

ABSTRACT

The Effect of Water Immersion Restraint Stress Towards Reward Effect of Nicotine in Mice Using Conditioned Place Preference Method

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Tobacco addiction is a chronically relapsing disorder caused by repeated exposure of addictive substance in cigarette, especially nicotine, which triggers an increase of dopamine release in the nucleus accumbens and produces reward effect. Previous preclinical studies showed that numerous compounds contained in cigarette smoke extract could enhance the psychoactive properties of nicotine. Stress is one of the main risk factors of drug addiction development and becoming a strong predictor of high rate of relapse to smoking. The aim of this research to investigate the effect of repeated stress in the extinction and reinstatement phase on the effect of nicotine reward on mice using CPP method. This research used 25 male Balb/C mice (20 – 30 g) that divided into five groups. The CPP method is using a biased design by pairing the least preferred compartment for pairing the drug. In conditioning, each group received a subcutaneous injection of saline, nicotine, or CSE before being place in each compartment. The dose of nicotine used is 0.5 mg/kg that resulting efficacy in reward effect. Repeated stress induced by water immersion restraint stress for eight consecutive days. This research showed that group injected with nicotine and CSE were able to produce a reward effect. In the period of extinction training, only nicotine with repeated exposure to stress group showed significantly decrease time spent in drug-paired chamber in day 7, but not in nicotine group. In reinstatement test, only nicotine with repeated stress group showed significantly increase time spent in drug-paired chamber. In conclusion, stress in period of abstinence is capable to decrease reward effect, resulting a negative emotional state that will lead to relapse.

Keywords: Addiction, Nicotine, Cigarette Smoke Extract, Stress, Conditioned Place Preference