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Brief report

Basal activity of the hypothalamic–pituitary–adrenal axis in patients with depersonalization disorder

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Abstract

Depersonalisation disorder may occur during severe anxiety or following a traumatic event, suggesting a possible role of stress hormones. This study investigated basal activity of the hypothalamic–pituitary–adrenal (HPA) axis in patients with depersonalisation disorder. Salivary cortisol levels were measured at four time points over 12 h in patients with depersonalisation disorder ($N = 13$), major depressive disorder (MDD, $N = 14$) and healthy controls ($N = 13$). Beck Depression Inventory scores were significantly higher in depersonalised subjects than controls, while MDD subjects demonstrated higher scores than both groups. Basal cortisol levels of depersonalised subjects were significantly lower than those of MDD subjects but not healthy controls. These results point to reduced basal activity of the HPA axis in depersonalisation disorder. This pilot study supports the distinction between depersonalisation disorder and major depressive disorder which should be examined in a larger sample.

Keywords: Depersonalisation disorder; Hypothalamic–pituitary–adrenal axis; Salivary cortisol

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1. Introduction

Depersonalisation is a subjective experience of being detached from one's mental processes or disconnected from one's body. It is frequently accompanied by *derealization,* a sense that the outside world is strange or unreal. Depersonalisation has received little research attention despite its etiology being unknown.

The DSM-IV defines depersonalisation disorder (DD) as *"persistent or recurrent experiences of depersonalisation"* which are *"sufficiently severe and persistent to cause marked distress"*. A recent case series found that the illness usually had a chronic course and caused marked interpersonal impairment (Simeon et al., 1997). Transient experiences of depersonalisation are known to occur in healthy individuals, particularly in association with stress or fatigue or following ingestion of psychomimetic drugs (Simeon and Hollander, 1993). Depersonalisation may also occur in neurological conditions, for example, temporal lobe epilepsy (Kenna and Sedman, 1965), and psychiatric disorders, including severe anxiety and depression (Brauer et al., 1970). Despite its occurrence in other conditions, depersonalisation may exist as a primary disorder where the symptoms pre-date other disorders and/or do not invariably coexist with them (Simeon et al., 1997).

The pathophysiology of DD is not understood. A biological basis for the disorder has been suggested (Sierra and Berrios, 1998), prompted in part by the association with organic conditions and pharmacological challenge (Simeon et al., 1995). Abnormalities in the HPA axis are well recognized in a significant minority of patients with depression (Scott and Dinan, 1998). Indeed there is some overlap in the symptoms of DD and those of major depression, for example, anhedonia and lack of emotional reactivity (Simeon et al., 1997), although in patients with primary DD, both anxiety and depression as measured by standardized self-report scales tend to be moderately elevated (Lambert et al., 2001). Preliminary studies have suggested reduced levels of serum cortisol in DD patients in contrast to depressives (Dubinina et al., 2000; Morozova et al., 2000).

Salivary cortisol samples are convenient to obtain and provide a reliable estimate of plasma cortisol (Goodyer et al., 1996). The objective of this study was to provide a preliminary investigation of the basal activity of the HPA axis using measures of salivary cortisol in patients with depersonalisation disorder compared with depressed patients and healthy controls.

2. Methods and materials

2.1. Subjects

Thirteen subjects (six male; seven female) were recruited from the Maudsley Hospital Depersonalisation Research Unit database [mean duration of illness = 16 years (range 0.5–29 years)]. All patients had received a psychiatric assessment and conformed exclusively to DSM-IV criteria for depersonalisation disorder. In addition, these patients were evaluated with the Present State Examination (Wing et al., 1974) and scored greater than one on either or both of the depersonalisation/derealization items, and had a Dissociative Experiences Scale depersonalisation taxon score greater than 13 (Simeon et al., 1998; mean = 35.7, range 15–68). None had major depression.

Fourteen patients with major depressive disorder (MDD, six male; eight female) recruited from General Practice clinics in the Newcastle area and 13 healthy volunteers (six male; seven female) recruited by advertisement were used as comparison groups. MDD patients currently met DSM-IV criteria for major depressive disorder on the basis of a standard clinical interview and did not meet the above criteria for depersonalisation disorder. None of the subjects had post-traumatic stress disorder or a history of substance abuse. All were psychotropic medication-free for a minimum of 4 weeks before testing, and were free from endocrine disorder or any serious medical condition. All subjects completed the Beck Depression Inventory (Beck et al., 1961). After complete description of the study to the subjects, written informed consent was obtained.

2.2. Measures

Samples for salivary cortisol measurement were collected in Salivette tubes (Sarstedt, Leicester, UK) at 08.00, 12.00, 16.00 and 20.00 h and stored at −25°C. Salivary cortisol was measured using a direct I^{125} disequilibrium radioimmunoassay. The assay sensitivity (defined as twice the standard deviation of maximum binding) was 0.1 nmol/l, the inter-assay variation was less than 10% and the intra-assay variation was less than 7.3%.

Salivary cortisol data were subjected to repeated measures analysis of variance (ANOVA) with time as the within- and diagnosis as the between-group factors. Logarithmic transformations (base 10) were applied to the data to normalize the distribution. Post hoc analyses were carried out using Fisher's Least Significant Difference (LSD) procedure across the time points combined.

3. Results

The three groups did not differ on age (depersonalised mean = 38.0 years, range = 27-58; MDD mean = 35.7, range = 21-55, control mean = 36.15, range = 22–55) or sex ($\chi^2 = 0.04$, d.f. = 2, $P = 0.98$). Beck Depression Inventory scores differed significantly between groups ($F = 58.43$, d.f. = 2,37, $P < 0.001$). MDD subjects (mean = 35.93, S.D. = 7.37) scored significantly higher than depersonalised subjects (mean = 18.54, S.D. = 12.22) and controls (mean = 1.46, S.D. = 1.81). Depersonalised subjects also scored significantly higher than controls (LSD, $P < 0.001$ for all groups).

Repeated measures ANOVA of salivary cortisol demonstrated a significant effect of time ($F = 112.9$, d.f. = 3,108, $P < 0.0005$) and a trend towards a significant effect of diagnosis ($F = 2.71$, d.f. = 2,36, $P = 0.08$). Post-hoc analysis showed depersonalised subjects to have lower cortisol levels than MDD subjects (LSD, $P = 0.026$; see Fig. 1), but there was no difference between depersonalisation patients and controls (LSD, $P = 0.21$) or MDD patients and controls (LSD, $P = 0.29$).

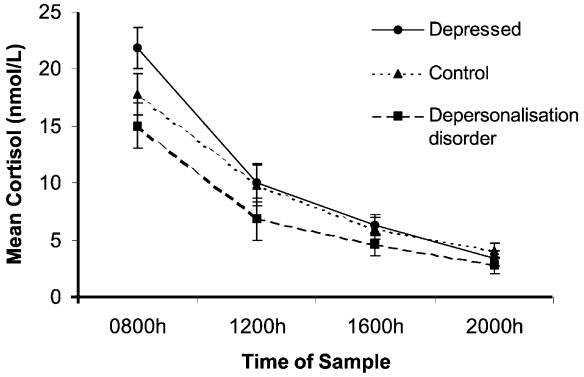

Fig. 1. Mean salivary cortisol values (±S.E.M.), 08.00 h–20.00 h for depressed ($n = 14$) and depersonalisation disorder ($n = 13$) patients and controls ($n = 13$). The depressed group had significantly elevated values compared with the depersonalisation disorder group ($P = 0.026$, see text for full statistics). Untransformed means are reported for clarity.

There was no significant interaction between time and diagnosis ($F = 0.12$, d.f. = 6,108, $P = 0.99$).

There were no significant correlations between overall cortisol output (calculated as trapezoid area under the curve) and BDI scores for either the MDD (Pearson's $r = -0.255$, $P = 0.38$) or depersonalisation group ($r = 0.137$, $P = 0.65$).

4. Discussion

Altered basal activity of the HPA axis is found in several psychiatric disorders. Increased basal cortisol secretion has been demonstrated in depressive illness (Scott and Dinan, 1998), whilst reduced HPA activity has been shown in chronic fatigue syndrome (Demitrack et al., 1991), post-traumatic stress disorder (Yehuda, 1998) and peri-menstrual mood changes (Odber et al., 1998). This preliminary study found that patients with depersonalisation disorder showed significantly lower basal cortisol secretion than patients with MDD and confirms recent work published in the Russian literature (Dubinina et al., 2000; Morozova et al., 2000). This result supports the existence of depersonalisation disorder as a condition with a pathophysiology, as reflected in the functioning of the HPA axis, distinct from depression,

despite the presence of moderately elevated BDI scores in many of the depersonalised subjects. It is also consistent with psychophysiological research that suggests reduced arousal in depersonalised individuals (Kelly and Walter, 1968) and preliminary functional neuroimaging data showing reduced cortical responses to emotive stimuli (Phillips et al., 2000). We failed to show a significant difference between healthy controls and either of the two patient groups, possibly due to the relatively small numbers studied and the limited time frame of our measures, but also because measures of basal HPA function may be relatively insensitive. Dysfunction of the HPA axis in depersonalisation disorder and related disorders may be more sensitively detected by examining the response of the HPA axis to provocation challenge (Gold et al., 1986). Indeed neuroendocrine studies of chronic fatigue syndrome have indicated that provocation tests are more sensitive to underlying deficits in cortisol secretion than resting or baseline measures (Parker et al., in press). The lack of effect in our depression group may reflect the less severe nature of their illness. Correlations between the BDI and non-suppression of cortisol secretion have been well documented (Schotte et al., 1997) although other rating scales with greater emphasis on physiological symptoms may have been more sensitive. Further neuroendocrine studies of activated HPA function may make a significant contribution to understanding the aetiology and pathophysiology of depersonalisation disorder.

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