months of age (PN180). We measured nicotinic acetylcholine receptor (nAChR) binding, choline acetyltransferase (ChAT) activity, a marker for ACh terminals, and hemicholinium-3 (HC3) binding to the choline transporter, an index of ACh presynaptic activity. By itself, adolescent nicotine exposure evoked sex-selective deficits in cerebrocortical HC3 binding while elevating ChAT in young adulthood in striatum and midbrain. Nicotine given in adulthood produced profound nAChR upregulation lasting 2 weeks after discontinuing treatment, and decrements in cerebrocortical and striatal HC3 binding emerged during withdrawal, indicative of reduced ACh synaptic activity. For all three parameters, adolescent nicotine altered the responses to nicotine given in adulthood, producing both sensitization and desensitization that depended on sex and brain region, effects that parallel the disparate behavioral outcomes reported for these treatments. The interaction seen here for the impact of adolescent nicotine exposure on adult nicotine responses was substantially greater than that found previously for the effects of prenatal nicotine exposure on adult responses. Our findings thus reinforce the importance of adolescence as a critical period in which the future responsiveness to nicotine is programmed.