Preclinical evidence showing that lisdexamfetamine (LDX) prevents compulsive and perseverative behaviour associated with binge eating
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ABSTRACT
Background Binge-eating disorder (BED) is a psychiatric condition characterised by compulsive, perseverative bouts of excessive consumption of palatable foods. LDX, a prodrug of lisdmefetamine, is approved to treat ADHD and is being assessed for BED (1). Rats given irregular, limited access to chocolate develop robust binge-eating (BE) and LDX decreases chocolate bingeing (2). We have investigated whether BE rats show compulsive and perseverative responding when given access to chocolate and the influence of LDX on these aspects.
Methods Thirty-four adult, female Wistar rats were given continuous access to chow and water. BE rats were given intermittent access to chocolate over 30 days. Non-binge (NB) controls were given an empty pot on these occasions. BE and NB rats were trained to perform the basic conditioned avoidance response (CAR) test in a 2-chamber shuttle-box, ie a presentation of a food stimulus (microwave-warmed food) in a food-associated compartment. After CAR training, a food-associated stimulus was repeated in the chocolate compartment of the shuttle box. When the rat entered this chamber, the conditioned stimulus was presented after a variable interval following 10s later by a foot shock if the rat did not initiate a trial and eat the food. BE rats spent ~75% of the session in the chocolate compartment vs empty pot (NB controls). BE rats showed compulsive and perseverative responding in a modified CAR test, LDX decreased chocolate bingeing and reduced the compulsive and perseverative behaviours of BE rats.

LEARNING OBJECTIVES
(1) Determine whether BE rats show compulsive and perseverative behaviours.
(2) Investigate whether LDX reduces compulsive and perseverative responding in BE rats.

INTRODUCTION
Binge-eating disorder (BED) is a psychiatric condition characterised by repeated, compulsive bouts of excessive consumption of palatable foods. Binge-eating is not associated with inappropriate compensatory purging, BED can be linked with obesity, but not all subjects with BED are overweight or obese with a significant proportion of subjects being in the normal body weight range. Lisdexamfetamine (LDX), a prodrug of d-amphetamine, is approved to treat ADHD and it has also recently gained approval in the US for the treatment of moderate to severe BED in adults (1).

Rats given irregular, limited access to chocolate maintain normal weight, but at the same time they develop robust binge-eating (BE). We have previously reported that LDX decreases chocolate bingeing (2) and in this study, we have investigated whether BE rats show compulsive and perseverative behaviour when given access to chocolate and whether LDX affects these responses.

METHODS
Thirty-four adult, female, Wistar rats with continuous access to standard chow and water were given intermittent 2 hr access to chocolate for 28 days. Non-binge (NB) controls were given an empty pot on the binge day. BE rats consumed ~40% of their daily food intake in 2hr chocolate binge. BE and NB rats were trained in the basic conditioned avoidance response (CAR) test in a 2-chamber shuttle-box, ie a tone/light stimulus was presented of a mild foot-shock 10s later if the rats did not move to the adjacent compartment. After rats were proficient in the CAR, the model was altered to a food-associated conflict test. A chocolate-filled jar was placed in 1 compartment of the shuttle-box. If the rat entered the chamber with the chocolate, the conditioning stimulus was presented after a variable interval and if the rat did not leave it received a food-shock.10s later. Residence in the “safe” chamber without a pot did not initiate a trial or administration of foot-shocks. LDX (0.8 mg/kg po [d-amphetamine base]) was tested. Results are presented as mean ± SEM.

REFERENCES
(2) Vickers SP et al. Effect of lisdexamfetamine in a rat model of binge-eating disorder. SPN 2013, abt 236.03

RESULTS
Figure 1 shows that there was no difference between the BE rats and NB controls for the rate of acquisition or proficiency in performing the CAR test. Figure 2 shows that BE rats consumed 35.2 ± 5.2 kJ of chocolate in the food-associated conflict test and LDX significantly reduced chocolate consumption by >50%.

Figure 3 shows:
- BE rats spent ~75% of the session in the chocolate-paired compartment vs empty pot (NB controls). BE rats showed compulsive and perseverative responding in a modified CAR test, LDX decreased chocolate bingeing and reduced the compulsive and perseverative behaviours of BE rats.
- Non-binge eating controls + vehicle (de-ionised water, 3 ml/kg po) vs Non-binge eating controls + LDX (0.8 mg/kg po) vs Binge-eating rats + vehicle (de-ionised water, 3 ml/kg po) vs Binge-eating rats + LDX (0.8 mg/kg po)

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