Lisdexamfetamine-induced suppression of binge-eating in rats is attenuated by the α₂-adrenergic antagonist, prazosin

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ABSTRACT
Binge-eating disorder (BED) is a common psychiatric condition, affecting ~2% of the adult population and presents as the frequent, compulsive, excessive consumption of highly palatable foods. We have recently developed and pharmacologically characterized a rat model of BED in which rats are given intermittent, limited access to a specific reward (chocolate). We report here the effects of the α₂-adrenergic antagonist, prazosin, on the development and expression of chocolate bingeing in this model.

INTRODUCTION
Binge-eating disorder (BED) is a psychiatric condition affecting ~2% of the adult US population. Binge-eating disorder is manifest as the compulsive, excessive consumption of highly palatable foods. Binge-eaters frequently experience intense feelings of guilt and anxiety after a binge, but do not indulge in purging. BED is often associated with obesity, but a significant proportion of sufferers are normal weight. Lisdexamfetamine dimesylate (LSDX) is a novel placebo that is metabolized to d-amphetamine primarily by red blood cells. LSDX is approved to treat ADHD in children (6-12 years) and adults.

METHODS
Female lean rats maintained on a reverse dark-light cycle were given free access to normal chow and water, and in addition were allowed access (2h), irregular access (4h) or no access to chocolate for periods of 4, 2, or 1 h respectively. During this period, rats were given intermittent access to chocolate to develop robust binge-eating behavior that consisted of prolonged hyperphagia of chocolate in combination with reductions in normal chow intake on the days immediately following the binge sessions. The bodyweights of the binge eating rats were not significantly different from the controls.

RESULTS
• Figure 1 shows that lean, female Wistar rats given intermittent, limited access to chocolate developed robust patterned bingeeating behavior. LDX dose-dependently reduced the rats' consumption of chocolate in the 2hr binge session (Figure 2A). In this experiment, LDX had no effect on the consumption of normal chow (Figure 2B). The doses of LDX used here were administered by either vehicle (ip), prazosin (0.1 or 0.3mg/kg), RX821002 (0.1 or 0.3mg/kg), SCH23390 (0.1 or 0.3mg/kg) or raclopride (0.1 or 0.5mg/kg ip).

REFERENCES

CONCLUSIONS
Lisdexamfetamine is effective in reducing binge-eating in binge-eating rats. At the doses used in the LDX interaction experiments, prazosin, RX821002, SCH23390 or raclopride did not affect chocolate consumption in their own right. The attenuation of chocolate bingeing produced by LDX was partially reversed in a dose-related manner by prazosin. RX821002 was without effect suggesting that the effect of LDX is not mediated by activation through α₂-receptors, but not α₂-adrenergic antagonists. SCH23390 and raclopride did not significantly modify the reduction of chocolate consumption produced by LDX treatment suggesting that LDX's effect is not mediated by dopamine release acting through D1 or D2 receptors.

Figure 1. Development of binge-eating in lean female Wistar rats induced by intermittent limited access to chocolate

Figure 2. Dose-dependence decreases in chocolate bingeing but normal chow intake by administration of lisdexamfetamine (LDX)

Figure 3. Effects of prazosin or RX821002 on the attenuation of chocolate bingeing produced by lisdexamfetamine (LDX)

Figure 4. Effects of SCH-23390 or raclopride on the attenuation of chocolate bingeing produced by lisdexamfetamine (LDX)

Table 1. Effects of noradrenergic and dopaminergic antagonists on chocolate and total food intake during a 2hr binge session