Hypothalamic obesity, Hyperphagia & Hyperinsulinaemia: time for a paradigm shift in assumptions?

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Background

- Hypothalamic obesity (HyOb) is a syndrome of ineradicable, treatment-resistant, morbid obesity seen after congenital (e.g. septo-optic dysplasia (SOD)) and acquired (e.g. suprasellar tumours) hypothalamic damage.
- HyOb is commonly associated with other features of the hypothalamic syndrome (panhypopituitarism, autism, sleep disturbances, temperature dysregulation).
- Its pathophysiology is poorly understood but often attributed to hyperphagia and increased caloric intake.
- Unclear whether hyperinsulinaemia is the cause or effect in HyOb.

Objectives

- To determine the frequency of hyperphagia in HyOb in comparison to simple obesity
- To examine the associations between hyperphagia and hyperinsulinaemia in HyOb and simple obese patients

Methods

- Multi-way case-control study of four subcohorts:
  - Hypothalamic obese (HyOb, BMI > +2 SDS) – congenital (SOD) vs. acquired (suprasellar tumour)
  - Hypothalamic lean (HyLean, BMI ≤ +2 SDS) – congenital (SOD) vs. acquired (suprasellar tumour)
  - Simple obese
  - Lean controls

- Dependent variables: Dykens’ Hyperphagia Questionnaire Scores (DHQS), fasting and 2-hour oral glucose tolerance test (OGTT)-stimulated glucose and insulin indices

- Statistical analyses (SPSS v22): Non-parametric Mann Whitney-U, Kruskal Wallis one-way ANOVA and χ² tests

Results

- Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>HyOb (14)</th>
<th>Tumour (13)</th>
<th>SOD (13)</th>
<th>Tumour (3)</th>
<th>SOD (20)</th>
<th>Lean control (14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age**</td>
<td>14.5 (10.2-16.3)</td>
<td>12 (9.1-18.0)</td>
<td>11.7 (7.3-12.3)</td>
<td>14.5 (8.1-14.5)</td>
<td>11.7 (8.9-13.8)</td>
<td>10.0 (6.1-12.8)</td>
</tr>
<tr>
<td>Female</td>
<td>6 (42.9%)</td>
<td>12 (70.6%)</td>
<td>7 (53.8%)</td>
<td>2 (66.7%)</td>
<td>10 (50.0%)</td>
<td>3 (21.4%)</td>
</tr>
<tr>
<td>Tanner stage*</td>
<td>2 (1-4)</td>
<td>3 (2-5)</td>
<td>1 (1-3)</td>
<td>1 (1-2)</td>
<td>2 (1-3)</td>
<td>1 (1-3)</td>
</tr>
<tr>
<td>Height</td>
<td>-0.4 (-0.9-0.8)</td>
<td>-0.9 (-1.9-1.5)</td>
<td>-1.8 (-2.0-0.9)</td>
<td>-0.9 (-2.6-0.4)</td>
<td>-1.2 (-1.2-1.1)</td>
<td>-2.4 (-2.4-2.0)</td>
</tr>
<tr>
<td>SDS</td>
<td>2.2 (1.9-2.7)</td>
<td>1.8 (1.4-2.6)</td>
<td>0.0 (-1.0-0.5)</td>
<td>0.9 (-1.1-1.3)</td>
<td>2.5 (1.6-3.5)</td>
<td>0.0 (-1.3-1.1)</td>
</tr>
<tr>
<td>Weight</td>
<td>2.8 (2.6-3.2)</td>
<td>2.6 (2.4-3.0)</td>
<td>2.0 (0.6-1.8)</td>
<td>1.6 (0.7-1.9)</td>
<td>2.8 (2.4-3.2)</td>
<td>0.3 (-1.0-1.3)</td>
</tr>
</tbody>
</table>

**p<0.05, ***p<0.01

Conclusions

- Hyperphagia not unique to HyOb and present in simple obesity
- Hyperinsulinaemia is a function of BMI and therefore unlikely to be primary driver of weight gain in HyOb
- The significant prevalence of IGT and type 2 diabetes in all obese children may indicate need for routine screening

References: