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A comparative phenotypic analysis of nicotine pharmacological effects and dependence behaviors in C57BL/6J and C57BL/6N mouse strains

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Significance: Mouse substrains can be a powerful source for discovery of genes and pathways regulating complex behavior. In this study, we report that C57BL/6J (B6J) (Jackson Lab) and C57BL/6NCrl (B6N) (Charles River) substrains, differ significantly in nicotine pharmacology and dependence after acute and chronic administration.

Methods: We characterized behavioral and pharmacological responses to nicotine male adult B6J and B6N mice in a battery of tests. We measured nicotine's acute effects (antinociception and hypothermia), repeated (locomotor sensitization), conditioned place preference (CPP) as well as withdrawal signs after chronic exposure to the drug.

Results: In general, B6N mice were less sensitive than B6J mice to nicotine's acute effects and nicotine CPP. In contrast, while both B6N and B6J expressed physical and affective withdrawal signs in nicotine-dependent mice, withdrawal signs were more intense in B6N mice. In addition, nicotine metabolism and levels did not differ between the two substrains after acute and chronic administration. We are currently testing whether the *Cyfp2* (S968F) mutation that is known to regulate psychostimulant response could also contribute to the differences seen in nicotine response.

Conclusions: Together, these results provide a thorough, simultaneous evaluation of the pharmacological and behavioral differences to experimenter-administered nicotine as measured in several behavioral tests of aspects that contribute to smoking behavior. These results suggest that these substrains may be useful for future genetic studies on nicotine behaviors.

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