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### **EFFECTS OF REPEATED NICOTINE VAPOR EXPOSURE ON WITHDRAWAL AND ANXIETY-LIKE BEHAVIOR**

**Background:** In recent years, there has been a dramatic increase in the consumption of nicotine "juice" vapor through the use of electronic nicotine delivery systems, particularly among adolescents. Pre-clinical studies have primarily investigated the rewarding and withdrawal effects of nicotine, through the use of nicotine injections, osmotic mini-pumps, and intravenous self-administration. Currently, there are only a handful of published studies investigating the effects of nicotine vapor exposure on nicotine reward and withdrawal. The goal of this study is to assess nicotine withdrawal signs and increases in anxiety following exposure to nicotine vapor in rats.

**Methods:** Fifty-six male rats were exposed to either 0, 12, or 24mg/ml of nicotine for 9 days. Separate groups of rats received daily injections of either 0.8mg/kg of nicotine or saline across these same exposure days. For all groups, blood samples were collected on day 6 of vapor exposure to assess nicotine metabolite levels. Physical withdrawal signs and anxiety-like behavior following s.c. injections of the nicotinic receptor antagonist mecamylamine were assessed on day 7 and day 9 of vapor exposure, respectively.

**Results:** An increase in cotinine levels was seen in groups exposed to nicotine vapor or injections, relative to those that were not. Similarly, an increase in physical withdrawal and anxiety signs during withdrawal days was seen in the groups exposed to nicotine vapor or injections, relative to those that were not.

**Conclusions:** The findings suggest that repeated exposure to nicotine vapor may lead to physical withdrawal comparable to that seen with more traditional routes of administration in rats. The proposed work will offer a foundation for future pre-clinical studies to identify the neurobiological mechanisms driving abuse and dependence to nicotine vapor consumed from e-cigarettes and improve government policies and educational campaigns for this novel nicotine delivery product.