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STRAIN-DEPENDENT ORAL NICOTINE INTAKE USING A FREE-CHOICE PARADIGM IN MICE

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Significance: Models to assess the addictive-like properties of nicotine in mice are limited. Therefore, we aimed to characterize and validate such model by using an oral nicotine free-choice paradigm in mice.

Methods: Adult male and female C57Bl/6J and DBA/2J mice as well as mice carrying deletions for the certain nicotinic acetylcholine receptor (nAChR) subunits, (n=8-10/group/sex) were given a choice of water or nicotine (a range of concentrations of 10 – 960 micrograms per milliliter) solution using two bottle free choice drinking assay.

Results: Oral nicotine intake and preference were higher in female compared to male C57Bl/6J mice without an effect on total fluid intake and body weight change. At the end of the study, absence of nicotine led to nicotine withdrawal. Intermediate access of nicotine exposure (every other day) resulted an escalation of nicotine consumption during the study and nicotine withdrawal at the end of the study. In addition, nicotine consumption varies in genetically modified mice due to subunit of nAChRs. In general, we observed that females consumed significantly more nicotine than males. While beta 2 nAChRs KO mice showed significant decrease on nicotine intake at all concentrations, deletion of alpha 5 nAChRs induced increase on nicotine consumption at high concentrations. In contrast to C57Bl/6J mice, DBA/2J mice showed very low nicotine preference and intake. These data are consistent with the findings of other models of nicotine reward and reinforcement.

Conclusions: We validated the two-bottle choice drinking paradigm to study nicotine's reward-like properties and nicotine withdrawal after oral nicotine exposure.