Eating disorders in adolescents: Correlations between symptoms and central control of eating behavior

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1. Introduction

There is considerable evidence showing that eating disorders (ED) and obesity rates are increasing worldwide (CDC, 2009; Lobstein, Baur, & Uauy, 2004; Tremblay & Lariviere, 2009). To understand the unhealthy eating behavior in obese individuals, it is necessary to consider the complex etiology of ED (Babio, Canals, Pietrobelli, Pérez, & Aria, 2009; Neumark-Sztainer, 2009; Schwartz & Henderson, 2009).

Eating disorders represent a heterogeneous diagnostic category that includes anorexia nervosa, bulimia nervosa, and eating disorder not otherwise specified (Schwartz & Henderson, 2009).

Bulimia nervosa is characterized by persistent binge eating and compensatory behaviors (e.g. self-induced vomiting, laxative use) to prevent weight gain (APA, 2000).

Studies have estimated that both anorexia and bulimia nervosa affect between 1% and 4% of the general population (Fairburn, 2003; Hoek, 2006; Hudson, Hiripi, Pope, & Kessler, 2007). Binge eating disorders exhibit binge eating episodes without the occurrence of compensatory methods, followed by intense feelings of shame and guilt (APA, 2000), affecting approximately 3% to 5% of the general population and about 20% to 30% of obese subjects (Azevedo, Santos, & Fonseca, 2004; Machado, Machado, Goncalves, & Hoek, 2007; Siqueira, Appolinario, & Sichieri, 2005).

Unhealthy eating habits in children and adolescents could be related to pubertal development, obesity, body satisfaction, as well as family and peer influences. Especially, obesity affects body-related self-esteem and satisfaction with appearance — factors that increase the risk of developing ED (Tremblay & Lariviere, 2009).

Since the second half of the 20 century, the possible mechanisms of ED and obesity have been attributed to hypothalamus, the key region in the central nervous system (SNC), which involves feedback control of appetite, food intake and energy storage (Konturek et al., 2005). Important advances have been made in the characterization of hypothalamic neuronal networks and neuropeptide transmitters, along with circulating peptides that send signals to the brain regarding the body’s nutritional status (Stanley, Wynne, McGowan, & Bloom, 2005), that control eating behavior.

It is currently accepted that the appetite is regulated by an interplay of hormonal an neural mechanisms, in brief, the arcuate nucleus of the hypothalamus houses two opposing sets of neural circuitry, an appetite-stimulating with neurons that express neuropeptide Y (NPY) and agouti and related protein (AgRP); and an appetite-inhibiting with neuron that expresses alpha melanocyt...
hormone (α-MSH), cocaine and amphetamine regulated transcript (CART), that are influenced by peripheral signals, such as leptin (anorexigenic factor), insulin (anorexigenic factor) and ghrelin (orexigenic factor) (Bloom, 2007).

However, the present acknowledgment is not able to describe the interactions between obesity, ED and anorexigenic and orexigenic central pathways, especially in adolescents. In this way, the aim of this study was to verify the relationship between symptoms of ED (binge eating and bulimia nervosa) and body image dissatisfaction with body mass index (BMI), anorexigenic and orexigenic factors in adolescents.

2. Methods

2.1. Participants

In an Ambulatory for Obesity treatment, a total of 32 adolescents (13 obese [BMI ≥ 95th] and 19 non-obese [25th ≤ BMI ≤ 85th]) (CDC, 2000), aged 14–19 years were selected and pubertal stage was assessed by means of the Tanner, stage 3 or 4 (Tanner & Whitehouse, 1976). This cross-sectional study was carried out in accordance with the principles of the Declaration of Helsinki and was formally approved by the ethical committee of the Federal University of São Paulo (#0135/04). Informed consent was obtained from all subjects and/or their parents.

2.2. Study protocol

Subjects were medically screened, had their pubertal stage assessed, anthropometric profile measured (height, weight, BMI and body composition) and symptoms of ED and body image dissatisfaction evaluated. After this, obese adolescents were submitted to a multidisciplinary long-term therapy as previously described (data not shown) (Lofrano-Prado et al., 2009).

2.3. Anthropometric measurements

Subjects wearing light clothing and no shoes were weighed on a Filizola scale to the nearest 0.1 kg. Height was measured to the nearest 0.5 cm by using a wall-mounted stadiometer (Sanny, model ES 2030). BMI was calculated as body weight divided by height squared. Body composition was estimated by plethysmography (Bod Pod®, Concord, CA) (Fields & Goran, 2000).

2.4. Serum analysis

Blood samples were collected after an overnight fast (≈08:00 a.m.). After collection, blood was immediately centrifuged for 10 minutes at 5,000 rpm and stored at −80 °C. Serum leptin, ghrelin, TNF-α, NPY, α-MSH, MCH and AgRP concentrations were measured using ELISA kits from Phoenix Pharmaceuticals Inc. (Belmont, California, USA). Insulin was determined by radioimmunoassay by the Molecular Research Center, Inc. kits (Cincinnati, OH, EUA).

2.5. Questionnaires

All questionnaires were applied as self-report questionnaires by a psychologist in a separate and quiet room.

2.5.1. BSQ — Body Shape Questionnaire

Translated into Portuguese and validated for the Brazilian population (Cordás, 2000) and validated for the Brazilian population (Manetta, 2002). A 34-item measure of body dissatisfaction assesses the frequency of concern and distress about body size/shape. The subjects could be classified into light (between 81 and 110 points), moderate (between 111 and 140), and severe (more than 140 points) body image dissatisfaction (Cooper, Taylor, Cooper, & Fairburn, 1987).

2.5.2. BES — Binge Eating Scale

Translated into Portuguese and validated for the Brazilian population (Freitas, Lopes, Coutinho, & Appolinario, 2001). BES is a 16-item self-reported questionnaire, designed specifically to identify behavioral and cognitive characteristics of binge eating. Based on BES scores, disturbed eating behavior is classified into three different levels of severity: non-bingers (scoring 17 or less), moderate bingers (scoring between 18 and 26), and severe bingers eaters (scoring 27 or above) (Gormally, Black, Daston, & Rardin, 1982).

2.5.3. BITE — Bulimic Investigation Test Edinburgh

Translated into Portuguese and validated for the Brazilian population (Cordás & Hochgraf, 1993). BITE is a 33-item self-report measure, designed to identify subjects with symptoms of bulimia or binge eating. The BITE consists of two subscales: the symptom scale and severity scale. Scores of the symptom scale can be subdivided into three groups: high scorers (score higher than 20); medium scorers (score between 10 and 19); and low scorers (score below 10). The severity scale measures the severity of bingeing and purging behavior, as defined by frequency (Henderson & Freeman, 1987).

2.6. Statistical analysis

All data were analyzed by STATISTICA 8.0 for Windows. Comparisons between obese and non-obese were made using independent t-tests. Correlation analyses between symptoms of eating disorders and body image dissatisfaction with BMI, leptin, insulin, ghrelin, TNF-α, α-MSH, MCH and NPY were performed by Pearson’s correlation test. Stepwise multiple regressions of BES, BITE and BSQ as dependent factors were performed. Data are presented as means ± sd. Significance were set at p < 0.05.

3. Results

Clinical characteristics of the volunteers are presented in Table 1. Obese adolescents had significantly higher BMI, body mass, fat mass (%), insulin, leptin and TNF-α than the non-obese. On the other hand, the former presented lower NPY, α-MSH and AGRP values. Obese

<table>
<thead>
<tr>
<th>Variables</th>
<th>Adolescents</th>
<th>Non-obese</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>17.17 ± 1.87</td>
<td>15.58 ± 1.12</td>
<td>0.005</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.66 ± 0.08</td>
<td>1.65 ± 0.08</td>
<td>NS</td>
</tr>
<tr>
<td>Body mass (kg)</td>
<td>100.06 ± 13.20</td>
<td>60.68 ± 11.85</td>
<td>0.000</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>36.63 ± 5.68</td>
<td>22.18 ± 3.11</td>
<td>0.000</td>
</tr>
<tr>
<td>Fat mass (%)</td>
<td>42.37 ± 7.42</td>
<td>19.93 ± 9.37</td>
<td>0.000</td>
</tr>
<tr>
<td>Insulin (µU/ml)</td>
<td>20.18 ± 13.45</td>
<td>5.20 ± 2.78</td>
<td>0.000</td>
</tr>
<tr>
<td>Leptin (ng/ml)</td>
<td>41.02 ± 13.34</td>
<td>1.47 ± 3.00</td>
<td>0.000</td>
</tr>
<tr>
<td>Ghrelin (ng/ml)</td>
<td>6.98 ± 4.30</td>
<td>6.87 ± 8.27</td>
<td>NS</td>
</tr>
<tr>
<td>TNF-α (ng/ml)</td>
<td>379.80 ± 151.59</td>
<td>69.02 ± 42.65</td>
<td>0.000</td>
</tr>
<tr>
<td>NPY (ng/ml)</td>
<td>2.71 ± 1.68</td>
<td>7.86 ± 5.10</td>
<td>0.001</td>
</tr>
<tr>
<td>α-MSH (ng/ml)</td>
<td>4.10 ± 1.17</td>
<td>16.46 ± 3.84</td>
<td>0.000</td>
</tr>
<tr>
<td>MCH (ng/ml)</td>
<td>16.23 ± 14.09</td>
<td>12.61 ± 7.93</td>
<td>NS</td>
</tr>
<tr>
<td>AgRP (ng/ml)</td>
<td>2.56 ± 0.60</td>
<td>5.23 ± 16.33</td>
<td>0.000</td>
</tr>
<tr>
<td>BITE</td>
<td>15.46 ± 4.13</td>
<td>6.16 ± 4.02</td>
<td>0.000</td>
</tr>
<tr>
<td>BSQ</td>
<td>115.31 ± 35.72</td>
<td>64.21 ± 28.55</td>
<td>0.000</td>
</tr>
<tr>
<td>BES</td>
<td>19.38 ± 5.31</td>
<td>8.16 ± 5.62</td>
<td>0.000</td>
</tr>
</tbody>
</table>

BMI = Body mass index; TNF-α = Tumor necrosis factor-alpha; NPY = Neuropeptide Y; α-MSH = Alpha-Melanocyte Stimulating Hormone; MCH = Melanin-concentrating hormone; AgRP = Agouti and related protein; BITE = Bulimic Investigative Test Edinburgh. BSQ = Body Shape Questionnaire; BES = Binge Eating Scale.
adolescents had higher symptoms of bulimia nervosa, binge eating and body image dissatisfaction than their non-obese counterparts.

In the present study, symptoms of binge eating, bulimia nervosa and body image dissatisfaction had a positive correlation with insulin, leptin (Fig. 1) and BMI (BES r = .663, p = .000; BITE r = .732, p = .000; BSQ r = .525, p = .002). TNF-α also had a positive correlation (BES r = .697, p = .000; BITE r = .727, p = .000; BSQ r = .595, p = .000), while α-MSH (Fig. 1) and AgRP had a negative correlation with BES (r = .536, p = .002), BITE (r = .587, p = .000) and BSQ (r = .504, p = .003). No correlations were verified in ghrelin, MCH and NPY. Correlations were performed in all volunteers (obese and non-obese).

Stepwise multiple linear regression analyses with BES, BITE and BSQ as a dependent variable showed that α-MSH, insulin and TNF-α provided the best model to explain the variability in BES (r² = .79, p < .000) and BITE (r² = .78, p = .003), to BSQ, the best model is composed of leptin, BMI, fat mass (%), insulin, AgRP and TNF-α (r² = .78, p = .010).

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**Fig. 1.** Simple correlation between symptoms of binge eating scores with a) insulin, b) leptin, c) α-MSH; and bulimia nervosa scores and d) insulin, e) leptin, f) α-MSH.
This study was the first to analyze the relationship between symptoms of ED and body image dissatisfaction with BMI, fat mass (%), anorexigenic and orexigenic factors in adolescents, the main findings were 1) a strong correlation between RES, BITE and BSQ scores with factors that are involved in the central control of eating behaviors; 2) obese adolescents have higher symptoms of ED, which is probably related to circulating levels of cytokines, hormones and neuropeptides.

In adolescents, body image dissatisfaction leads to low self-esteem, negative affect, depression and changes in eating behaviors (Mori, Sekine, Yamagami, & Kagarimimori, 2009). The relationship between the level of body dissatisfaction and weight status has shown that overweight adolescents report greater body dissatisfaction than their normal weight peers (Rinderknecht & Smith, 2002). ED are related to biological, developmental, psychological and sociocultural factors (Schmidt, 2003). Our results revealed that BMI and fat mass increase the risk of developing ED and body image dissatisfaction. Similarly, Kayano et al. (2008) demonstrated that as BMI increased, the higher were the abnormal eating behaviors.

It has been postulated that pro-inflammatory cytokines may play a key role in the pathogenesis of ED (Corcos et al., 2003). In experimental animals, peripherally and centrally secreted or injected TNF-α induces changes in biochemical, behavioral and physiological parameters which have also been observed in ED patients (Plata-Salaman, 1998). Holden and Fukula (1996) have proposed a psychoneuroimmunological model of ED in which a deregulation of the immune system, involving certain cytokines (TNF-α) could initiate a cascade of reactions and biochemical interactions, which may result in either anorexia or bulimia nervosa. Nakai, Hamagaki, Tagaki, Taniguchi, and Kurimoto (2000) reported elevated TNF-α levels in individuals with bulimia nervosa. Likewise, in the present study we found a higher TNF-α in obese adolescents and a strong positive correlation between TNF-α and symptoms of ED.

Many studies have demonstrated a possible correlation between the hypothalamic control of energy balance and ED (Corcos et al., 2001, 2003; Hermosdorff, Vieira, & Monteiro, 2006; Raymond et al., 2000). Once and again, our results support this hypothesis. Insulin and leptin are the two main factors to signalize hypothalamus about energy status, both inhibit food intake, modulating neurons that express NPY, thus stimulating α-MSH release and inhibit AGRP. Therefore, whenever leptin and insulin are elevated, α-MSH will be elevated. However, obese individuals often have increased leptin. This hyperleptinemia could result in desensitization for the leptin signal, a phenomenon referred to as leptin resistance (Meier & Gressner, 2004), what could explain the lower levels of α-MSH and obese, and the negative relation between α-MSH and ED, and a positive relation with leptin, insulin and ED.

As expected, in the present study, obese adolescents had higher leptin, insulin and TNF-α plasma values than the non-obese, as well as lower values of NPY, AGRP and α-MSH. These results are in agreement with previous studies (Nicklas, You, & Pahor, 2005; Viso Gonzalez, Solano, Sanchez, Portillo, & Lovera, 2005). It is important to note that Dostalova, Sedlaclova, Papезová, Nedivková, and Haluzik (2009) found no differences in individuals with or without bulimia.

In the present study we did not find any association between ghrelin values and ED. Conversely, Tanaka et al. (2002) verified a positive relationship of ghrelin and binge eating and purging. These controversial results may be due to the sample differences since we analyzed obese and non-obese adolescents, while Tanaka et al. observed only normal weight adults.

One weakness of this study is the fact that all evaluations were performed in plasma, not in cerebrospinal fluid (CSF). Also, the shuttle of peripheral signals across blood brain barrier and receptor expression in the hypothalamus were not assessed, which could limit our conclusions. It is important to note that this is the first study addressing that insulin, leptin, α-MSH and TNF-α, could be markers of ED symptoms in adolescents, and this information is essential to prevent and treat ED. In conclusion, we could suggest that there is a link between blood levels of hormones, cytokines, neuropeptides and BMI and symptoms of bulimia, binge eating and body image dissatisfaction in adolescents. Moreover, obese adolescents are at greater risk to develop abnormal eating behaviors; however, it is not clear which is the cause and which is the consequence. Thus, future research must be conducted in order to answer these questions.

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Contributors
MCLP: design, data collection, interpretation of data and drafting the manuscript. WLP, AP, DAC, LT, CMON, LOM: data collection, analysis and interpretation of data. ST, MTM and ARD: Design and critically revising of the manuscript. All authors read and approved the final manuscript.

Conflict of Interest
Nothing to declare.

References


