Deep Brain Stimulation of the Nucleus Accumbens Attenuates Binge Eating in Mice: Preliminary Evidence for A Potential Therapeutic Role of Neuromodulation in Treatment-Refractory Obesity

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INTRODUCTION

Deep brain stimulation (DBS) of the nucleus accumbens (NAc) may be an effective treatment for psychiatric disorders. Here, we examine whether NAc DBS can modulate the rewarding aspects of a highly palatable diet in a mouse model of binge eating.

Hypothesis (Fig. 1):

NAc DBS modulates the rewarding aspects of highly palatable food.

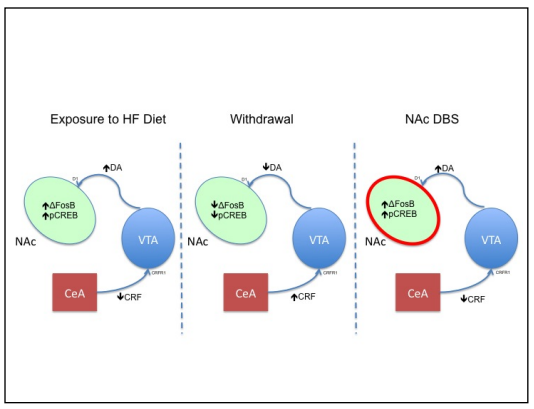

Figure 1. CRF decreased and pCREB and deltaFosB increased during exposure to HF, which reverse during withdrawal. NAc DBS is hypothesized to prevent these changes which may underlie moduation of binge eating. Central nucleus of amygdala (CeA), Ventral tegmental area (VTA), Dopamine (DA), DA receptor-1 (D1), CRF receptor-1 (CRFR1)

METHODS

Animals

Male mice (C57Bl/6:129; 8–10 wks)

Diet

High fat (HF); (45% fat, Research Diets)

House Chow (Purina)

Binge eating

7 days of limited exposure of HF (1hr/d).

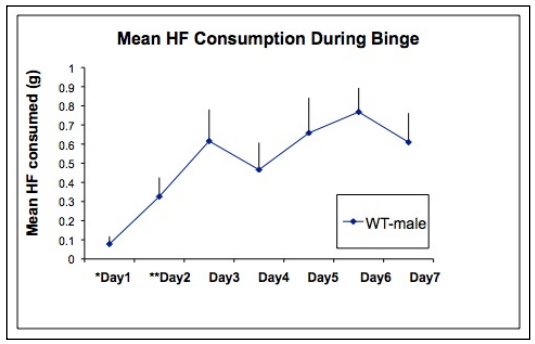

Figure 2. Mean HF consumption. *Differs from days 2-7 ($p<0.05$); **differs from days 3-7 ($p<0.05$).

METHODS (cont'd)

Unilateral NAc DBS and binge eating

Based on our validated binge eating model (Fig. 2), during Days 1-4, no stimulation was administered (DBS-off). DBS was turned on at Day 5 (3V, 20KOhm, 160Hz, 60us) and biphasic symmetrical pulses were delivered through bipolar tungsten electrodes (75 um, 125um apart). Binge eating was then re-examined with DBS-off.

RESULTS

Attenuation of binge eating is seen on Day 5 with unilateral NAc DBS. Mice return to binge eating when DBS is turned off. See Figs. 3 and 4.

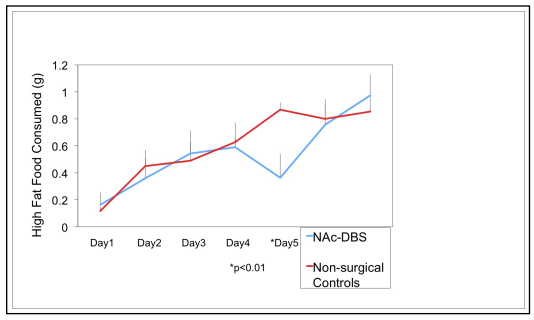

Figure 3. Effect of Nac DBS on binge eating. *p<0.01

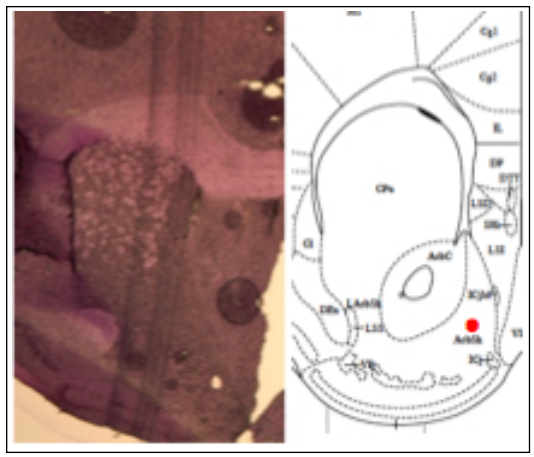

Figure 4. Electrolytic lesion confirming location of electrode in the nucleus accumbens

CONCLUSIONS

DBS of the NAc significantly attenuated binge-eating behavior in mice compared to non-surgical controls in this preliminary experiment, providing impetus for additional studies with larger sample sizes, within-group comparisons, and control for anatomic specificity. Given the significant prevalence of binge eating disorder in obesity, our findings provide preliminary evidence for a potential therapeutic role of DBS for treatment-refractory obesity.

Learning Objectives

By the conclusion of this session, participants should be able to: 1) Describe the importance of investigating deep brain stimulation in animal models of eating disorders 2) Discuss, in small groups the possible therapeutic role for deep brain stimulation in obesity 3) Identify an effective treatment for eating disorders associated with treatment refractory obesity that needs to be studied in greater detail in animal models.

References

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