INTRODUCTION

Binge-eating disorder (BED) is a psychiatric condition affecting ~2% of the US adult 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 session, but do not indulge in purging. BED is often associated with obesity, but a significant proportion of sufferers are normal weight. Lisdexamfetamine dimesylate (LDX) is a novel produg that is metabolized to d-amphetamine primarily by red blood cells. LDX, is approved to treat ADHD in children (6–12 years) and adults.

We have developed a rodent model of BED in which freely-fed rats are given irregular, limited access to chocolate. The rats develop robust, hyperphagia of this palatable food. They show concomitant reductions in consumption of normal chow and so maintain a normal bodyweight [1]. This rodent model mirrors human BED without obesity. We have reported that LDX is able to selectively decrease the consumption of palatable food without decreasing the intake of normal chow [1]. Recent evidence has linked eating disorders with CNS dopaminergic dysregulation [2,3]. Therefore, we have explored dopaminergic neurochemistry in the brains of binge-eating rats.

METHODS

Forty-five adult female Wistar rats were housed individually on reverse-phase lighting with free access to standard diet and water. Ground milk chocolate was offered to each rat for 2h periods at irregular intervals over a 28-day period during which time they developed robust binge-eating behaviour. Control rats were treated identically except that an empty glass jar was placed in their cages during the binge sessions. Rats were killed 1 hr after the final binge session. Dopamine (DA) and its metabolites (dihydroxyphenylacetic acid [DOPAC], homovanillic acid [HVA] and 3-methoxytyramine [3-MT]) were measured in striatum, prefrontal cortex (PFC) and hypothalamus by HPLC-EC. D1 and D2 receptors were quantified by saturation binding analysis in STR membranes using [3H]SCH23390 and [3H]raclopride, respectively, and dopamine reuptake transporters (DAT) sites with [3H]GBR12935.

RESULTS

- Figure 1 shows when rats were given irregular, limited access to chocolate for approximately 4 weeks, they developed robust, reproducible binge-eating behaviour. The episodes of chocolate-induced hyperphagia were accompanied by concomitant reductions in the intake of normal chow.
- Figure 2 shows striatal D2 receptors were reduced by 39% (p<0.01) in binge-eating rats, but the numbers of D2 receptors and DAT sites in the striatum were unaltered.
- The affinities (Kd’s) of striatal D1, D2 receptors and DAT sites were unchanged in the brains of binge-eating rats (Figure 2).
- Binge-eating behaviour did not alter the concentration of dopamine or its metabolites in the striatum, PFC or hypothalamus (Figure 3).
- Compared with controls, dopamine turnover (seen as a reduction in the DA/DOPAC ratio) was increased by 18% (p<0.05) in the hypothalamus of the binge-eating rats (Figure 4). Dopamine turnover was unchanged in the striatum and PFC (Figure 4).

CONCLUSIONS

- Binge-eating decreased the number, but not the affinity, of striatal D2 receptors without altering the number of D3 receptors and DAT sites, the size of the dopamine neuronal pool, or the rate of dopamine turnover.
- The results indicate that binge-eating is associated with decreased dopaminergic signalling via D3 receptors in the striatum, and possibly as a consequence, an imbalance of striatal D2/D3 signalling.
- Dopaminergic neurotransmission was not altered in the PFC. However, increased dopamine turnover suggests that dopaminergic signalling in the hypothalamus, which controls food intake, may also be dysregulated in binge-eating.

REFERENCES

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CONFLICT OF INTEREST

SC Cheetham, J Gosden, MP Prow & DJ Heal are employees of RenaSci Ltd.
PH Hutson is an employee of Shire Development Inc