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   2021T007

2. Title
   Elucidation of Nicotine-Induced Neuroplastic Changes in the Brain and the Underlying Mechanisms of the Behavioral Aspects of Nicotine Addiction

3. Period
   2021-2024

4. Summary
   In the present study, we aimed to develop an animal model of nicotine-administration-related behavioral addiction and investigate the cellular and neuronal mechanisms of smoking addiction. To this end, a conditioned place preference (CPP) protocol was used for the establishment of an animal model of nicotine-administration-related behavioral addiction to mimic smoking addiction. Behavioral examination revealed that nicotine administration induced a dose-dependent behavioral preference. Voxel-based statistical analysis showed regional brain activity, particularly in the medial prefrontal cortex (mPFC), was altered in response to behavioral addiction. Moreover, the CPP score was positively correlated with mPFC activity. To further examine whether and how endogenous opioid signaling in the mPFC modulates nicotine-associated behavioral preference, we chemogenetically manipulated neuronal activity within the mPFC–NAcShell circuit or in MOR-positive neurons in the mPFC. Chemogenetic experiments clearly demonstrated that selective activation of MOR-positive neurons in the mPFC or suppression of the mPFC–NAcShell circuit abolished both the formation and retention of nicotine-associated behavioral preference. These results indicate that MOR-positive neurons in the mPFC regulate the behavioral aspects of nicotine addiction through their interaction with excitatory projections to the NAcShell, thereby providing new insights into the development of effective therapeutic strategies.