Elevated ratio between acylated and unacylated ghrelin in children and young adults with Prader-Willi syndrome

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Conclusions

• PWS have a higher AG/UAG ratio than controls due to higher AG levels and similar UAG levels.
• The switch to excessive weight gain and hyperphagia in PWS is associated with an increase in the AG/UAG ratio.

Background

Prader-Willi syndrome (PWS) is characterized by a switch from failure to thrive to excessive weight gain and hyperphagia in early childhood. Hyperghrelinemia may be involved in the underlying mechanisms of the switch.

Ghrelin exists in two forms. Acylated ghrelin (AG) stimulates appetite and induces a positive energy balance. Unacylated ghrelin (UAG) acts as a functional inhibitor of AG. Thus the AG/UAG ratio may be crucial.

Aim

To evaluate AG and UAG levels in PWS compared to healthy and obese controls and investigate their associations with hyperphagia.

Participants & Method

138 children and young adults with PWS aged 0-29 years from 3 PWS expert centers in the Netherlands and France, compared with 39 age-matched healthy and 50 obese controls. AEBSF was added to the blood samples to inhibit deacylation of AG.

Table 1a. Ghrelin levels in the three groups

<table>
<thead>
<tr>
<th>Parameter</th>
<th>PWS n=138</th>
<th>Controls n=39</th>
<th>Obese n=50</th>
</tr>
</thead>
<tbody>
<tr>
<td>AG (pg/ml)</td>
<td>129.1 [67.1-227.9]</td>
<td>82.4 [56.3-130.4]</td>
<td>40.3 [26.4-82.5]</td>
</tr>
<tr>
<td>UAG (pg/ml)</td>
<td>135.3 [66.0-284.2]</td>
<td>157.3 [79.3-261.0]</td>
<td>35.8 [26.0-64.4]</td>
</tr>
<tr>
<td>AG/UAG ratio</td>
<td>1.00 [0.57-1.49]</td>
<td>0.61 [0.37-0.81]</td>
<td>1.16 [0.92-1.43]</td>
</tr>
</tbody>
</table>

Table 1b. Comparison between the groups

<table>
<thead>
<tr>
<th>Parameter</th>
<th>p between groups*</th>
<th>PWS vs Controls*</th>
<th>PWS vs Obese*</th>
<th>Obese vs Controls*</th>
</tr>
</thead>
<tbody>
<tr>
<td>AG (pg/ml)</td>
<td>&lt;0.001</td>
<td>0.016</td>
<td>&lt;0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>UAG (pg/ml)</td>
<td>&lt;0.001</td>
<td>0.868</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AG/UAG ratio</td>
<td>&lt;0.001</td>
<td>0.001</td>
<td>0.069</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*p-value between the groups

This boxplot shows the AG/UAG ratio of children and young adults with PWS in the 6 nutritional phases and of healthy controls and obese controls.

Results

• Compared to healthy controls, both PWS and obese controls have a high AG/UAG ratio but the mechanisms seem different.
• Compared to healthy controls:
  - PWS had high AG levels and similar UAG levels
  - Obese controls had low AG and low UAG levels
• Children and young adults with PWS without weight gain or hyperphagia had normal AG/UAG ratios, while those with weight gain and/or hyperphagia had higher AG/UAG ratios than controls.