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Circulating ghrelin is decreased in non-obese and obese women with binge eating disorder as well as in obese non-binge eating women, but not in patients with bulimia nervosa

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Summary Ghrelin is a peripheral gastric peptide involved in the regulation of eating behavior and energy homeostasis. While changes in ghrelin plasma levels have been found in anorexia nervosa, bulimia nervosa (BN) and obesity, no study has assessed circulating ghrelin in binge eating disorder (BED). Therefore, we measured plasma levels of this peptide in women with BED as compared to women with BN, obesity and healthy controls. One hundred and eighty-two drug-free women (56 bulimics, 13 non-obese and 34 obese BED subjects, 28 obese non-binge eating women and 51 non-obese healthy women) underwent psychopathological and nutritional assessments and blood sample collection for glucose and ghrelin assays in the morning. As compared to non-obese healthy women, both non-obese and obese BED women as well as obese non-binge eating women had significantly increased values of body weight, body mass index and body fat mass. Moreover, plasma ghrelin concentrations were significantly decreased in both non-obese ($P<0.01$) and obese ($P<0.0001$) BED women as well as in obese non-binge eating women ($P<0.001$) but not in women with BN. No significant correlations emerged between plasma ghrelin values and the frequency of binge/vomiting in BN subjects or the frequency of bingeing in BED individuals. The reduction of plasma ghrelin in non-obese and obese binge eaters as well as in obese non-binge eaters may represent a secondary change aiming to counteract their positive energy imbalance.

1. Introduction

Ghrelin is a 28-amino acid peptide initially characterized as an endogenous ligand of the growth hormone (GH) secretagogue receptor, which

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regulates the pituitary GH secretion (Kojima et al., 1999; Hosoda et al., 2000; Takaya et al., 2000). Although identified in various tissues, the highest ghrelin concentrations were found in the stomach and duodenum (Kojima et al., 1999). The physiological relevance of such a localization remained unclear up to when it was demonstrated that ghrelin is involved also in regulating food intake and energy homeostasis. Indeed, in rodents, systemic and intracerebroventricular injections of ghrelin increase food intake, fat deposition and weight gain (Tschöp et al., 2000; Wren et al., 2000; Nakazato et al., 2001; Shintani et al., 2001). Similarly to rodents, ghrelin stimulates appetite and enhances food consumption when administered intravenously to humans (Wren et al., 2001). Now, it is widely accepted that this gastric peptide is part of the peripheral system signalling to the brain short-term changes in the energy balance. In fact, in humans, circulating ghrelin progressively increases over short-term fasting and rapidly decreases after food ingestion (Ariyasu et al., 2001; Otto et al., 2001; English et al., 2002; Muller et al., 2002), suggesting that it promotes meal initiation during fasting and favours meal termination after food consumption.

The importance of ghrelin in the control of feeding behaviour in humans is further supported by the evidence that, beside short-term changes in energy balance, nutritional state and eating patterns affect circulating ghrelin. In fact, plasma ghrelin concentrations have been found to be increased in malnourished underweight subjects with anorexia nervosa (AN) (Ariyasu et al., 2001; Otto et al., 2001; Shiiya et al., 2002; Nedvidkova et al., 2003; Tanaka et al., 2003a,b; Soriano-Guillén et al., 2004), increased or normal in patients with bulimia nervosa (BN) (Tanaka et al., 2002; Tanaka et al., 2003a; Monteleone et al., 2003) and decreased in obese individuals (Tschöp et al., 2001; Shiiya et al., 2002; Soriano-Guillén et al., 2004). Moreover, in patients with AN or BN as well as in obese subjects plasma ghrelin responses to food ingestion have been reported to be suppressed, blunted or delayed (English et al., 2002; Tanaka et al., 2003b; Nedvidkova et al., 2003; Monteleone et al., 2003). After dietary interventions, plasma ghrelin concentrations have been reported to increase in obese people and to decrease in AN patients (Hansen et al., 2002; Soriano-Guillén et al., 2004).

Patients with binge eating disorder (BED) exhibit alterations of their eating behaviour similar to those of bulimics, as they compulsively binge; however, differently from people with BN, they do not engage in compensatory behaviours and, as a consequence, do not incur malnutrition. As a matter of fact, these individuals are almost always overweight or clearly obese. Therefore, both changes in the eating pattern and a positive energy imbalance occur in BED, which make investigation of ghrelin production of great interest. To the best of our knowledge, there is no information in the literature regarding plasma ghrelin levels in BED patients. Therefore, to further investigate the role of ghrelin in eating disorders, we measured morning circulating levels of ghrelin in a sample of obese and non-obese women with BED and compared them with those of non-obese healthy women, normal weight women with BN and non-binge eating obese women.

2. Methods

2.1. Subjects

A total of 182 women were recruited for the study. They were 131 outpatients attending the Eating Disorder Center of the Department of Psychiatry of the University of Naples SUN, and 51 healthy controls. None of them had participated in previous studies on ghrelin physiology. According to the criteria of the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) (American Psychiatric Association, 1990), 56 patients fulfilled the diagnosis of BN and 47 the diagnosis of BED. Diagnostic assessment was made by a trained interviewer using the Structured Clinical Interview for DSM-IV Axis I disorders (SCID-I) (First et al., 1995). Moreover, according to the obesity criteria of the World Health Organization (World Health Organization, 1998), 13 BED patients with a body mass index (BMI) $<30\ kg/m^2$ were classified as non-obese patients with BED, the remaining ones with a BMI $\geq 30\ kg/m^2$ were classified as obese patients with BED. Twenty-eight patients suffered from obesity (BMI $\geq 30\ kg/m^2$) without binge eating. All endocrine diseases known to cause obesity were excluded.

Patients with BN were all of the purging subtype, with self-induced vomiting as the main compensatory behaviour; their BMI ranged 17.29–25.56 kg/m^2. Four of them had a past-history of AN; 14 had a comorbid major depression, and seven had a comorbid anxiety disorder (two a generalised anxiety disorder, one an obsessive-compulsive disorder and four a panic disorder). None of BED women had a previous history of AN or BN; four of them had a comorbid major depression and four a comorbid anxiety disorder (three a panic disorder