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GENOME TO PHENOME IMPLICATIONS OF SOCIAL STRESS-INDUCED NICOTINE PREFERENCE: A CONSPECIFIC AGGRESSOR-INDUCED SOCIAL STRESS MODEL INTEGRATED WITH A NICOTINE TWO-BOTTLE CHOICE PARADIGM

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Social stress (SS), a major burden of the modern day lifestyle, is associated with a number of comorbidities including substance abuse. The lack of a robust treatment strategy for SS-induced addiction aggravates the condition. We postulate that a comprehensive understanding of the mechanism underlying SS-induced addiction would be highly valuable for determining an intervention strategy. A SS model was adapted from a resident-intruder model to engineer stressful interactions with a conspecific companion, and a two-bottle choice (2BC) paradigm for nicotine self-administration was integrated with the SS model. Naïve C57BL/6j mice were co-housed within a protective cage inside the homecage of aggressor SJL mice, for 6hx10d. Control mice had no interaction with aggressor mice. Post-SS, both control and stressed mice were presented with nicotine in a serially increasing concentration of 10 to 240 ug/mL over a 20-day timespan. Nicotine preference (NP) was measured by calculating the longitudinal trend in nicotine consumption over water, as both liquids were offered per the 2BC paradigm. Both control and stressed mice had a nearly 50% NP at the lowest nicotine concentration. At the highest nicotine concentration, NP for control mice was reduced by 50% from the lowest nicotine dose, but that of stressed mice remained the same; as such, the difference in NP between the groups was statistically significant. Brain transcriptomic data also showed some relevant networks linked to SS-induced NP. These data will be the foundation of future validation projects to evaluate the applicability of the gene candidates as future therapeutic targets.