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Cortisol response to the Trier Social Stress Test in obese and reduced obese individuals

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ABSTRACT

Impact of body weight loss, body fat distribution and the nutritional status on the cortisol response to the Trier Social Stress Test (TSST) was investigated in this study. Fifty-one men (17 non-obese, 20 abdominally obese and 14 reduced obese) and 28 women (12 non-obese, 10 peripherally obese and 6 reduced obese) were subjected to the TSST in fed and fasted states. The TSST response was determined using salivary cortisol measurements. The nutritional status (being fed or fasted) had no effect on the cortisol levels during and following the TSST. Reduced obese men exhibited lower cortisol levels than non-obese men. Cortisol levels in obese men were not different from those of non-obese and reduced obese subjects. In women, there was no significant difference between groups. These finding suggest that weight status in men influences cortisol reactivity to a psychological stress and the different responses seen among genders could be linked to the different fat distributions that characterize men and women.

1. Introduction

In humans, high levels of glucocorticoids have been reported to promote the deposition of abdominally located visceral fat and its associated metabolic alterations (Björntorp, 1993, 2001; Chalew et al., 1995; Drapeau et al., 2003; Epel et al., 2001; Marin et al., 1992; Pasquali and Vicennati, 2000). One of the most acknowledged examples of the link existing between hypercortisolemia and abdominal (visceral) obesity is the Cushing's syndrome patient, in whom normalization of cortisol levels is followed by a decrease in visceral fat (Peeke and Chrousos, 1995; Rebuffe-Scrive et al., 1988). In addition, psychological and socioeconomic factors leading to sustained HPA axis activation have also been shown to promote visceral obesity (Larsson et al., 1989; Rosmond and Björntorp, 1999, 2000; Wing et al., 1991). In male cynomolgus monkeys, social stress-induced hypercortisolemia leads to the deposition of intra-abdominal adipose tissue (Jayo et al., 1993). Similarly, in dominated cynomolgus monkeys, social subordination, which stimulates HPA axis, is also strongly associated with a preferential deposition of visceral fat (Shively et al., 1997).

Increase in the HPA axis activity seems to not only be a source of visceral obesity but may also be a consequence of excessive deposition of abdominal fat, which has the capacity to release cytokines stimulating the HPA axis (Mastorakos et al., 1993; Yudkin et al., 1999). We indeed recently demonstrated that a reduction in waist circumference in men could reduce the awakening cortisol response (ACR) (Therrien et al., 2007), which is used to assess the HPA axis function (Fries et al., 2009; Schmidt-Reinwald et al., 1999). The proposition that visceral fat can stimulate the cortisol secretion to stress based on ACR needs to be further substantiated, using other types of stress such as the one we propose in the present study.

The observation that visceral fat loss can reduce the activity of the HPA axis contrasts with findings demonstrating that weight loss and associated behaviors restricting energy intake increase HPA axis activity. In laboratory animals, weight loss and fasting are associated with a HPA axis activation that has been demonstrated to be rather extreme in the obese Zucker rat, in which fasting may represent a psychogenic stress (Timofeeva and Richard, 1997). Studies conducted in humans have also demonstrated that fasting and weight loss may increase circulating levels of cortisol (Beer et al., 1989; Dallman et al., 2004; Fichter et al., 1986; Vance and Thorner, 1989) to potentially increase appetite in order to 'defend' an existing body weight (Doucet et al., 2000). This stimulating response appears to be more apparent in women in which subcutaneous fat could eventually protect against stress.

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The goal of the present study was to investigate the effect of body weight and fat loss on the secretion of cortisol in response to the Trier Social Stress Test (TSST). The TSST is a standardized psychosocial stress test that has been extensively used. Because of the apparent importance of the nutritional status on the HPA axis activity, the TSST was performed in fed and fasted states. Based on previous data (Therrien et al., 2007), we predicted (i) that weight loss in men, in whom fat is predominantly deposited in the abdominal cavity, would reduce (compared to non-obese subjects) stress-induced cortisol secretion, and (ii) that weight loss in women, in whom fat is largely subcutaneous, would increase the stress response and that the increase would be enhanced by food restriction.

2. Methods

2.1. Subjects

Eighty two healthy men (n = 51) and women (n = 28), aged between 23 and 51 years old, were recruited through media advertisements or advertising posters disseminated on the *Université Laval* campus. Women who were selected had normal menstrual cycles and were not using oral contraceptives. Exclusion criteria were any history of depression or psychiatric disorders, cardiovascular diseases, smoking and regular alcohol consumption (more than 2 alcoholic beverages per day or 9 per week). Subjects had to be medication free during the protocol and were required to abstain from alcohol consumption and physical activity from 24 h before until the end of the testing days and from caffeine during the testing days.

The subjects were selected to form three groups according to their body mass index (BMI), waist circumference (WC) and weight loss: Non-obese—BMI < 27 kg/m^2, WC < 100 cm for men and < 90 cm for women; obese—BMI 30–35 kg/m^2, WC > 100 cm for men and < 100 cm for women; reduced obese—minimal weight loss of 5 kg, still trying to loose weight or just stabilized (maximum two weeks). Prior to weight loss, the reduced obese had a BMI > 30 kg/m^2 (WC > 100 cm in men and < 100 cm in women). Reduced obese subjects all lose weight through solely improving their lifestyle habits (dieting or dieting + physical activity). We verified that no drastic diets were used. Self-reported weight loss was accepted, but when available, a proof of the initial weight and historic of weight loss was provided.

All subjects were invited to the laboratory for three visits within a two-month period. At their first visit, subjects were submitted to medical examination, blood sampling, psychological assessment and anthropometric measurements. Participants were then asked to come back twice to the laboratory in order to perform the TSST in both fed and fasted states (see below). This study protocol was approved by the Medical Ethic Committee of *Université Laval* (project # 152-99) and all participants signed a written consent.

2.2. Medical examination and general psychological assessment

During the first visit to the laboratory, subjects underwent a medical exam consisting of a brief auscultation and a medical history to ascertain their health status. All subjects were asked to answer questionnaires about eating disorders [Eating Disorders Inventory; EDI-2 (Garner, 1991) and Binge Scale (Hawkins and Clement, 1980)], eating behaviors [Three-Factor Eating Questionnaire; TFEQ (Stunkard and Messick, 1985)] and depression symptoms [Beck Depression Inventory; BDI (Spielberger, 1983)]. Participants were also screened for the presence of psychiatric and personality disorders through the Structured Clinical Interview for DSM-III [SCID (Spitzer et al., 1990)]. The scores for all these questionnaires served as excluding factors for some of the subjects with eating behavioral and psychiatric disorders liable of affecting the HPA axis activity. One woman from the obese group was excluded because she was determined as suffering from binge eating disorder.

2.3. Anthropometric measurements

Body weight was assessed on a balance beam scale, to the nearest 0.1 kg with participants in underwear, and height was measured to the nearest centimeter. The BMI was calculated by dividing the weight by the height in m^2. WC was measured twice at the midpoint between the lowest rib and iliac crest, and the hip circumference was measured twice at the maximum width of the buttocks (Lohman et al., 1988). Body density was determined by hydrodensitometry (Behnke and Wilmore, 1974), and the Siri formula was used to estimate the percentage body fat from body density (Siri, 1956). The closed-circuit helium dilution method was used to assess residual lung volume (Meneely and Kaltreider, 1949). Because the protocol was extended on a few weeks (maximum two months), participants were weighted on each visit.

2.4. Psychosocial stress test

The TSST essentially consists of two tasks: a mental arithmetic task and a free speech in front of a fictive audience (Kirschbaum et al., 1993). The test has been shown to be a reliable protocol to induce a moderate psychological stress in a laboratory setting. This protocol is also one of the most effective to provoke a noticeable HPA response because it combines both uncontrollable and social-evaluative characteristics (Dickerson and Kemeny, 2004).

Subjects performed the TSST in fed and fasted states. Because of the known habituation effect between the first and second administration of this test (Epel et al., 2000), the order of the two conditions was randomly assigned to each subject. In the fed–state test, participants were instructed to eat a standardized breakfast at home at around 0800 h and to arrive at 1100 h to the laboratory where a meal (buffet type meal—*ad libitum* intake) was served at 1130 h. In the fasted state test, participants were instructed to refrain from eating from 2000 h (the day before) until the end of the TSST. They were however allowed to drink water *ad libitum* and also asked to arrive at the laboratory at 1100 h. At 1500 h, subjects were introduced to the TSST (2 min) and were then exposed to a mental arithmetic task (5 min) consisting of serial subtractions. Participants were thereafter asked to prepare a speech (10 min) and to perform in front of the fictive audience (5 min). The speech was videotaped. Because subjects had to perform the TSST twice, the numbers in the arithmetic task and the speech topic were changed at each visit. Participants rested for 60 min after the TSST. Saliva was collected before and immediately after the stress as well as 10, 20, 30, 40 and 60 min after the TSST. A blood sample was also taken 30 min before the beginning of the test, to measure estrogen levels in women.

2.5. Anxiety assessment

Anxiety in relation to the TSST was assessed using a French version of the Spielberger's state-trait anxiety inventory (STAI) (Spielberger, 1983). The state portion of the STAI, which measures the actual anxiety level of a subject, was administered immediately before and after the TSST. The difference between these two anxiety levels was used as an indicator of the effect of the TSST on the anxiety status.

2.6. Saliva and blood sampling

Saliva samples were collected with a Salivette sampling device (Sarstedt; Nuembrecht, Germany), consisting of a standard centrifugation tube filled with a small cotton swab. Saliva samples were centrifuged at 6000 rpm during 30 min and then stored at −25 °C and salivary cortisol levels were determined by radioimmunoassay (Medicorp inc., Montreal, Canada). Plasma concentrations of estradiol in women were measured by radioimmunoassay (Medicorp inc., Montreal, Canada).

2.7. Statistical analysis

Data are presented as means ± standard errors in the text, tables and figures. A two-way ANOVA was first performed to determine the main and interaction effects of the factors 'group' and 'sex' on all variables. Data from state anxiety measured before and after the TSST were analyzed using a four-way ANOVA (nutritional status, sex, group, time and interactions), where time was defined as a repeated measure. Regarding the cortisol levels, a crossed-nested design was used to analyze (i) the effects of four experimental factors (group, nutritional status, sex and time), and (ii) the block effect of a random factor (subject). Time was analyzed as a repeated measure. The value measured just before the TSST was used as a covariate. The same statistical techniques were used to analyze cortisol increases (deltas), which were calculated as the maximum cortisol levels reached following the TSST minus the baseline cortisol values. For some variables, the graphical analyses of residuals with predicted values revealed a relationship between variances and means. The logarithm transformations were then applied as judged appropriate and statistical results from these parameters were expressed with the log-transformed values. Non-transformed data are however presented in tables and figures. The univariate normality assumption was verified using a graphical representation and the Brown and Forsythe's variation of Levene's test statistics and was used to verify the homogeneity of variances. Multivariate normality was verified with Mardia's tests. The Tukey Kramer test was used for post hoc comparisons. The Pearson correlation coefficient was used to measure relationship between variables. The results were considered significant with p values ≤ 0.05. The data were analyzed using the statistical package programs SAS v9.1.3 and JMP software v3.2.2 (SAS Institute Inc.).

Because of the known influence of sex hormones on the response to psychosocial HPA axis stressors (Kajantie and Phillips, 2006), we assessed the influence of estrogen levels on cortisol for women and there was no significant effect (p = 0.43).

3. Results

Descriptive characteristics of the participants in the three groups of subjects are presented in Table 1. In the reduced obese group, mean body weight loss was 11.0 ± 4.9 kg (12.5 ± 5.8 kg for men; 8.9 ± 2.2 kg for women), which corresponded to a decrease of 11.0 ± 4.5% from the initial weight (12.2 ± 5.4% for men; 9.6 ± 3.0% for women). Reduced obese individuals all kept a stable weight during the protocol, except one man who regained 2.3 kg between the two TSST sessions. Testing on that patient was delayed until the