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Associations of childhood trauma with hypothalamic-pituitary-adrenal function in borderline personality disorder and major depression

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Summary
Background: Alterations of the hypothalamus-pituitary-adrenal (HPA) axis are hallmarks in major depressive disorder (MDD) and there is some evidence about similar patterns in borderline personality disorder (BPD). This study examines HPA axis abnormalities with respect to clinical characteristics in both BPD ($n = 24$) and MDD patients ($n = 33$) as well as in healthy control participants ($n = 41$).
Method: A 0.5 mg dexamethasone suppression test was administered to evaluate basal cortisol release and HPA feedback sensitivity via salivary cortisol. Traumatic experiences in childhood as well as severity of borderline and depressive symptom severity and dissociation were obtained by self-report questionnaires.
Results: Compared to the healthy control group, BPD and MDD patients exhibited both enhanced cortisol concentrations before and after the administration of 0.5 mg dexamethasone. Higher cortisol levels were positively correlated to a history of childhood trauma, current dissociative symptoms and severity of borderline and depressive symptoms. Regression analyses revealed that some aspects of early trauma were associated with cortisol release before and after dexamethasone, whereas psychopathology did not contribute to the regression model.

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Conclusions: HPA dysfunctions appear to be related rather to childhood trauma than to psychopathology in adulthood. Exposure to childhood trauma may contribute to long-lasting alterations in HPA activity and might enhance the risk for the development of later mental disorder.

1. Introduction

Dysfunctions of the hypothalamic-pituitary-adrenal (HPA) axis have been proposed to play an important role in the psychopathology of major depressive disorder (MDD). Hypersecretion of cortisol is a prominent neuroendocrine finding in MDD (Pariante and Lightman, 2008; Schlosser et al., 2011) and there is increasing evidence that alterations in HPA activity may also contribute to borderline personality disorder (BPD) (Zimmerman and Choi-Kain, 2009; Wingenfeld et al., 2010b). Likewise, enhanced basal cortisol concentrations were also reported for BPD patients (Lieb et al., 2004; Wingenfeld et al., 2007a), but alterations of the HPA axis function in BPD seem to be influenced by comorbid symptomatology. Comorbid depressive symptoms were found to be positively related to cortisol levels in BPD, whereas severity of posttraumatic stress symptoms was negatively associated to basal cortisol release (Wingenfeld et al., 2007a).

In addition to the assessment of basal cortisol levels, the dexamethasone suppression test (DST) has extensively been used to detect abnormal HPA axis feedback regulation. Several studies demonstrated that depressed patients failed to suppress endogenous cortisol release after dexamethasone administration (Handwerger, 2009), indicating a reduced feedback sensitivity (Holsboer, 2000; Pariante and Miller, 2001; Pariante and Lightman, 2008). In BPD, findings were heterogeneous and DST results again varied by patterns of comorbid psychopathology (Wingenfeld et al., 2007b, 2010b; Zimmerman and Choi-Kain, 2009). A reduced cortisol suppression has been associated with comorbid depression (Rinne et al., 2002). Of note, reduced cortisol suppression to dexamethasone was also obtained in non-depressed BPD patients (Lieb et al., 2004), indicating that reduced feedback inhibition in BPD may depend not only on additional MDD diagnosis. However, there are also inconsistent results showing increased feedback inhibition in BPD patients (Carrasco et al., 2007).

Alterations of the HPA stress response system are supposed to be an important vulnerability factor for developing MDD (Dedovica et al., 2010) and might also influence some of the symptomatology associated with BPD (Wingenfeld et al., 2010b). Although the origin of these HPA axis abnormalities still remains not fully understood, traumatic experiences in childhood are supposed to play a major role in HPA axis irregularities (Heim et al., 2008a). Preclinical and clinical studies have frequently presumed that early life stress has long-lasting effects on the activity of the HPA axis by altering glucocorticoid receptor functioning (Kaufman et al., 2000; Teicher et al., 2003; Heim et al., 2008b). Likewise, exposure to childhood trauma is recognized as major antecedent for BPD and MDD (Zanarini et al., 1997; Johnson et al., 1999; MacMillan et al., 2001; Molnar et al., 2001). Consequently, HPA axis dysregulations have been suggested to act as one potential mechanism that mediates the effects of early life adversities on developing mood-related psychiatric symptoms.

In MDD, neuroendocrine research offered considerable evidence for a link between childhood maltreatment experiences and altered HPA function (Heim et al., 2008b). In BPD patients with a history of sustained childhood abuse, Rinne et al. (2002) also observed HPA axis dysregulations, but the relation between early traumatization and HPA alterations in BPD remain to be sufficiently clarified. It has been speculated that distinct symptom profiles may have different neuroendocrine correlates (Zimmerman and Choi-Kain, 2009) as, for example, dissociative symptoms were shown to be correlated with HPA reactivity (Simeon et al., 2007). Moreover, abnormal HPA axis functions have also been reported in other psychiatric disorders related to trauma experience like posttraumatic stress disorder (PTSD) and stress-related bodily disorders (e.g. fibromyalgia) (Heim et al., 2000; Wingenfeld et al., 2007c). Interestingly, and in contrast to MDD, the some of these findings suggested PTSD and bodily disorders to be associated with hypocortisolism (Heim et al., 2000; Yehuda, 2002; Wingenfeld et al., 2007c). However, HPA abnormalities related to childhood trauma experiences have also been found in the absence of current and lifetime psychopathology (Carpenter et al., 2009; Klaassens et al., 2009). In sum, research on the link between childhood adversities and HPA axis dysfunctions has revealed contradictory findings with both increased and decreased cortisol levels, suggesting that factors like different types of maltreatment and the psychiatric sequelae of early life stress contribute differentially to the observed HPA irregularities (Miller et al., 2007; Flory et al., 2009).

The objective of our study was twofold. Firstly, we compared basal cortisol levels and feedback sensitivity of the HPA axis between patients with MDD and BPD and healthy control subjects, as previous results were inconsistent, especially for BPD patients. We hypothesized that MDD as well as BPD patients would show an enhanced basal cortisol secretion and a reduced feedback sensitivity of the HPA axis in comparison to the healthy control group. Secondly, we further aim to investigate the association of childhood traumatic experiences and psychopathology with cortisol release, hypothesizing childhood trauma to be potent predictor of HPA axis dysregulations.

2. Methods

2.1. Participants

The clinical group consisted of 24 patients with BPD and 33 patients with MDD as primary diagnosis. All patients were consecutively recruited from the Clinic of Psychiatry and Psychotherapy Bethel, Ev. Hospital Bielefeld, and at the Department of Psychosomatic Medicine and Psychotherapy, University Medical Center Hamburg-Eppendorf & Schoen-Klinik Hamburg-Eilbek, Germany. The control group included