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Effects of Naltrexone on Alcohol and Nicotine Use in Female P Rats

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Background/Introduction

According to the National Institutes of Health, although underage drinking and binge drinking have declined in the past decade, alcohol (EtOH) is still the most commonly abused substance in the United States (NACAOA, 2015) and worldwide (Falk et al., 2016). In addition, approximately 80% of people with an EtOH use disorder also use tobacco, which equates to more than 46 million co-abusers of EtOH and nicotine in the United States (Miller & Gold, 2008). Furthermore, the co-use of EtOH and nicotine increases the difficulty of cessation of either substance (Mittle & Weinberg, 2013). However, there is currently no single medication to treat the co-abuse of EtOH and nicotine, despite the two substances having similar mechanisms of action.

The objective of the present study was to determine the effectiveness of the opioid antagonist naltrexone at reducing the consumption of EtOH and nicotine in female alcohol-prefering (P) rats. P rats have been selectively bred to have a genetic predisposition for alcohol abuse, which allows them to be used as an animal model of alcoholism. P rats readily self-administer iv nicotine (Izumiylova & Shoah, 2010; Guy et al., 2014), and in addition, naltrexone reduces EtOH self-administration in rats (Williams & Broadbridge, 2009) and nicotine self-administration in rats (Izumiylova & Shoaib, 2010; Guy et al., 2014). In addition, naltrexone has been FDA approved for alcohol use disorder based on its ability to treat alcohol dependence. Animal studies have shown that naltrexone decreases nicotine self-administration in rats (Izumiylova & Shoah, 2010; Guy et al., 2014). Active and inactive lever presses for nicotine in a headmount/catheter connected to the jugular vein.

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Method

- Twelve adult female P rats
- EtOH administration by opioid receptor agonist and antagonists in rats.
- Allowing naltrexone to be used in very few previous studies. It also measured choice for water (natural reward) and inactive lever presses (non-reinforced behavior) to determine if naltrexone had any effect on those behaviors. Because the highest dose of naltrexone (0.6 mg/kg) reduced water drinking, we did not increase the test dose beyond that point. Further research must be conducted to find medications to treat the co-use of EtOH and nicotine.

Results

In Phase 1 (EtOH alone), naltrexone did not have any significant effect on EtOH or water consumption. However, in the co-use phase, naltrexone dose-dependently reduced EtOH consumption; water consumption was also reduced, but only at the highest dose tested (0.6 mg/kg). Also, in the co-use phase, naltrexone significantly reduced inactive lever presses for nicotine at the lowest dose (0.15 mg/kg), but it had no effect on active lever presses for nicotine. Thus, naltrexone is more effective in treating EtOH use when tested in combination with nicotine rather than when tested alone.

In the P rat model, naltrexone did not have any significant effect on EtOH or water consumption during adolescence that is similar to that seen in adulthood, and operantly also reduces EtOH self-administration in rats given alternating access to either EtOH or respond for EtOH until they are impaired/intoxicated (Bell et al., 2006). Thus, P rats are a reduce the co-use of EtOH and nicotine.

Modified Operant Chamber

- ETOh and water bottles located on left wall of chamber.
- Active and inactive levers for nicotine self-administration located on right wall of chamber.
- Naltrexone

Naltrexone

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Literature Cited