Serum Metabolite Signature in an animal model of binge eating by Nuclear Magnetic Resonance Spectroscopy
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Target Audience: NMR Scientists, Psychiatrics and Psychologists, Nutritionist Scientists.

Purpose- Binge Eating (BE) episodes are characterized by uncontrollable, distressing eating of a large amount of highly palatable food (HPF). These episodes represent a central feature of bingeing related eating disorders, such as binge eating disorder, bulimia nerviosa, and binge/purge subtype anorexia nervosa. Considerable evidence suggests that BE may be caused by a unique interaction between dieting and stress. In the model adopted by our group, BE for HPF is evoked in rats by the combination of cyclic food restrictions and stress. The model uses female rats in relation to the higher prevalence of BE disorders in women. Moreover, according to the inverse association between plasma estradiol levels and BE, we recently demonstrated that during the estrous phase, BE was not induced in our experimental conditions in female rats (Figure 1). In order to investigate Binge Eating behavior in female rats, for the first time, we analyzed the metabolic profile obtained from biological fluids (serum) of rats exposed or not to cycles of dieting and stressful exposure to food: as well as building blocks for all other biochemical species including proteins, nucleic acids and cell membranes.

Materials and Methods- Animals. Female Sprague-Dawley rats (Charles River, Calco, Como, Italy), 52-day-old at the beginning of the experiment, were used. Rats were acclimated to individual cages under a 12-h light/dark cycle. Diets. Animals were offered standard rat food pellets (4RF18, Mucedola, Settimo Milanese, Italy; 2.6 kcal/g) and a HPF. The HPF was a paste in texture, prepared by mixing: (a) 52 % Nutella (Ferrero, Alba (TO), Italy) chocolate cream (5.33 kcal/g; 56%, 31%, and 7% from carbohydrate, fat and protein, respectively), (b) 33 % grounded food pellets (4RF18), (c) 15 % water.

Purpose

Figure 1: BE for HPF is evoked in rats by the combination of cyclic food restrictions and stress

Table 1 The Schedule Adopted to Evoke Binge Eating in R+S respect to NR+NS group.

<table>
<thead>
<tr>
<th>Group</th>
<th>NR-NS</th>
<th>R-S</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days 1-4</td>
<td>Ad lib chow</td>
<td>Ad lib chow</td>
</tr>
<tr>
<td>Days 5-6</td>
<td>Ad lib chow</td>
<td>Restricted chow 66% + HPF (2 h)</td>
</tr>
<tr>
<td>Days 7-8</td>
<td>Ad lib chow</td>
<td>Restricted chow 66% + HPF (2 h)</td>
</tr>
<tr>
<td>Days 9-12</td>
<td>Ad lib chow</td>
<td>Ad lib chow</td>
</tr>
<tr>
<td>Days 13-14</td>
<td>Ad lib chow</td>
<td>Restricted chow 66% + HPF (2 h)</td>
</tr>
<tr>
<td>Days 15-16</td>
<td>Ad lib chow</td>
<td>Ad lib chow</td>
</tr>
<tr>
<td>Days 17-20</td>
<td>Ad lib chow</td>
<td>Restricted chow 66% + HPF (2 h)</td>
</tr>
<tr>
<td>Days 21-24</td>
<td>Ad lib chow</td>
<td>Ad lib chow</td>
</tr>
<tr>
<td>Days 25</td>
<td>Restricted chow 66% + HPF (2 h)</td>
<td>Stress</td>
</tr>
</tbody>
</table>

Figure 2: Convolutional presaturated 1H (a) spectra: zgcppr, (b) cpmg, (c) kid and 2D COSY (d). Lipids, macromolecules and small metabolites contributions are labelled: Ala: alanine; Ac: acetate; Lac: lactate; Glu: glutamate; Cr: creatinine; Gly: glycine; Myo: myo-inositol; Ser: sarcosine; GPC: glycerophosphocholine; PA: fatty acid; Thr: threonine; Lys: lysine; α-Glc: α-glucose; β-Glc: β-glucose; Val: valine; Leu: leucine; N(CH3)2: phospholipid component. The quantification of metabolites. Peak areas were determined using Mnova software (MestReNova, ver. 8.1.0, 2012 Mestrelab Research S. L., Santiago de Compostela, Spain). Statistical analysis. Data were reported as means ± standard errors. P<0.05 was considered to indicate a statistically significant difference. (Figure 3) Discussion- Significant differences were found in small metabolites such as glutamine, lactate, and glycero phosphochoylcholine. Another important difference is in the amount of lipids more evident in the R+S animals model of BE compared to relative NR-NS animals. Lipids amount may be is related to the Adipocyte fatty acid binding protein (A-FABP), that has been suggested to play an important role in fat metabolism linking obesity and the metabolic syndrome. The variation in A-FABP plasma levels reflect alterations in nutritional status and proinflammatory cytokines in patients with anorexia nervosa. The results will be used for the study of innovative pharmacotherapeutic strategies. References- 1 Cifani C. et al. A preclinical model of binge-eating elicited by yo-yo dieting and stressful exposure to food: effect of sibutramine, fluoxetine, topiramate and midazolam. Psychopharmacology 2009;204:113–25. 2 Micioni Di B MV et al. 2010 Appetite 54:663. 3 Violante IR et al. Cerebral activation by fasting induces lactate accumulation in the hypothalamus. Magn Reson Med. 2009; 62:729-83. 4 Engle MJ. et al Biochimica et Biophysica Acta 2001; 1511: 369-80.