Hypothalamic–pituitary–adrenal axis response in borderline personality disorder without posttraumatic features

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Summary Hypothalamic–pituitary–adrenal (HPA) axis sensitivity was investigated in 32 non-medicated patients with borderline personality disorder without comorbid post-traumatic syndromes and in 18 normal individuals using a modified dexamethasone suppression test (0.25 mg). Enhanced cortisol suppression was found in the patients *v.* controls ($P<0.05$) and the percentage of participant's with non-suppression was smaller in the patient (34%) than in the control group (89%) ($P<0.01$). Baseline cortisol levels in the patients were also lower than in the controls ($P<0.05$). The 0.25 mg dexamethasone suppression test reveals increased feedback inhibition of the HPA in borderline personality disorder.

Declaration of interest None.

Hypothalamic–pituitary–adrenal (HPA) axis response in borderline personality disorder is a controversial issue according to previous reports in the scientific literature. Several studies published two decades ago reported high rates of non-suppression with the 1 mg dexamethasone test in patients with borderline personality features, suggesting an association of the condition with affective disorders (Sternbach *et al*, 1983). However, recent studies of the disorder suggest some similarities with HPA axis disturbances found in post-traumatic stress disorder (PTSD). Studies of people with PTSD have reported lower cortisol levels than in a normal comparison group, increased lymphocyte glucocorticoid receptor density and enhanced cortisol suppression with a 0.5 mg dexamethasone test (Rinne *et al*, 2002; Yehuda *et al*, 2004). On the other hand, several studies with the 0.5 mg dexamethasone test have reported enhanced cortisol suppression in patients with borderline personality disorder and comorbid post-traumatic symptoms (Grossman *et al*, 2003, Lange *et al*, 2005), but not in patients with this personality disorder but without PTSD. However, cortisol suppression was very high in the normal control group in these studies, ranging from 70% to 85%, which might have reduced the discriminatory power of the 0.5 mg test. A preliminary study with a lower dose (0.25 mg) of dexamethasone (Carrasco *et al*, 2003) reported enhanced cortisol suppression in borderline personality disorder with no comorbid PTSD compared with other personality disorders and demonstrated high specificity for detection of cortisol suppression. However, the conclusions were limited by the absence of a comparison group of normal individuals.

METHOD

Patients were selected at the emergency room for repetitive self-aggressive behaviour (at least two episodes of self-aggression in the preceding 6 months) and were evaluated by a senior psychiatrist with the Structured Clinical Interview for DSM–IV Axis I Disorders (SCID–I; First *et al*, 1995) and Axis II Personality Disorders (SCID–II; First *et al*, 1997), as well as with the Childhood Trauma Questionnaire (Bernstein *et al*, 2003) and the Zanarini Rating Scale for Borderline Personality Disorder (ZAN–BPD; Zanarini *et al*, 2003).

Fifty-one patients with a diagnosis of borderline personality disorder were selected. Patients with comorbid PTSD ($n=4$) were excluded, as were patients with current major depression ($n=9$) or substance dependence ($n=4$) and a lifetime history of bipolar disorder ($n=1$) or schizophreniform disorder ($n=1$). Finally, 32 patients with no major metabolic or hormonal disease entered the study and were admitted to the hospitalisation unit for a wash-out period to eliminate medication and other drugs. The control group included 18 healthy individuals recruited from a healthcare prevention programme and matched with the patient group for age and gender.

Biological tests followed a wash-out period of at least 1 week for anxiolytic medication and 3 weeks for other medications and illicit drugs (5 weeks for fluoxetine). Participants were admitted to the psychoendocrinology research unit at 07.30 h on day 1. An intravenous catheter was inserted at 08.00 h, allowing subsequent blood sampling exempt from the stress-inducing effects of needle-sticks. After 30 min, a blood sample was taken for measurement of plasma cortisol. At 23.00 h on day 1 the participants were administered an oral capsule containing 0.25 mg dexamethasone, and on day 2 at 08.00 h blood samples were taken again for cortisol measurement. Participants were tested under strictly controlled conditions, including minimal activity, 8 h fasting and sleep from 23.00 h the previous night.

Between-group comparisons employed analysis of covariance (ANCOVA) for differences in percentage cortisol suppression and chi-squared tests for differences in the rate of non-suppressor participants. Within the patient group relationships between variables were explored using Pearson's correlation coefficients. All statistical analyses were two-tailed with a 0.05 level of significance.

RESULTS

Distribution of age (patients, mean 30.6 years, s.d=6.4; controls, mean 29.7 years, s.d.=5.5) and gender (patients, 59% female; controls, 61%) showed no significant difference between groups. Across all groups, cortisol suppression was 55% (s.d.=31.4) in women and 50% (s.d.=35.0) in men, with no significant difference ($t=0.52$, d.f.=41, $P=0.6$).

Cortisol non-suppression was defined as a post-test cortisol level >5 μg/dl. In the borderline personality disorder group, 10 out of 29 patients (34%) were non-suppressors, *v.* 14 of 16 control participants (88%) ($\chi^2=11.6$, d.f.=1, $P<0.01$). Analysis of covariance revealed that the patient group had significantly lower cortisol levels pre-test ($F=4.0$, d.f.=1, $P<0.05$) and post-test ($F=19.8$, d.f.=1, $P<0.01$) compared with controls, as well as a significantly greater percentage cortisol suppression ($F=11.09$, d.f.=1, $P>0.01$) (Table 1). The difference in cortisol levels was not significantly altered by reanalysis with age, anxiety or depression scores as covariates.

Percentage cortisol suppression significantly correlated with severity of disorder on the Zanarini scale (r=0.42, P<0.05) but not with scores on the Childhood Trauma Questionnaire (r=0.068, P=0.73). Scores on the trauma questionnaire were higher in the patient group (mean 30.1, s.d.=8.1, range 16–54) than the controls (mean 23.2, s.d.=9.7, range 15–48; t=3.0, d.f.=66, P<0.01).

DISCUSSION

Significantly low baseline cortisol levels and enhanced cortisol suppression with 0.25 mg dexamethasone in borderline personality disorder without comorbid PTSD seem to be contrary to findings in previous studies (Rinne *et al*, 2002; Grossman *et al*, 2003; Lange *et al*, 2005) reporting enhanced cortisol suppression in borderline personality disorder to be associated specifically with PTSD symptoms. The relationship of enhanced cortisol suppression and borderline personality disorder in our study is further supported by significant correlation with severity of disorder (ZAN–BPD) and the lack of significant correlation with childhood trauma scores.

Interestingly, the rate of comorbid PTSD in our patient sample (10%) was lower than that reported in previous studies (Grossman *et al*, 2003; Lange *et al*, 2005), which found rates of PTSD comorbidity of 25–50%. This suggests that the patients in our sample might have been clinically different from those in other studies, who were recruited by advertisements or from veterans' hospitals or facilities for abused women. Our sample specifically included patients with a common symptom (repetitive self-aggression) associated with impulsivity and affective instability (Siever & Davis, 1991). This might have increased homogeneity, thereby favouring detection of biological abnormalities in borderline personality disorder, which is composed of different clinical and biological domains.

The different composition of the sample might also explain the discrepancy of our results with previous studies reporting high salivary baseline cortisol levels and high rates of dexamethasone non-suppression in women with borderline personality disorder (Lieb *et al*, 2004). In addition, methodological differences in cortisol measurement might also lead to different results. We used a laboratory method with strictly controlled conditions of environmental stress, including 30–60 min of relaxed delay before sample extraction. Ambulatory conditions for cortisol salivary sampling in the previously mentioned study might not be free of external stress influences, which could account for increased cortisol levels.

The very low dose (0.25 mg) of dexamethasone might be responsible for the strong group effect which was not found in previous studies using 0.5 mg doses. As predicted, 0.25 mg dexamethasone produced milder cortisol suppression in the control group than the 0.5 mg dose as reported in previous studies (31% *v.* 60–80%) (Rinne *et al*, 2002; Grossman *et al*, 2003; Lange *et al*, 2005). Furthermore, 65% of the patients in our study were categorised as complete suppressors (cortisol level <5 μg/dl) compared with only 12% of controls, suggesting that the 0.25 mg dexamethasone test could be useful for discriminating abnormal HPA axis functioning in personality disorders.

In conclusion, our results show a pattern of low plasma cortisol levels and enhanced cortisol suppression in a 0.25 mg dexamethasone suppression test in individuals with borderline personality disorder with no PTSD compared with healthy controls. Increased HPA feedback inhibition probably reflects increased lymphocyte glucocorticoid receptor density, which might in turn be secondary to previous intense and persistent stress in both disorders (Yehuda *et al*, 2004). However, these results apply to a specific subgroup of patients selected by the presence of repetitive self-aggressive behaviours in the previous 6 months, and should not be generalised to all people with borderline personality disorder.

Table 1 Cortisol suppression in the 0.25 mg dexamethasone test in the borderline personality disorder (BPD) and control groups

	BPD group	Control group
Cortisol level, μg/dl: mean (s.d.)		
Baseline[1]	17.2 (5.4)*	20.8 (7.0)
Post-test[2]	5.7 (5.5)**	13.9 (6.4)
Cortisol suppression, %: mean (s.d.)[2]	63.2 (30.1)**	31.5 (30.5)
Post-test cortisol levels, *n* (%)		
0–≤5 μg/dl	19 (66) b	2 (12)
>5–10 μg/dl	5 (17)	3 (19)
>10 μg/dl	5 (17)	11 (69)

1. BPD group n=32, control group n=18.
2. BPD group n=29, control group n=16.
*P<0.05, **P<0.01.

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