Brief report

Enhanced cortisol suppression in eating disorders with impulsive personality features

Marina Díaz-Marsá,⁎ Jose L. Carrasco, Elena Basurte, Jerónimo Sáiz, Juan J. López-Ibor, Eric Hollander

Department of Psychiatry, Hospital Clínico San Carlos, C/ Martín Lagos s/n, 28040 Madrid, Spain
Department of Psychiatry, Hospital Ramón y Cajal, Ctra Colmenar Km 9, 20034 Madrid, Spain
Department of Psychiatry, Mount Sinai School of Medicine, One Gustave Levy, New York City, United States

Received 22 May 2006; received in revised form 22 December 2006; accepted 24 June 2007

Abstract

Evidence of both blunted and enhanced cortisol suppression with the dexamethasone test (DST) is available in eating disorders (ED), suggesting that different subtypes of ED might be characterized by distinct neurobiological stress response dysfunctions. Other evidence indicates that ED patients with impulsive clinical features might have enhanced cortisol suppression similar to patients with impulsive personality disorders. A group of 52 patients with restrictive anorexia, binge eating-purging anorexia and bulimia nervosa were studied with a very low dose (0.25 mg) dexamethasone test and measures of phenomenology, personality and impulsivity. Patients with bulimic symptoms had significantly higher rates of cortisol suppression than controls and than restrictive anorectic patients. Percent cortisol suppression showed a strong and significant correlation with the patient’s score on the Barratt Impulsiveness Scale. A hypersensitive cortisol response to dexamethasone, which might reflect hypothalamic-pituitary-adrenal axis dysfunctions might be specifically associated with impulsive subtypes of eating disorders.

© 2007 Elsevier Ireland Ltd. All rights reserved.

Keywords: Eating disorders; Cortisol; Dexamethasone; Impulsive disorders; Personality disorders; Impulsivity

1. Introduction

Research with the dexamethasone suppression test (DST) in eating disorders (ED) in the last two decades demonstrated that cortisol suppression after a 1-mg dose of dexamethasone was inhibited in 40–50% of patients (Schweitzer et al., 2001; Estour et al., 1990; Brambilla et al., 1993), which closely resembles the findings in major depression. However, research in recent years has suggested that non-suppression is more frequent in anorectic than in bulimic patients (Fichter et al., 1990; Neudeck et al., 2001). Furthermore, research with a low-dose (0.5 mg) dexamethasone suppression test suggests that cortisol suppression might be even larger than normal in those ED patients with associated posttraumatic stress features, which are particularly frequent in ED patients with bulimic and with other impulsive symptoms (Diaz-Marsa et al., 2000; Steiger et al., 2001). These observations are concordant with studies on impulsive personality disorders reporting enhanced cortisol suppression with a 0.5 mg dexamethasone test (Schweitzer et al., 2001; Grossman et al., 2003) and with a 0.25 mg dexamethasone test (Carrasco et al., 2003) when compared with normal subjects. Therefore,
hypersensitive HPA axis response to dexamethasone might be associated with the presence of impulsive clinical features across several diagnostic conditions.

Doses of 0.5 mg and 0.25 mg of dexamethasone can be used for detection of excessive cortisol suppression. However, the specificity of the 0.5 mg DST might be reduced due to high rates of cortisol suppression in normal controls, ranging from 50 to 85% (Barton et al., 2002). Lower doses of dexamethasone (0.25 mg) for the DST have been used in previous studies with impulsive disorders demonstrating marked sensitivity and discrimination between patients and controls (Carrasco et al., 2003). In this study, a 0.25 mg dexamethasone dose was used with the aim of increasing discrimination of cortisol hypersuppression between patients and controls and also between different clinical subtypes of eating disorders.

2. Methods

2.1. Selection of samples

The study was approved by the institutional review board. After complete description of the study to the subjects, written informed consent was obtained.

Patients with a current diagnosis of anorexia or bulimia nervosa were included in the study. Subjects were selected consecutively at the Eating Disorders Unit of the hospital and evaluated by a senior psychiatrist with structured interviews for mental disorders (SCID-I) and for personality disorders (SCID-II).

A group of 52 female patients with DSM-IV eating disorders – 9 restrictive anorexia nervosa (ANr), 14 binge eating-purging anorexia (ANbp) and 29 bulimia nervosa (purging type) – were selected. Patients had a severity score on the Clinical Global Impression scale (CGI) ≥ 4 (moderate) and were free of medication for at least 2 weeks at the time of the study.

Age distribution (22.5 years, s.d 4.8 in ANr, 21.9, s.d. 5.6 in ANb-p, 23.7, 6.3 in BN and 24.3, s.d. 4.2 in controls) did not differ significantly between the groups. Mean duration time of the disorder was 2.4 years (range 10.1–1.3 years). Average body mass index (BMI) was 16.8 in anorexia nervosa (range 14.9–17.7) and 18.9 in bulimia nervosa(range 17.5–21.4). Amenorrhea was present in all patients with AN, but the duration was variable (range 7–42 months).

Patients who had lost weight over the last 2 weeks were excluded from the study until they stabilized or started to gain weight. Unstable physical conditions requiring hospitalization constituted an exclusion criterion, as did medical diseases that could affect hormonal regulation. Current diagnosis of major depression or substance use disorders and lifetime bipolar or schizophreniform disorders were also criteria for exclusion. The control group included 28 healthy women recruited from a health care prevention program and matched with the ED group for age and sex.

2.2. Clinical and psychological variables

Bulimic symptoms were rated with the BITE questionnaire (Henderson and Freeman, 1987). Personality disorders were evaluated with the SCID-II interview for DSM-IV axis II. Personality features were assessed with the Eysenck Personality Questionnaire (Eysenck, 1967) and the Temperament and Character Inventory (Cloninger et al., 1993). Impulsivity was specifically assessed with the Barratt Impulsiveness Scale (Patton and Barratt, 1992). All patients and controls underwent the entire clinical and personality evaluation.

2.3. Biological tests

Biological tests followed a washout period of at least 2 weeks for anxiolytic medication and 3 weeks for other medications and drugs (5 weeks for fluoxetine).

Subjects were admitted to the Psychoendocrinology Research Unit at 7.30 a.m. of day 1. An IV catheter was inserted at 8.00 a.m. allowing for blood sampling exempt from the stress-inducing effects of later needle sticks. After 30 min, a blood sample was taken for plasma cortisol. At 11.00 p.m. of day 1 the participants were administered an oral capsule containing 0.25 mg of dexamethasone and, on day 2, at 8.00 a.m., blood samples were taken again for cortisol with the same method as on day 1. Subjects were tested under strictly controlled conditions, including minimal activity, 8 h fasting and sleep from 11.00 pm on the previous night.

Blood samples were extracted and immediately placed on ice; after centrifugation the plasma was kept frozen at −70 °C until analysis. Cortisol plasma levels were measured by RIA techniques using commercially available assays. The intrassay and interassay coefficients of variation were less than 10%.

2.4. Statistical tests

Between-group comparisons employed analysis of covariance (ANCOVA) for differences in percent cortisol suppression and Chi-square test for differences in the rate of non-suppressor subjects. Within the ED group, relationship between variables were explored by Pearson’s correlation coefficient. All statistical analyses were two-tailed with a 0.05 level of significance.
3. Results

Impulsivity scores on the Barratt scale were significantly higher in patients with bulimia (45, s.d. 9.5) and in patients with binge eating-purging anorexia (36.4, s.d. 9.2) than in controls (19.3, s.d. 6.8) (F(3,80)=8.1, \( P<0.01 \)). No differences were found between restrictive anorectic patients (21, s.d. 5.6) and controls (\( P=0.69 \)). Significant differences in other personality measures between controls and the different clinical subtypes of ED (Table 1) were found for novelty seeking, harm avoidance, neuroticism and persistence.

No significant differences in baseline cortisol were found between ED patients and controls, or within the different subgroups of ED (ANr, AN b-p and BN).

Cortisol non-suppression was defined accordingly to standard practice as a cortisol concentration greater than 5 \( \mu \)g/dl after dexamethasone administration. In the ED group, 66.7% of patients were non-suppressors versus 94.4% of subjects in the control group (88.8%) (Chi square \( F(3, 50)=10.01, \ P<0.01 \)). In addition, significant differences were found between patients with anorexia (71.2% were non-suppressors) and patients with bulimia nervosa (58.8% were non-suppressors) (Chi square \( F(3,50)=7.2, \ P<0.05 \)) (Table 2).

ANOVA of percent cortisol suppression showed significant differences between the clinical subtypes of ED. Patients with binge eating-purging anorexia and with bulimia nervosa had greater percent cortisol suppression than controls and than patients with restrictive anorexia nervosa (\( F(2,50)=8.2, \ P<0.05 \)) (Table 2).

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Personality dimensions in patients and controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPQ</td>
<td>Neuroticism</td>
</tr>
<tr>
<td>AN r</td>
<td>38.4*</td>
</tr>
<tr>
<td>AN bp</td>
<td>48.4*</td>
</tr>
<tr>
<td>BN</td>
<td>51.2**</td>
</tr>
<tr>
<td>Control</td>
<td>13</td>
</tr>
<tr>
<td>TCI</td>
<td>Novelty seeking</td>
</tr>
<tr>
<td>Anr</td>
<td>13.4</td>
</tr>
<tr>
<td>AN bp</td>
<td>33.3***</td>
</tr>
<tr>
<td>BN</td>
<td>40.6***</td>
</tr>
<tr>
<td>Control</td>
<td>35.4</td>
</tr>
<tr>
<td>Abbreviations: Anr, restrictive anorexia. Anbp, binge eating-purging anorexia. BN, bulimia nervosa. TCI, Temperament and Character Inventory. EPQ, Eysenck Personality Questionnaire.</td>
<td></td>
</tr>
</tbody>
</table>

*Difference with controls \( P<0.05 \).

**Difference with controls \( P<0.01 \).

***Difference with other subtypes of eating disorders \( P<0.05 \).

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Effects of administration of 0.25 mg oral dexamethasone on cortisol in patients with eating disorders and normal controls (Anorexia R: restrictive anorexia nervosa. Anorexia b-p: binge eating and purging anorexia nervosa. Bulimia N: bulimia nervosa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline cortisol</td>
<td>Anorexia restrictive</td>
</tr>
<tr>
<td>&lt;0=5 ( \mu )g/dl</td>
<td>28.6%</td>
</tr>
<tr>
<td>&gt;5 ( \mu )g/dl</td>
<td>71.4%</td>
</tr>
<tr>
<td>Percent (%):</td>
<td></td>
</tr>
<tr>
<td>Cortisol suppression</td>
<td>( p&lt;0.05 )</td>
</tr>
</tbody>
</table>

To explore a possible relationship of hypothalamic-pituitary-adrenocortical (HPA) axis dysfunction with criteria for impulsive personality features, the sample of ED patients was divided into patients with BPD (five diagnostic criteria for BPD), with subsyndromal BPD (three or four criteria for BPD) and without BPD. Significant differences were found for percent cortisol suppression between groups (ED with BPD 71.1%, s.d. 32.7; ED with subsyndromal BPD 48.7%, s.d. 28.0 and ED without BPD 29%, s.d. 21.3) (ANOVA, \( F(2,50)=10.2, \ P<0.01 \)).

Percent cortisol suppression significantly correlated with impulsivity-related measures like the BITE severity score (\( r=0.29, \ P<0.05 \)) and the total score of the Barratt Impulsiveness Scale (\( r=0.51, \ P<0.05 \)).

The difference of cortisol levels was not significantly altered by reanalysis of age, body-mass index, duration of illness, duration of amenorrhea, anxiety scores or depression scores (on the Hamilton scales) as covariates.

4. Discussion

Enhanced cortisol suppression on the DST is found in this sample of ED patients, reflecting some abnormalities in the HPA axis response mechanisms. This HPA abnormality has also been reported in association with impulsive symptoms and traits in patients with severe personality disorders (Carrasco et al., 2003; Westrin et al., 2003, Lange et al., 2005). Consequently, enhanced cortisol suppression might also be expected in a subgroup of eating disorders with prominent impulsive symptoms, as is frequently observed in a number of bulimic patients (Neudeck et al., 2001). In our sample, cortisol suppression is significantly associated with the presence of bulimic symptoms (bulimia nervosa and binge eating-purging anorexia nervosa).
anorexia), while no significant difference in cortisol suppression was found between restrictive anorexia and controls. Other possible explanations for differences between restrictive and bulimic patients, such as weight loss, amenorrhea or baseline hypercortisolism in restrictive anorexia were eliminated by statistical analysis.

In addition, the intensity of cortisol suppression is statistically associated with the presence of borderline personality features. The relationship of increased HPA axis feedback inhibition with affective instability has been reported in previous studies of patients with borderline personality disorder (Grossman et al., 2003). Emotional instability is often present in ED patients (Díaz-Marsá et al., 2000), especially in those with bulimic symptoms, and might therefore be related to enhanced suppression of cortisol.

Some authors have proposed that increased cortisol feedback inhibition in impulsive disorders results from the association with comorbid posttraumatic stress features (Rinne et al., 2002; Grossman et al., 2003) and is related with findings in PTSD (Yehuda et al., 2004). In eating disorders, childhood traumatic events are particularly frequent in patients with bulimic symptoms (Lacey, 1990) and in eating disorders with comorbid borderline personality disorder (Grilo et al., 1996). Consequently, hypersensitive DST results in a subgroup of ED patients might be related to history of trauma, a factor that should be further explored.

In summary, enhanced cortisol suppression in our sample of eating disorders is significantly associated with the severity of bulimic symptoms and with impulsive personality features, which might reflect an association of a subtype of ED with other impulsive disorders.

The conclusions are limited by the small size of the ED subgroups. Defining a consistent association of HPA axis increased feedback inhibition with specific clinical subtypes of eating disorders requires larger samples; nevertheless, the results in our study might at least show a tendency for an association with impulsive eating disorders. The absence of stability measures for the DST is another limitation of the study. The possibility that DST findings are influenced by external and internal state variables related to stress cannot be excluded. To reduce the risk of confounding variables, strict control of associated psychopathological factors and external conditions during test administration was attempted throughout the study.

Acknowledgement

This study was partially supported by a grant from the Spanish Government (Health Research Fund).

References


