Urinary cortisol and psychopathology in obese binge eating subjects.

Research report

Urinary cortisol and psychopathology in obese binge eating subjects ☆

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Abstract

Background: Investigations on the relationship between obesity, binge eating and the function of hypothalamic–pituitary–adrenal (HPA) axis have led to inconsistent results. General psychopathology affects HPA axis function. The present study aims to examine correlations between binge eating, general psychopathology and HPA axis function in obese binge eaters. Methods: Twenty-four hour urinary free cortisol (UFC/24 h) was measured in 71 obese binge eating women. The patients were administeredpsychometric tests investigating binge eating, psychopathology and clinical variables. The relationship between binge eating, psychopathology and urinary cortisol was investigated, controlling for age and BMI. Results: We found an inverse correlation between UFC/24 h and binge eating, depression, obsessive-compusive symptoms, somatization and sensitivity. In a regression model a significant inverse correlation between urinary cortisol and psychopathology was confirmed. Conclusions: Urinary cortisol levels in obese patients with binge eating disorder show an inverse correlation with several dimensions of psychopathology which are considered to be typical of a cluster of psychiatric disorders characterized by low HPA axis function, and are very common in obese binge eating patients. If these results are confirmed, UFC/24 h might be considered a biomarker of psychopathology in obese binge eaters.

Introduction

Binge eating disorder (BED) is characterized by recurrent episodes of binge eating in the absence of purging or other compensatory behaviors (American Psychiatric Association, 2000); it is thought to be a frequent condition in individuals seeking treatment for obesity (Spitzer et al., 1993). The role of HPA (hypothalamic–pituitary–adrenal) axis in obesity and its comorbidities is currently debated (Abraham, Rubino, Sinaii, Ramsey, & Nieman, 2013). Dysfunctions in the HPA axis are thought to play a role in eating disorderpsychopathology (Lo Sauro, Ravaldi, Cabras, Faravelli, & Ricca, 2008); in particular binge eating episodes are often preceded by stress and negative affect (Laessle, Schulz, 2009 and Levine, Marcus, 1997) and a growing body of research shows that cortisolreleased during stress might promote hunger and feeding behavior (Tataranni et al., 1996). Indeed, some studies found an augmented cortisol secretion as a result of laboratory stress in obese BED subjects compared to non-BED obese subjects (Gluck, 2006, Gluck et al, 2004 and Gluck et al, 2004); in another study patients who developed weight gain after a stressful event have been found to show higher twenty-four hour urinary free cortisol (UFC/24 h) than patients who did not identify a stressful event before the onset of weight gain (Vicennati, Pasqui, Cavazza, Pagotto, & Pasquali, 2009). These data might suggest the presence of higher baseline cortisol levels in some obese BED patients. However, one study examining the HPA in BED found normal cortisol suppression after dexamethasone suppression test (Yanovski, Yanovski, & Gwirtsman, 1993). Some studies that relied on single measurements of evening (Coutinho, Moreira, Spagnol, & Appolinario, 2007) and morning (Monteleone et al, 2000 and Monteleone et al, 2003) cortisol levels in women with BED reported normal levels.

Some authors also reported opposite findings. Two more recent studies in patients with BED suggested a blunted HPA function in obese patients with binge eating disorder (Larsen et al, 2009 and Rosenberg et al, 2013).

The difficulty in replicating the anomalies in HPA activity in eating disordered patients with binge eating might be related to other dimensions of psychopathology that affect HPA function.
Dysregulation of the HPA axis in humans has been documented in mood and anxiety disorders (Nemeroff et al., 1999). Particularly, a considerable amount of research has been done in posttraumatic stress disorder (de Kloet et al, 2006 and Delahanty et al, 2000), chronic fatigue syndrome (Kumari et al., 2009) and depression (Vreeburg et al., 2009); some studies have also been done on psychosis (van Venrooij et al., 2012).
It has been proposed that the alterations of the HPA axis could be specific for different disorders (Handwerger, 2009 and Sriram et al, 2012) and patients with eating disordersare known to suffer from a variety of psychiatric comorbidities (Hudson, Hiripi, Pope, & Kessler, 2007).
Given the previous findings, it appears relevant to take the effects of comorbidpsychopathology into account when studying HPA axis function in obese binge eating subjects.
Urinary free cortisol excretion rate in 24 hours (UFC/24) is an integrated measure of HPA axis function which has been proposed to characterize different phenotypes of obesity (Duclos et al, 2005 and Pasquali et al, 2008), and it has been used to investigate HPA axis activity in relation to previous stressful events in obese women (Vicennati et al., 2009).
The present study attempts to investigate whether UFC/24 h levels are associated with binge eating and/or general psychopathology in a sample of obese women with BED.

Methods and materials

Of 86 female patients initially recruited from the Center for Eating Disorders of the University of Torino, 4 were excluded from the study because of known endocrinedisorders, 7 were excluded because they were diagnosed with a psychotic or bipolar spectrum disorder. Two patients returned incomplete psychometric tests. Two patients had urinary cortisol values above the normal range; they were referred to an endocrinologic assessment and excluded from the study sample. A total of 71 patients met inclusion criteria, accepted to participate in the study and completed thepsychometric assessment.
Sociodemographic and psychometric data are reported in Table 1 and Table 2.

Table 1.
Baseline demographic data and cortisol values. BMI = body mass index.

	Mean	SD
Age (years)	40.5	12.4
BMI (kg/m^2)	40.8	7.5
Urinary cortisol (µg per L in a 24 h sample)	22.8	17.1

Table 2.
Psychometric tests.

		Mean	SD
	BES	22.7	10.7
SCL90R	Somatization	21.2	9.7
	Obsessive-compulsive	14.9	8.6
	Interpersonal sensitivity	13.6	7.5
	Depression	21.0	12.2
	Anxiety	13.2	9.3
	Hostility	6.3	5.0
	Phobic anxiety	4.5	4.8
	Paranoid ideation	7.8	5.9
	Psychoticism	8.6	8.1
	Total	120.3	67.5

SCL-90-R = Symptom Checklist 90 Revised; BES = Binge Eating Scale.

The BMI of the sample was 40.8 ± 7.5 kg/m2 (mean ± SD). The diagnostic assessment was made by psychiatrists with experience in the diagnosis and treatment of eating disorders; BED was diagnosed following the criteria proposed by DSM-IV-TR for further study. Patients with illnesses like diabetes or other endocrine disorders were excluded. Patients diagnosed with schizophrenia or related psychoses or bipolar disorder were also excluded; patients diagnosed with anxiety disorder not otherwise specified,dysthymic disorder and major depressive disorder of mild to moderate intensity were included as long as they were not taking psychotropic drugs at the time of assessment. The patients were administered the Binge Eating Scale (BES) and the Symptom Checklist 90 Revised (SCL-90-R) at their first visit to our Centre. The BES is a self-administered questionnaire designed to assess the behavioral and psychological correlates of binge eating (Gormally, Black, Daston, & Rardin, 1982); the SCL-90-R is a self-report tool used to assess several dimensions of psychopathology (see Derogatis, Rickels, & Rock, 1976 for details). HPA activity was assessed dosing UFC per liter of urine in a 24-hour urine sample. UFC (µg/day) was evaluated by CMIA (chemiluminescent microparticle-based immunoassay) automated on Architect i2000 platform (Abbott Diagnostics, Abbott Park, IL, USA). It is a non-invasive, integrated measure that can be collected in the subject's environment. Patients were instructed to collect all urine for 24 hours starting from the next day at 8:00 am, and then were requested to bring the sample to the laboratory of our hospital.
The study has been carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki). Ethical approval for the study protocol was also given by the local Ethics Committee. All the patients provided written informed consent to the study.

Data analysis

For statistical analysis, we used the Statistical Package for Social Sciences (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.). Partial correlations were calculated between UFC/24 h and psychopathologyvariables, using age and BMI as confounding variables. The significant correlations were further tested with bootstrapping by creating 1000 bootstrap samples and robust confidence intervals were computed. The variables

which were significantly associated with urinary cortisol were then used as predictors in a regression model, where urinary cortisol was the dependent variable, and BMI and age were used as covariates to control for confounding. In case of multicollinearity between the psychological variables, principal component analysis (PCA) was used to obtain uncorrelated principal components to be used in the regression model as predictors.

Results

Partial correlations

Significant correlations were found between UFC/24 h and the following variables: BES ($r = -.29$; $p = .016$, 95% CI = −.09, −.45); somatization ($r = -.24$; $p = .041$, 95% CI = −.04, −.42); obsessive–compulsive ($r = -.32$, $p = .007$, 95% CI = −.11, −.48); sensitivity ($r = -.30$, $p = .012$, 95% CI = −.07, −.5) and depression ($r = -.30$, $p = .011$, 95% CI = −.47, −.11). Age and BMI were used as covariates; coefficients and confidence intervals were calculated with bootstrapping (1000 bootstrap samples).

The psychometric scales that showed a correlation with urinary cortisol were examined in a correlation matrix as a preliminary step to fitting the regression model (Table 3). We identified a significant degree of correlation between the variables: five out of ten of the pairwise correlations were greater than 0.7 in absolute value, indicating harmful collinearity (Slinker & Glanz, 1985). The other five correlations (0.32–0.59), although smaller, should also be considered problematic for a regression model (Van Steen et al., 2002).

Table 3.
Correlation matrix for BES and SCL-90-R variables. Som = somatization; obs-comp = obsessive–compulsive; sensit = sensitivity; depr = depression. All the correlations are significant ($p < 0.01$).

	BES	SCL-90-R som	SCL-90-R obs-comp	SCL-90-R sensit	SCL-90-R depr
BES	1				
SCL-90-R som	0.32	1			
SCL-90-R obs-comp	0.48	0.78	1		
SCL-90-R sensit	0.56	0.59	0.81	1	
SCL-90-R depr	0.54	0.74	0.88	0.83	1

Principal component analysis

An explorative principal component analysis was performed on the five psychometric scales to investigate the underlying structure of our variables, as suggested by Van Steen et al. (2002) as a means to manage problematic multicollinearity. The Kaiser–Meyer–Olkin measure of sampling adequacy verified the adequacy of the sample for the analysis (KMO = 0.84). An initial analysis was run to obtain eigenvalues for each factor in the data. The analysis identified only one component (Component 1), which had eigenvalues over Kaiser's criterion of 1 and explained 73.7% of the variance. Component scores were obtained with the Anderson–Rubin method for all

the subjects. Given that only one factor was extracted no rotation was used. Table 4 reports component loading. All the variables had high loadings on the component (from 0.6 to 0.9).

Table 4.
Component matrix. Loading of the psychopathology variables on the component obtained with principal component analysis.

	Component 1
SCL-90-R depression	0.94
SCL-90-R somatization	0.94
SCL-90-R obsessive compulsive	0.89
SCL-90-R sensitivity	0.81
BES	0.65

Regression model

Component 1 obtained in the principal component analysis was used in a linear regression model with UFC/24 h as the outcome variable; age and BMI were added as covariates in order to avoid confounding effects. The model was statistically significant ($F = 3.45$; $p = .021$; $R2 = .13$). Component 1 predicted significantly UFC/24 h (Beta = −.33, $p = .015$). Coefficients and confidence intervals were calculated with bootstrapping (1000 bootstrap samples).

The graph in Fig. 1 shows the relationship between Component 1 and UFC/24 h.

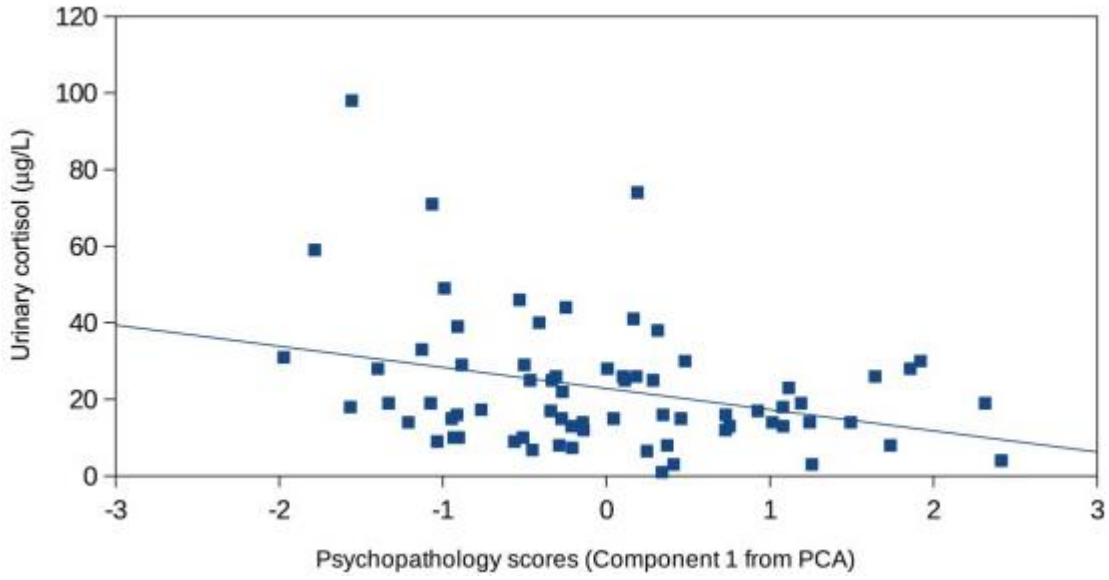

Fig. 1.

The graph shows the relationship between the concentration of urinary cortisol (µg/L in a 24 h urine sample) and Component 1 obtained with the Anderson–Rubin method in principal component

analysis (PCA). Component 1 is loaded by the Binge Eating Scale (BES) and somatization, obsessive–compulsive, depression and sensitivity scales from SCL-90-R.

Discussion

The present study examined correlations between binge eating, generalpsychopathology and UFC24/h in obese binge eating women. Several associations were found that are consistent with published studies.

The inverse association between HPA axis function and depression is consistent with some studies on chronic (Pintor et al., 2007) and atypical (Fries, Hesse, Hellhammer, & Hellhammer, 2005) depression. It is important to note that overeating is one of the symptoms of atypical depression, and that patterns of subjective and objective binge eating also tend to have a chronic course (Peterson et al., 2012).

Somatization too shows an inverse correlation with UFC24/h, which is consistent with many studies identifying lower levels of HPA axis activity in disorders characterized by functional somatic symptoms, like fibromyalgia and low back pain (Griep et al., 1998). Intriguingly, recent studies highlighted the high prevalence rates of obesity in fibromyalgia patients (Ursini & Naty, 2011).

The negative correlation between sensitivity and UFC/24 h is consistent with a study reporting an association between rejection sensitivity and hypocortisolism (Tops, Riese, Oldehinkel, Rijsdijk, & Ormel, 2008).

The BES showed an inverse correlation with UFC/24 h in our sample.

If confirmed, this finding would be in line with the cited studies which suggest a down-regulation of the HPA axis in patients with binge eating (Larsen et al, 2009 and Rosenberg et al, 2013).

However, our results appear to be at odds with Gluck et al., who found higher cortisolsecretion in obese women with BED compared to obese women without BED, and the women with BED also showed a nearly significant greater area under curve in cortisol response after a cold pressure test (Gluck, 2006, Gluck et al, 2004 and Gluck et al, 2004). The authors interpreted these results as evidence for a hyperactive HPA system in obese BED patients. The discrepancy in these results can be explained in several ways. It is possible that HPA activation under stress might show a different property of the system compared to baseline levels (i.e., the subjects might have a lower mean HPA function, but a higher response to stress). Secondly, baseline cortisol levels were assessed by means of dosing cortisol in a single blood sample. As noted by Larsen and colleagues, a single measure of cortisol might not be the best way to characterize HPA function (Larsen et al., 2009). UFC/24 h is an integrated measure of HPA function that assesses the production during the whole day, and might provide a more stable estimate of HPA function. Lastly, it is important to remember that this study doesn't have a control group, making thus impossible to compare UFC/24 h values in our patient population with those of healthy subjects and define whether they appear relatively “high” or “low”. However, the present data show a relationship between urinary cortisol and different dimensions of psychopathology. Raison and Miller suggested that insufficient glucocorticoid signaling does not necessarily imply an absolute deficiency, but rather it signifies that the glucocorticoid message is not getting through in an adequate manner in order to perform its regulatory function (Raison & Miller, 2003). According to these authors, glucocorticoid insufficiency (and associated psychological symptoms) could exist even in the case of glucocorticoid hypersecretion (for example, if sensitivity in the target tissues is reduced) (Raison & Miller, 2003). Therefore, testing whether UFC/24 is associated with psychological symptoms and testing whether UFC/24 is lower than normal in obese binge eaters might represent two different research questions. Our study investigated the first issue; the second requires future studies comparing UFC/24 in obese subjects with BED, obese subjects without BED and in healthy controls.

The principal component analysis and the regression model suggest that eating and other psychopathology dimensions are highly correlated in obese binge eaters, and that psychopathology in general is inversely correlated with HPA function assessed with urinary cortisol (see graph in Fig. 1).
Some authors have described a cluster of psychiatric disorders and physical conditions (i.e. atypical depression, burn-out, somatizations, chronic fatigue) that are thought to have a common origin in prolonged stress and are characterized by insufficient glucocorticoid function ("hypocortisolism") (Fries et al, 2005, Heim et al, 2000 and Raison, Miller, 2003). Some of the symptom scales that show inverse correlations with UFC/24 h in our sample seem to fit in this description: depression, hyperfagia (binge eating) and rejection sensitivity (two features of atypical depression), and somatization. The fact that they load on the same component in the PCA might suggest that they are an expression of the same pathophysiological mechanism. The question could thus be raised whether BED might be considered part of so-called "hypocortisolemic" disorders. Future studies should compare associations of urinary cortisol with psychopathology in populations with obesity and binge eating, in patients with atypical depression and somatization and in healthy controls, taking into account stressful life events.

This study has some limitations.

It was not possible to identify the separate contributions of the psychopathology values in the regression model, because of the substantial correlations between the psychopathology dimensions that generated multicollinearity between the predictors. The size of the correlations we found between psychopathology and urinary cortisol is small. Nonetheless, the sample size appears adequate for the analysis, and the fact that the results are confirmed by bootstrapping suggests that our estimates of the correlations are robust. Another limitation pertains to the lack of an assessment of stressful life events. Stressful life events are known to be frequent in binge eating (Pike et al., 2006) and obese (Gunstad et al., 2006) patients, and they can lead to HPA alterations (Ehlert, 2013, Gunstad et al, 2006 and Miller et al, 2013). There is preliminary evidence that these alterations might mediate the relationship between stress and overeating (Tomiyama et al, 2011 and Tryon et al, 2013). Although clinical experience and the scientific literature support the frequent presence of stressful life events in this patient population, in this study lifetime and recent stressful events were not assessed, therefore we cannot directly test hypotheses about the role of stress in determining psychopathology through the modulation of HPA function.

In conclusion, the present study suggests the presence of correlations between binge eating, general psychopathology and UFC/24 h. The spectrum of symptoms that show an overlap with binge eating and correlate inversely with UFC/24 h is considered by some authors typical of hypocortisolemic stress-related conditions. Future studies on psychopathology and HPA function in obese BED patients could provide a framework for achieving a better understanding of the causes, pathophysiology, and possibly new treatment approaches for obese binge eating patients.

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