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Increased testosterone levels and cortisol awakening responses in patients with borderline personality disorder: Gender and trait aggressiveness matter

Juliane Rausch[a], Andrea Gäbel[a], Krisztina Nagy[a], Nikolaus Kleindienst[b], Sabine C. Herpertz[a], Katja Bertsch[a,*]

[a] Department for General Psychiatry, Center of Psychosocial Medicine, University of Heidelberg, Germany
[b] Department of Psychosomatic Medicine, Central Institute of Mental Health Mannheim, Medical Faculty Mannheim, Heidelberg University, Heidelberg, Germany

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Summary
Background: Borderline personality disorder (BPD) is characterized by antagonism, negative affectivity, disinhibition, and impairments in interpersonal functioning, including enhanced impulsive aggression. Interpersonal dysfunctions may be related to alterations in endocrine systems. The current study investigated alterations in basal activity of the hypothalamus—pituitary—gonadal (HPG) reproductive and the hypothalamus—pituitary—adrenal (HPA) stress system in BPD patients and their association to anger-related aggression with a particular focus on effects of gender and comorbid conditions of depression and posttraumatic stress disorder (PTSD).
Method: Saliva testosterone levels as well as cortisol awakening responses were assessed in 55 medication-free female and male patients with BPD and compared to 47 gender-, age-, and intelligence-matched healthy volunteers. In addition, analyses controlling for current depression and PSTD and bivariate correlations between testosterone and cortisol levels on the one hand and anger and aggressiveness on the other hand were performed.
Results: The results revealed increased saliva testosterone levels in female and male patients with BPD as well as elevated cortisol awakening responses in female, but not male patients with BPD compared to healthy volunteers. Cortisol awakening responses were positively related to anger and aggressiveness in female patients with BPD, but no associations were found with testosterone levels.

* Corresponding author at: Department of General Psychiatry, Center for Psychosocial Medicine, University of Heidelberg, Voßstraße 4, 69115 Heidelberg, Germany. Tel.: +49 6221 56 36502; fax: +49 6221 56 5374.
E-mail address: Katja.bertsch@med.uni-heidelberg.de (K. Bertsch).

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Conclusion: In line with previous reports, the present results suggest endocrine alterations in BPD which may be associated with interpersonal impairments, such as increased anger-related aggressive behavior and could have implications for the development of new (psychopharmaco-) therapeutic interventions that may help to restore the alterations in the HPA and HPG systems.

1. Introduction

Borderline personality disorder (BPD) is a severe mental disorder characterized by antagonism, negative affectivity, disinhibition, and impairments in interpersonal functioning, including enhanced anger-related impulsive aggression (American Psychiatric Association, 2013). Interpersonal problems such as impulsive aggression may be related to endocrine alterations. In healthy volunteers and highly aggressive populations, there is some evidence for associations between the hypothalamus–pituitary–gonadal (HPG) and hypothalamus–pituitary–adrenal (HPA) stress axis functioning and aggression (for reviews, see Van Honk et al., 2010; Carre and Mehta, 2011; Haller, 2013, 2014). Although results are inconsistent (Archer et al., 2005), increased basal testosterone levels have been reported in more aggressive individuals, and (weak) positive correlations between testosterone and aggression were found — particularly in those with low basal cortisol secretion (Popma et al., 2007; Carre and Mehta, 2011). As for cortisol secretion, positive associations with aggression have been found with both decreased and increased levels in healthy volunteers and aggressive individuals (e.g., Gerra et al., 2007; van Goozen et al., 2007; Böhnke et al., 2010a, 2010b) suggesting a general association between HPA axis dysregulations and aggressiveness (Haller, 2013, 2014).

In BPD, only few studies have investigated endocrine alterations and their association with the patients' interpersonal impairments. This is surprising as structural and functional alterations in brain regions that are crucially involved in the processing of social threats, the regulation of the fight/flight response, and the endocrine system have been reported in BPD. Besides reduced hippocampal and amygdalar gray matter volumes, which are the most consistent structural alteration in BPD (for meta-analysis, see Nunes et al., 2009), abnormalities in gray matter volume of the anterior cingulate cortex (e.g., Hazlett et al., 2005; Minzenberg et al., 2008), the hypothalamus (Kuhlmann et al., 2013), and pituitary (Garner et al., 2007) have been observed. In addition, exaggerated and prolonged amygdala responses (e.g., Herpertz et al., 2001; Hazlett et al., 2012) seem to be a neural correlate for BPD patients' hypersensitivity to social threats (Bertsch et al., 2013a). Patients with BPD also report more frequent and intense daily hassles (Jovev and Jackson, 2006) and elevated levels of stress-associated inner tension (Kuo and Linehan, 2009), which often precede self-injury and impulsive aggression (Kleindienst et al., 2008). As about 80% of patients diagnosed with BPD report traumatic childhood experiences, early stress and related HPA axis alterations have been discussed to play a prominent role in the etiology of BPD (Herman et al., 1989; Ogata et al., 1990). Although results of the few previous studies on HPA axis functioning are heterogeneous and may be influenced by comorbid disorders, in particular current major depression and post-traumatic stress disorder (PTSD; for review, see Zimmerman and Choi-Kain, 2009; Wingenfeld et al., 2010), there is evidence for elevated cortisol secretion and thus a basal HPA hyperactivity in BPD (Lieb et al., 2004; Wingenfeld et al., 2007; Carvalho Fernando et al., 2012). Regarding HPG activity, so far only one study investigating the occurrence of polycystic ovary (PCO) syndrome in a small group of partly medicated female patients with BPD and healthy women has shown increased plasma testosterone levels that could not be explained by PCO status or weight (Roepke et al., 2010).

Taken together, elevated basal cortisol and testosterone secretion have been reported in BPD who are characterized by more frequent and intense reactions to potential social threats and stressors and elevated stress-related inner tension which often triggers dysfunctional behaviors, such as anger-related impulsive aggression. However, little is known about effects of gender and comorbid disorders — current major depression and PTSD, in particular — as well as trait anger and aggressiveness with respect to HPG and HPA axes functioning in BPD.

The current study therefore aimed to investigate alterations in HPG and HPA axes functioning in female and male patients with BPD compared to healthy women and men controlling for comorbid conditions of current major depression and PTSD and their relationship with self-reported anger and aggressiveness. Therefore, we recruited a relatively large clinical sample of medication-free female and male patients with a current DSM-IV diagnosis of BPD and healthy women and men who provided two saliva samples to assess mean saliva testosterone levels as well as eight saliva samples at four fixed time points after awakening on two consecutive weekdays to assess the cortisol awakening response, a reliable measure for the HPA axis functioning (Schmidt-Reinwald et al., 1999; Hellhammer et al., 2007). In addition, anger and aggressiveness — as well as depressiveness, borderline symptom severity, and history of childhood traumatization — were measured with self-report questionnaires. Based on previous results, we hypothesized increased saliva testosterone levels and cortisol awakening responses in patients with BPD compared to healthy volunteers. We also expected increased testosterone levels in male compared to female patients and healthy volunteers and explored group by gender interactions as well as associations between endocrine data and self-reported anger and aggressiveness in BPD.

2. Material and methods

2.1. Participants

Participants were 55 patients with a current DSM-IV diagnosis of BPD (including self-injury and/or aggression; BPD;