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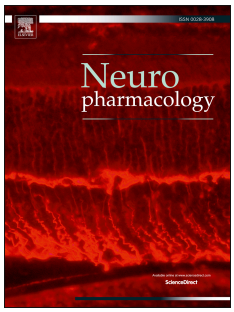

The effect of *N*-acetylcysteine or bupropion on methamphetamine self-administration and methamphetamine–triggered reinstatement of female rats

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The effect of N-acetylcysteine or bupropion on methamphetamine self-administration and methamphetamine–triggered reinstatement of female rats.

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Abstract

N-acetylcysteine and bupropion are two promising candidate medications for treatment of substance use disorder. The effects of N-acetylcysteine or bupropion on methamphetamine self-administration of female rats are not well understood. To fill this gap, this study assessed the effects of N-acetylcysteine (0, 30, 60, or 120 mg/kg) and bupropion (0, 10, 30, and 60 mg/kg) on methamphetamine self-administration of female rats across the natural estrous cycle. Following a completed dose-response curve, responding for methamphetamine self-administration was extinguished and the effects of N-acetylcysteine or bupropion on methamphetamine-triggered reinstatement was evaluated in separate experiments. N-acetylcysteine did not decrease responding maintained by methamphetamine or methamphetamine-triggered reinstatement. Bupropion significantly decreased methamphetamine self-administration and methamphetamine-triggered reinstatement in female rats with highest dose (60 mg/kg) also significantly decreasing general chamber activity. In a companion experiment, testing the effect of bupropion on responding maintained by sucrose, we confirmed non-specificity of bupropion's effects as bupropion also decreased responding for sucrose. Considered together, our findings suggest that while N-acetylcysteine has considerable promise for treatment of cocaine dependence it may not generalize to other stimulants like methamphetamine. Furthermore, although bupropion has been shown to effectively decrease methamphetamine self-administration, and presently methamphetamine-triggered reinstatement, its locomotor and reward suppressing effects warrant further investigation including both sexes.

Key words: methamphetamine, N-acetylcysteine, N-acetyl-L-cysteine, bupropion, drug self-administration, female rat,

1. Introduction

United Nations Office on Drugs and Crime estimates that there are 0.3 to 1.1% of amphetamine-type stimulants users worldwide (13.8-53.8 millions; Burns, 2014). In the US alone, methamphetamine use places a significant economic and societal burden, costing an estimated 23 billion dollars annually (Nicosia et al., 2009). Despite a slight global downward trends in methamphetamine use, approximately 7-8% decrease from 2009-2013, methamphetamine use is increasing in parts of North America and Europe. Although many users desire to quit using methamphetamine, majority of users are not able to do so due to lack of efficacious treatment strategies (Burns, 2014; Nicosia et al., 2009; Substance Abuse and Mental Health Services Administration, 2014).

The primary model of drug taking in the rat is the intravenous drug self-administration. This model has a high degree of face validity as drugs that are abused by humans are generally self-administered by laboratory animals (Brady et al., 1987; Yokel, 1987). In addition, this method models two key features of addiction – namely, drug seeking and drug relapse (Stewart, 2008). Surprisingly, few preclinical studies have examined

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