

Social behavior and anxiety predicts nicotine self-administration in adolescent outbred rats

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It is well documented that emotional and social traits interact with genetic factors to influence smoking behavior. Using olfactogustatory stimuli as the sensory cue for nicotine intravenous self-administration (IVSA), we previously established a socially acquired nicotine IVSA model where social learning of a nicotine-associated odor cue reversed conditioned flavor aversion and promoted nicotine intake. We also showed that carbon disulfide, a component of rodent breath, is a critical component of the social signal. We used this unique model to identify factors contributing to voluntary nicotine intake. We have completed phenotyping of over 800 adolescent heterogeneous stock rats in their open field, novel object interaction, social interaction, elevated plus maze, and marble bury behaviors. These rats were then phenotyped on socially acquired nicotine self-administration for 10 sessions. Nicotine metabolism was measured in 92 rats. The level of plasma cotinine showed no correlation with nicotine intake ($r = 0.01$, $p=0.96$). Data from 35 social and emotional phenotypes were analyzed using principal component analysis, where PCs 2 and 6 were loaded with anxiety-related traits, and PCs 3, 4 and 7 had strong loading with social behavior. We then conducted a multiple regression analysis using the first eight PCs. We found in males, PC3, PC6 and PC7 were significant for total nicotine intake during the first three sessions. These PCs explained 15.7% of the variance in nicotine intake. In females, PC2 and PC4 were significant, with the model explaining 5.1% of the variance. We then analyzed total nicotine intake for the first 10 sessions. In males, PC3, PC6, and PC7 were significant, explaining 7.5% of the variance. In females, PC3, PC4, and PC5 were significant, with the model explaining 5.2% of the variance. These data strongly indicated that both social behavior and anxiety are contributors to nicotine intake in our model. Genetic analysis is currently underway.

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