Name: Belle Buzzi Email: buzzib@vcu.edu
PI Name: Dr. M. Imad Damaj PI email: m.damaj@vcuhealth.org

Nicotine reward and preference in C57BL/6J and C57BL/6N mouse strains

Belle Buzzi[1], Vivek Kumar[2] and M. Imad Damaj[1]

[1]Department of Pharmacology and Toxicology, Virginia Commonwealth University, 1217 E Marshall St, Richmond, VA 23298, USA; [2]Jackson Laboratory, Bar Harbor, ME 04609, USA

Significance: Mouse substrains can be a powerful source for discovery of genes and pathways regulating complex behaviors. In this study, we report that C57BL/6J (B6J) (Jackson Lab) and C57BL/6NCrl (B6N) (Charles River) substrains, differ significantly in nicotine preference in the conditioned place preference (CPP) test.

Methods: We characterized the effects of nicotine at different doses (0.1, 0.5 and 1 mg/kg) after s.c. administration in male and female adult B6J and B6N mice in the CPP test. Mice were conditioned for 7 days, and their preferences assessed in a drug free state. We created an allele swap of the Cyfip2 S968F mutation in B6J and B6N substrains.

Results: B6N mice were less sensitive than B6J mice to nicotine CPP. We tested whether the *Cyfip2* (S968F) mutation that is known to regulate psychostimulant responses could also contribute to the differences seen in nicotine preference. B6J mice with *Cyfip2* (S968F) mutation (B6J-*Cyfip2*$^{N/N}$), a mutation that exists in all B6N substrains, showed a reduction in nicotine preference at 0.5 mg/kg compared to B6J WT mice. In contrast, B6N mice corrected for *Cyfip2* (S968F) mutation (B6N-*Cyfip2*$^{J/J}$) showed an increased nicotine preference at 0.5 mg/kg compared to B6N WT mice.

Conclusions: Together, these results significant differences in nicotine reward in B6J and B6N substrains. In addition, our data showed that *Cyfip2* (S968F) mutation may play an important role in these differences in nicotine reward. These results suggest that these substrains may be useful for future genetic studies on nicotine behaviors.

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