**Effect of lisdexamfetamine in a rat model of binge-eating disorder**

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**INTRODUCTION**

Binge-eating disorder is a common psychiatric condition that affects around 2% of the adult European population. The prevalence of binge-eating disorder is approximately equal in women and men and it occurs most frequently in older adults.

Binge-eating disorder is manifest as the compulsive, excessive consumption of highly palatable foods and it may or may not be associated with obesity. Binge eaters frequently experience intense feelings of guilt and anxiety after a binge session, but do not indulge in purging. Lisdexamfetamine dimesylate (Vyvanse®), a novel prodrug that is metabolised to d-amphetamine primarily by red blood cells,[1] is approved in North America, Brazil and some European countries for treatment of ADHD in children and adults in the USA. Lisdexamfetamine is currently undergoing clinical evaluation in the USA as a potential treatment for binge-eating disorder.

This study compared the acute effects of lisdexamfetamine in rats trained to binge eat chocolate with its active metabolite, d-amphetamine, and sibutramine, which has been reported to be moderately effective in clinical trials of binge-eating disorder [2].

**METHODS**

Adult, lean, female Wistar rats (44 started study, 40 completed) were housed individually on reversed-phase lighting with free access to standard diet and water at all times. A pot containing ground milk chocolate was offered to each rat for 2 hour periods at irregular intervals to establish binge eating. An empty pot was placed in the cages of the control rats. Lisdexamfetamine, d-amphetamine and sibutramine were administered orally. On Days 29, 42 and 56, animals were dosed with compound (2 week washout period between each compound) and 60 min later were given a pre-weighted amount of chocolate for 24 hours.

To facilitate comparisons, doses of lisdexamfetamine and d-amphetamine are expressed as mg/kg d-amphetamine base.

**RESULTS**

Figure 1 shows that when rats were given irregular, limited access to chocolate for approximately 4 weeks, reproducible binge eating was evident. The episodes of chocolate-induced hyperphagia were accompanied by concomitant reductions in the intake of standard diet.

Figure 2 shows that intermittent episodes of chocolate binge eating did not change the bodyweights of the rats compared with control rats maintained on standard diet.

Lisdexamfetamine (0.1-1.5 mg/kg po) reduced chocolate bingeing by 08% (p<0.001) at the highest dose (Figure 3A). The intermediate dose of lisdexamfetamine, ie 0.3 mg/kg po, reduced chocolate consumption by 40% (p<0.001) while having no effect on the consumption of standard diet (Figure 3A).

Lisdexamfetamine did not decrease rats’ bodyweight compared with the control group given vehicle (Table 1).

d-Amphetamine (0.1-1.0 mg/kg po) decreased chocolate bingeing at 0.5 mg/kg (35%; p<0.01) and 1.0 mg/kg (56%; p<0.001) (Figure 3B). d-Amphetamine did not significantly reduce the simultaneous consumption of standard diet (Figure 3B), but it produced a 13% decrease of bodyweight (p<0.01) at the highest dose (Table 1).

Sibutramine (0.3-5.0 mg/kg po) reduced chocolate bingeing by 44-91% (p<0.001) at doses of 1.0-5.0 mg/kg; however, there were similar 74-97% (p<0.01) reductions of standard diet consumption at these doses (Figure 3C). At 1.0-5.0 mg/kg, sibutramine also produced small 1.5-6.1% (0.05<p<0.001) decreases of bodyweight (Table 1).

**CONCLUSIONS**

Animals allowed irregular, limited access to chocolate developed robust, intermittent hyperphagia that mirrored binge-eating disorder without any associated obesity.

Binge eating of chocolate was markedly reduced by a single treatment with lisdexamfetamine or its metabolite, d-amphetamine.

Some doses of lisdexamfetamine and d-amphetamine reduced chocolate binge-eating without simultaneously decreasing the consumption of standard diet. In contrast sibutramine dose-dependently decreased chocolate bingeing and the consumption of standard diet.

These results provide preclinical evidence to support the clinical evaluation of lisdexamfetamine as a potential treatment for this disorder.

References


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