Binge-eating behaviour in rats induces changes in dopamine and opioid receptor binding in the brain

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 that are freely-fed on standard chow are given intermittent, limited access to chocolate along with normal chow. Over a period of 4 weeks, the rats develop robust binge-eating of the chocolate with concomitant reductions in their consumption of normal chow. Body weights remained at the same level as control rats maintained on normal chow. We have, therefore, proposed that this paradigm models BED without obesity (Vickers et al., 2013).

To further our understanding of the neurochemical changes underlying this behavior, a study was conducted to determine whether the development of binge-eating was associated with changes in dopaminergic or μ-opioid receptors (both of which are thought to be implicated in BED). Davis et al. (2009) in various brain regions of binge-eating rats.

**METHODS**

Two cohorts of lean, female, Wistar rats (Study 1 = 10 and Study 2 = 30) maintained on a reverse dark-light cycle were given free access to normal chow and water. They were given brief (2hr), irregular access to powdered milk chocolate over 4 weeks. Groups of controls (Study 1 = 10 and Study 2 = 25) were treated identically except that an empty glass jar was placed in their cages during the binge sessions. On Day 28 of the irregular access protocol, the rats were killed and their brains taken 1 hr after the final chocolate binge session or (Study 1 = 10 and Study 2 = 25) were treated identically except that an empty glass jar was placed in their cages during the binge sessions. The brains were then dissected under a dissecting microscope and the striatum and frontal cortex were dissected and stored at -80°C. The dopamine and opioid receptor binding was determined by saturation binding analysis using [3H]raclopride (8 concentrations from 0.125-12nM) defined with (-)sulpiride (1µM). Striatal dopamine reuptake transporter (DAT) sites were labelled with [3H]GBR 12935 (10 concentrations from 0.125-250nM) defined by mazindol (1µM). In Study 2, the number and affinity of μ-opioid receptors in the striatum and frontal cortex were quantified using [3H]DAMGO (8 concentrations from 0.0025 - 125nM) defined by naloxone (50μM). Results are presented as mean ± SEM; n = 6-10/group. NS = not significantly different.

**RESULTS**

As shown in Figure 1, when rats were given intermittent access to chocolate they developed robust patterns of binge-eating which consisted of compulsive chocolate consumption in the binge sessions with reductions in the intake of normal chow. The bodyweights of the binge-eating rats were not significantly different from their respective control group (data not shown).

Binge-eating was associated with a reduced number of striatal D1 receptors (Figure 2) with no change in their affinity (Table 1). Binge-eating did not alter the number of striatal D2 receptors or DAT binding or cortical μ-opioid receptor binding. It has been postulated that there are changes in dopaminergic and opioid systems in subjects with BED (Davis et al., 2009). The findings in our rat model of BED suggest that dysregulation of the dopamine and opioid reward systems in the striatum also have a role in the development of binge-eating in rats.

**CONCLUSIONS**

The results show that binge-eating behaviour in lean, female rats is associated with a 39% reduction of striatal D1 receptor density together with a concomitant 29% increase in the number of striatal μ-opioid receptors. Binge-eating did not alter the number of D2 receptors and DAT binding striatum or μ-opioid receptors in the frontal cortex. It has been postulated by Davis et al. (2009) that there are dopamine and opioid dysregulations in subjects with BED [2]. The findings from our rat model of BED suggest that dysregulation of the dopamine and opioid reward systems in the striatum also have a role in the development of binge-eating in rats.

**REFERENCES**