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Influence of Genotype and Sex on Oral Nicotine Consumption in Founder Strains of Diversity Outbred Mice

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Background and Goals. Smoking continues to be a worldwide health problem. Nicotine, a natural alkaloid of tobacco, is largely responsible for initiation and maintenance of tobacco dependence. Genetic factors play a significant role in nicotine dependence (ND). While the heritability of ND is well-documented, the contribution of specific genetic variants to specific phenotypes such as intake and preference has not been closely examined. The present study characterizes nicotine intake, preference, and aversion in both sexes of six founder strains of the diversity outbred (DO) populations: C57BL/6J, A/J, 129S1/SvImJ, PWK/PhJ, NOD/ShiLtJ, and CAST/EiJ.

Methods. The two-bottle choice paradigm was used to assess oral nicotine intake, nicotine preference, and total fluid intake in male and female mice of each strain at increasing nicotine concentrations (10-480 µg/mL). Conditioned place preference (CPP) was performed to evaluate the rewarding effects of nicotine (0.5 mg/kg, sc) in selected strains. Oral quinine (60-300 uM) and saccharine (0.3%) preference were measured to distinguish influence of taste in selected strains.

Results. We found a significant interaction of genotype and sex on nicotine intake and preference. The highest nicotine consuming strain in both males and females was 129/SvImJ while the lowest was A/J. Genetic heritability for total nicotine intake was calculated and found to be 0.53 in males and 0.25 in females. Quinine and saccharin data did not suggest that taste influenced nicotine consumption. CPP results revealed a higher preference in 129S1/SvImJ than A/J mice.

Conclusion. Characterization of nicotine consumption in the founder populations informs genomic and genetic studies.