Effects of Nicotine Exposure During Adolescence on Adult Cognition, Dendritic Morphology, and Epigenome

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Early adolescent smoking is associated with working memory deficits, and late adolescent smokers exhibit cognitive deficits that emerge after initiation of smoking. Here, we present findings across multiple studies using a mouse model of adolescent nicotine exposure, for which C57BL/6 mice receive a chronic exposure to nicotine in adolescence via osmotic minipump (12.6 mg/kg/day, freebase) and are tested in hippocampus-dependent learning tasks in adulthood. Overall, we have found that chronic nicotine exposure in adolescence is associated with impairments in contextual fear learning and accompanying reduced dendritic length in the hippocampus. The changes observed with adolescent nicotine exposure were not observed with adult exposure. Additionally, we found that chronic adolescent nicotine exposure leads to differential gene methylation patterns in the adult hippocampus that may be related to learning impairments and changes in dendritic morphology. PANTHER (GO-Ontology) analysis identified over-represented functional gene categories in 453 differentially methylated genes. Chromatin remodeling genes showed the highest enrichment of the differentially methylated genes identified. Finally, we present findings suggesting that a choline-enriched diet in adolescence reversed later contextual fear learning deficits as well as methylation patterns associated with adolescent nicotine exposure. These results suggest that adolescence is a period of susceptibility to long-term behavioral and physiological changes mediated by epigenetic changes in methylation and chromatin induced by nicotine exposure.