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**Genetic Association of Socially Acquired Nicotine Self-administration in Adolescent Outbred Rats Identifies Candidate Genes Shared with Human Smoking GWAS**

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The social environment significantly influences cigarette smoking behavior. To model this in rodents, we established a socially acquired nicotine intravenous self-administration (IVSA) procedure in adolescent rats. In this model, nicotine delivery is paired with a contingent flavor cue that includes both odor and taste. The transfer of the nicotine-associated odor cue is crucial for initiating nicotine self-administration. We conducted a genetic association study on socially acquired nicotine IVSA using a population of outbred adolescent heterogeneous stock rats (n=1995, balanced for sex, IVSA started on postnatal day 41). Each rat was genotyped at 5,489,880 sites. We analyzed 63 phenotypes (heritability range: 0.05 to 0.26, mean: 0.165, SD: 0.04) and found 50 genome-wide significant loci linked to various aspects of nicotine IVSA. Among them, 30 contain genes with human orthologs related to smoking behaviors. For instance, total nicotine intake in rats is associated with Chr16:78175034, which harbors *Arhgef7*, associated with *PackYears* (lifetime cigarette consumption) in human GWAS. Additionally, PheWAS revealed shared genetic influences between nicotine motivation and social or anxiety-related phenotypes. For example, chr4:151349337 was associated with time spent in a social zone as well as nicotine intake during the first three IVSA sessions. These findings shed light on the intricate genetic control of nicotine motivation within a social context. Establishing the causality of these candidate genes could pave the way for successful treatments for nicotine addiction. This research was supported by NIDA grant P50DA037844.