Oxytocin deficiency is associated with hyperphagia & weight gain in hypothalamic & common obesity: a first-in-humans proof-of-concept study

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INTRODUCTION

- Hypothalamic obesity (HyOb) is a syndrome of intractable morbid obesity seen in congenital (e.g. septo-optic dysplasia [SOD]) and acquired (e.g. suprasellar tumours) hypothalamic damage.
- It is commonly associated with the hypothalamic syndrome (panhypopituitarism, autism, sleep & temperature disturbances).
- Its pathophysiology has been attributed to hyperphagia and hyperinsulinemia.
- More recently the wider role of oxytocin (OXT) in regulating appetite and weight has emerged from animal studies and pilot trials of intranasal OXT in humans with common obesity.
- We aimed to determine if hypoxytocinaemia and hyperinsulinemia were more prevalent in HyOb compared to common obesity and to examine the relationship between OXT concentrations, appetite and weight.

METHODS

- Multiwave case-control study, 4 subcohorts:
  - Hypothalamic obese (HyOb, BMI > +2SDS) – congenital (SOD) vs. acquired (suprasellar tumour)
  - Hypothalamic lean (HyLean, BMI ≤ +2SDS) – congenital vs. acquired
  - Common obese (Ob)
  - Lean controls (Lean)
- Independent variables: Age, sex, height/weight/BMI SDS, Tanner stage, endocrine morbidity score (EMS), frequency of hypothalamic syndrome features (autism, temperature dysregulation, sleep disturbances)
- Dependent variables: Dykens’ Hyperphagia Questionnaire Score (DHQS), fasting and 2-hour oral glucose tolerance test-stimulated Insulin and OXT concentrations using internally validated ELISA
- Statistical analyses using SPSS v22

RESULTS

- **Hyperphagia is not unique to HyOb**
- **Hyperinsulinemia is not more severe in HyOb**
- **OXT is decreased in all forms of obesity**
- **OXT is associated with an increased appetite**

CONCLUSIONS

- Hyperphagia and hyperinsulinemia are common to both HyOb and common obesity, and therefore unlikely to be primary drivers of HyOb.
- First-in-humans study supporting the role of OXT as an anorexigen with additional possible effects on weight & BMI.
- No correlation between OXT concentrations and other features of the hypothalamic syndrome or diabetes insipidus
- 6.5% had impaired glucose tolerance and 1 patient (1.1%) had frank type 2 diabetes.
- Further recruitment needed to power study sufficiently, with possible need for OXT trials in HyOb and common obesity.

**References:**