Protein Kinase C Epsilon (PKCε) involvement in Nicotine Addiction

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Background

- Alcohol and nicotine addition are often co-morbid
- The current annual costs associated with nicotine addiction is 300 billion[1]
- Neuronal nicotinic acetylcholine receptors (nAChRs) are involved in the mechanisms of drug action and are found throughout the central nervous system (CNS)[2]
- The brain reward system is comprised of dopaminergic neurons that are found in the ventral tegmental area (VTA) that release dopamine in the nucleus accumbens (Nac)[3]
- Nicotine can interact with nAChRs and the brain reward system to produce rewarding, and addictive, effects[4]
- Protein kinase C (PKC) are a family of enzymes that are believed to modulate drug addiction[4]
- PKCε is involved in many CNS signaling pathways and is known to act upon nAChRs
- Previous studies have shown male mice with the deletion of the PKCε gene have reduced nicotine consumption. Therefore, PKCε may be a good drug target to reduce nicotine consumption in males.[4]
- The role of PKCε in nicotine addiction in female mice has not been previously invesigated
- Our work suggests a sex by genotype difference exists in the contribution of PKCε in nicotine consumption

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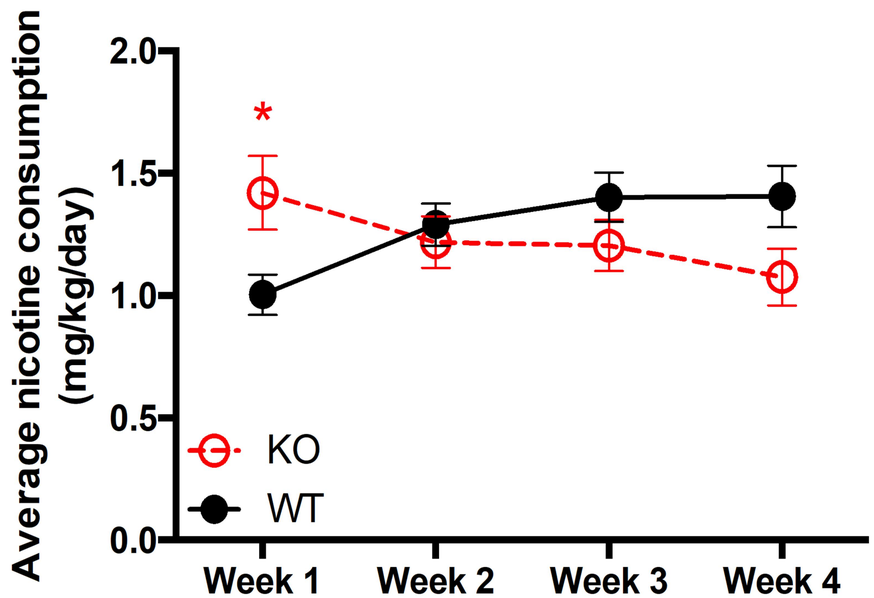
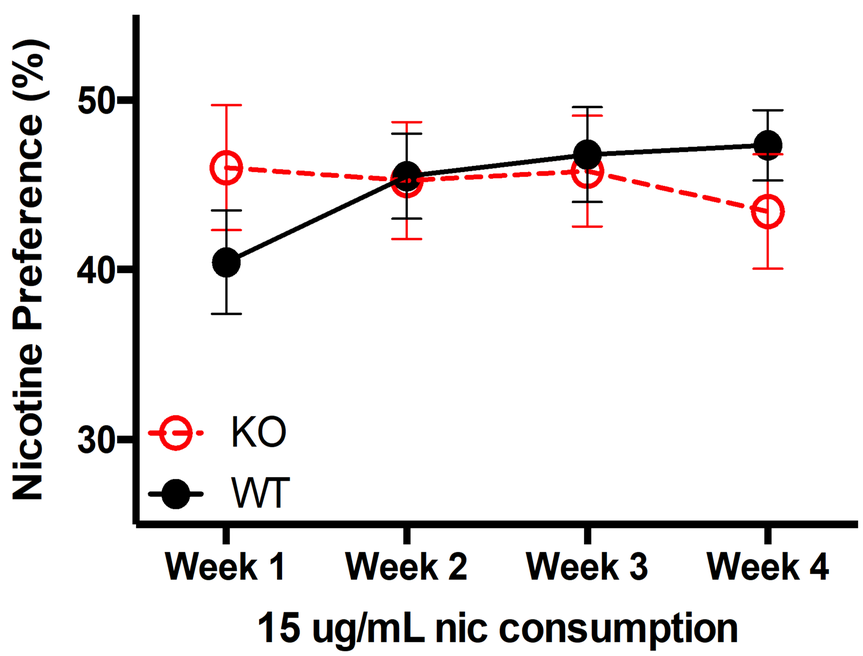
Female PKCε Knock- Out Mice Consumed More Nicotine Compared to Wild-Type Mice in the First Week of the Experiment



Nicotine Preference Between Genotypes was not Significantly Different over the Four Week Experiment



Methods

Continuous Access 2-Bottle Choice: Female PKCε wild-type (n= 35) and knockout mice (n= 30) were presented with a water bottle containing 2% Saccharine, and a nicotine bottle containing a solution of 2% Saccharine and 15µg/mL nicotine. The bottles were presented to the mice for four weeks. There were no changes in nicotine concentration presented over the four weeks of measurements.

Statistical Analysis: Average daily nicotine (mg/kg/day) was calculated based on the differenced in weights of the bottles and weights of each mouse. Nicotine preference was also determined. The consumption data was compared using 2-way repeated ANOVA with multiple comparisons.

Summary and Conclusions

- Female PKCε knock-out mice consumed more nicotine compared with wild-type mice in the first week.
- Thereafter, female PKCε knock-out mice had similar nicotine consumption compared with wild-type mice.
- Our results indicate that a sex by genotype difference exists in the contribution of PKCε to nicotine consumption
- .These results contribute may play a role in future development of treatment options for nicotine addiction.

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