# Endogenous oxytocin is associated with compassion and recalled upbringing in Borderline Personality Disorder

Short title. Oxytocin, compassion and upbringing in Borderline Personality Disorder

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**Abstract**

**Background/Objective** The role of the neuropeptide oxytocin (OT) in Borderline Personality Disorder (BPD) is not well understood and recent findings depict a complex mode of action of OT. In this study we aimed to examine the association of oxytocin levels in the plasma of BPD patients with the experience of compassion and recalled parental behavior during childhood.

**Methods** Fifity-seven BPD patients and forty-three healthy controls participated in the study. OT plasma levels were obtained and analyzed by radioimmunological assay. Subjects additionally completed questionnaires focusing on fears of compassion (FOC) and recalled upbringing by their parents ("Questionnaire of Recalled Parental Rearing Behavior/Fragebogen zum erinnerten elterlichen Erziehungsverhalten", FEE).

**Results** BPD patients had significantly lower OT plasma levels than healthy controls. Additionally, both groups differed significantly on all FOC and FEE scales; BPD patients had higher FOC scores (indicating more aversion of being compassionate and receiving compassion from others) and differed in recalled parenting. In the BPD group, scores of the CES scale "Responding to the expression of compassion from others" were negatively correlated with oxytocin levels. Moreover, recalled "emotional warmth" of their parents during childhood was positively correlated with oxytocin plasma levels of BPD subjects. No such correlations were found in the control group.

**Conclusion** Our results corroborate findings from previous studies reporting lower OT levels in patients with BPD. Moreover, peripheral OT seems to be linked with the tolerance of compassion and recalled parental upbringing style. This is consistent with the assumption that OT is an important mediator of the experience of emotional warmth from others.

Keywords: Oxytocin, compassion, Borderline Personality Disorder, upbringing, rearing

## Introduction

Borderline Personality Disorder (BPD) is a psychiatric disorder characterized by emotional instability, impulsive behavior and difficulties in interpersonal relationships (American Psychiatric Association, 2013). With a lifetime prevalence of up to six percent (Grant et al., 2008), BPD is one of the most frequent personality disorders (Sansone and Sansone, 2011).

It is well known that deficits in certain domains of social cognition may contribute to the difficulties BPD patients experience in social interaction. With regard to emotion processing, for instance, patients with BPD seem to experience problems in correctly identifying emotions or intentions when of others (Preißler et al., 2010) and they may, at times, exhibit deficits in both emotional as well as cognitive empathy (Dziobek et al., 2011). Conversely, other studies showed intact or even enhanced empathic abilities (Flury et al., 2008; Lynch et al., 2006; Matzke et al., 2014; Wingenfeld et al., 2014), or a "seventh sense" regard to others mentalities (Krohn, 1974), referred to as "empathy paradox" (Dinsdale and Crespi, 2013).

Empathy, however is a mental competency that can be used for both prosocial and antisocial motives; empathy can give one a competitive advantage (Zaki, 2014). In contrast, compassion is linked to caring motivations (Mayesless, 2016)which evolved with oxytocin (Carter, 2012) and the myelinated parasympathetic system (Porges, 2007). Compassion is defined as a ‘sensitivity to distress and suffering in self and others with a commitment to try to alleviate and prevent it (Gilbert, & Choden, 2013). This aspect of caring is essential for the evolution of attachment where the parent is sensitive to the distress of their infant and seeks to prevent and alleviate it; thus acting as a provisioning protecting and rescuing agent (Bowlby, 1969, 1973; Maylesless 2016). Importantly, not only is the parent sensitive to the infants needs and distress the infant has to be responsive to the inputs from the parent in order to be soothed or comforted

(Gilbert 1989/2016). Although caring and attachment behaviour involve much more than compassion (for example providing a secure base that promotes exploration and development) distress sensitivity and responsiveness are core features (Gilbert. 1989/2016; Mayesless, 2016).

Compassion can then be experienced in three orientations; the compassion we feel for others; an openness and sensitivity the compassion we feel that others have towards us; and self-compassion. In the last 20 years there has been considerable research exploring the physiological and psychological impact of promoting compassion motives in these three orientations ( ) with good evidence that all forms of compassion are associated range of physical and mental health benefits (Keltner et al., 2015). Partly for these reasons 'compassion' has become a focus for cultivation, training and therap- (Gilbert, 2010; 2014; Hoffman et al., 2011; Jazaieri et al., 2014). Compassion however is known to have facilitators and inhibitors. It is easier to be compassionate to and receive compassion from people we like than people we don't; people who seem like us people rather than people who seem very different; and when we can empathise with their difficulties.

During the clinical development of compassion focused therapy (CFT) it became clear that many clients had a fear of self—compassion, and also being open to compassion from others (Gilbert, 2000, 2010). Sometimes the feelings of being cared for in the therapy stimulated a grieving process, but at other times anxiety because in the past caring others had also been harmful. Indeed, Bowlby, (1980) noted that sometimes patients with disturbed attachments could respond to kindness as if it were a threat. In addition, self-criticism, which is known to be linked to attachment difficulties is associated with 'imagining compassion from another' as threatening as measured by changes in heart rate variability (Rockliff, 2008). Some self-critical people respond to oxytocin intranasal spray with negative affect, possibly linked to chronic sense of loneliness (Rockliff, et al., 2010).

In order to explore the fears of compassion Gilbert et al., (2011, 2013 developed scales for each orientation. Is also compassion were highly correlated with fears of receiving compassion but less so with fears of being compassionate. Fears of compassion have also been shown to be associated with depression and anxiety in clinical populations ( ).

Neurochemically, evidence is mounting that the experience of compassion for self and others is related to the activity of oxytocin (OT). Oxytocin, a nonapeptide present in both men and women, was primarily known for its role in parturition and lactation (Leng et al., 2015). During the last decades, research has focused on the role of OT in social cognition and behaviour in both nonhuman animals and humans, including patients with BPD (reviewed in Brüne, 2015). OT in BPD seems to exert differential effects on fear and affiliation and trust, whereby fear reduction is not paralleled by an increase in trust and prosocial behaviour (Bartz et al. 2011, Ebert at al., 2013; Brüne et al., 2015). In addition, peripheral OT seems to be lower in BPD patients (Bertsch et al., 2013) and children who experienced maltreatment (Mizushima et al., 2015) as well as OT levels in the cerebrospinal fluid of women with a history of traumatisation (Heim et al., 2009), whereby girls with a history or abuse showed an increase of salivary OT following a social stress test (Seltzer et al., 2014). Finally, in mothers who were asked about their recalled upbringing three months after giving birth, an inverse connection between OT plasma levels and negative features of the remembered paternal behavior emerged (Eapen et al., 2014).

More specifically to its role in compassion, intranasal application of OT improves individuals' performance in a compassion-focused imagery task, though this effect is modulated by attachment style and self-criticism (Rockcliff et al., 2011). Interestingly, the compassion enhancing effect of OT seems to be larger when listening to female voices than to male voices (Palgi et al., 2015). The same group also found a compassion-enhancing effect of administered OT in traumatized subjects exclusively towards females (Palgi et al., 2016).

Based on the evidence outlined above, we aimed to explore possible associations of peripheral OT with the fears and resistance to compassion and recalled parenting in BPD. We hypothesized that OT would inversely correlate with fears of compassion and with negative memories of one's upbringing, but positively correlated with recalled emotional warmth from both parents. In addition, we predicted lower serum OT levels in BPD compared to controls.

## Methods

### Participants

We included 96 female inpatients from a specialized ward of our hospital (LWL-University Hospital Bochum, Germany) diagnosed with Borderline Personality Disorder according to DSM-IV criteria and a Structured Diagnostic Interview for DSM-IV (SCID-II, German version, Wittchen et al., 1997). Inclusion in the study was performed immediately after BPD patients had been admitted to the ward in order to exclude therapy effects on the results of our study. All participants had given informed consent, both orally and in writing. Healthy controls were recruited with the help of notices. The study was performed in accordance with the Declaration of Helsinki (1964) and approved by the Ethics Committee of the Medical Faculty of the Ruhr-University Bochum, Germany.

After exclusion of the subjects who could not be analyzed due to missing data, 57 female BPD patients and 43 female control subjects were included; the mean age was 24.8 years (SD ± 4.7) in the BPD group and 23.4 years (SD ± 3.3) in the control group. General exclusion criteria were substance dependence, psychosis, bipolar disorder, acute suicidal ideation, neurological or severe somatic disorders; control subjects had additionally to be free of pre-existing psychiatric disorders. Most patients were on stable psychopharmacological medication, mainly serotonin reuptake inhibitors.

**Laboratory analyses**

Blood samples were collected using EDTA tubes which contained the protease inhibitor aprotinin to prevent OT degradation (Vacutainer with 1,5 mg/ml $K_3$EDTA and 250 KIU aprotinin, BD, Heidelberg, Germany). Blood samples were immediately placed on ice. They were subsequently centrifuged for 15 min at 4 °C. Afterwards, the supernatant plasma was aliquoted into cryogenic vials which were instantly stored at -80 °C. After completion of the study, all samples were sent to the commercial RIAgnosis laboratory (Sinzing, Germany) on dry ice. OT plasma levels were determined via a radioimmunological assay (RIA) following extraction of the samples and the quantification of OT concentrations via an antibody-antigen reaction (Landgraf, 1985).

**Tests and questionnaires**

*Fears of Compassion Scales (FOS)* (Gilbert, McEwan, Matos, & Rivis, 2011*_)*

The fears of compassion scale comprise three different scales. Fears of compassion *for Self* scale comprises 15 items (e.g. "Getting on in life is about being tough rather than compassionate"); fear of compassion *from Others* scale comprises 13 items (e.g. "Wanting others to be kind to oneself is a weakness"); fear of compassion *for Others* scale comprises 10 items (e.g. "I fear that being too compassionate makes people an easy target"). The items are rated on a five-point Likert scale (0 = Don't agree at all, 4 = Completely agree). In the original study these scales showed good reliability with Cronbach's alpha's of .92 *for self*, .85 *from others*, and .84 *for others* in a student sample.

*Recalled Parental Upbringing Style*

Recalled parental rearing style was examined using the German version of the "Recalled Parental Rearing Behavior Questionnaire" ("Fragebogen zum erinnerten elterlichen Erziehungsverhalten", FEE; Schumacher et al., 1999 and 2002), first published in Swedish as "Egna Minnen Beträffande Uppfostran" (EMBU; Perris et al., 1980). The EMBU or FEE is a self-report measure of subjects' memorised experiences concerning their upbringing. Several domains are evaluated separately for both parents: "emotional warmth", "rejection and punishment" and "control and over-protection", resulting in six different subscales.

### Statistics

All analyses were carried out by applying the commercial statistics software "IBM SPSS Statistics" Version 23 (IBM Corp., Armonk, NY, USA). Statistical significance levels were set at $p < 0.05$. We did not assume a Gaussian distribution in our sample, therefore we used Wilcoxon rank sum test as a non-parametric method for comparing means. For correlation analyses we used the non-parametric Spearman's rho correlation coefficient.

## Results

### Oxytocin levels in BPD patients and controls

We performed a non-parametric analysis for independent groups (Mann-Whitney-U-Test) to compare differences between oxytocin plasma levels of BPD patients and healthy controls (see Fig. 1 and Tab. 1). Oxytocin levels differed significantly between both groups, BPD patients had lower mean oxytocin levels (2.1 pg/ml; SD ± 0.90) than controls (2.4 pg/ml; SD ± 0.85; $p = 0.047$).

**CES and FEE scores in patients and controls**

Another set of Mann-Whitney-U-Tests were carried out in order to compare scores on the FOC and the FEE-Questionnaires. BPD patients and healthy control subjects differed significantly on all three FOC and all six FEE scales (three scales for both maternal and paternal behavior). BPD patients scored significantly higher FOC in all three orientations (all $p < 0.001$). In addition they scored significantly higher on "negative" FEE scales ("rejection and punishing" and "control and over-protective behavior") and lower on the FEE scale "emotional warmth" (all $p < 0.001$). For details see Table 1.

--- please insert Fig. 1 and Table 1 about here ---

**Oxytocin levels, compassion and upbringing in BPD patients**

*Oxytocin levels and compassion/upbringing*

In order to test for putative connections between oxytocin levels and compassion, we performed a correlation analysis; Spearman's rho correlation coefficient was used. fears of compassion from others was inversely correlated with oxytocin levels ($r = - 0.35$; $p = 0.008$) in the BPD group (see Fig. 2). Fears of compassion to others and fears of self-compassion were not significantly correlated with OT levels; although there was a tendency regarding scale 3 ("control and over-protective behavior"; $r = -0.23$; $p = 0.09$).

--- Please include Fig. 2 and Fig. 3 about here ---

Oxytocin plasma levels and FEE values were also analyzed (Fig. 3); "emotional warmth" was positively correlated (both maternal and paternal measures) with OT levels (mother: $r = 0.37$; $p =$

0.005; father: r = 0.39, p = 0.006). In contrast, "rejection and punishing", as well as "control and over-protective behavior" were not correlated with oxytocin levels ($p > 0.05$). For detailed values please see Table 1.

Computing partial correlation analysis incorporating OT levels and CES scale 2 resp. FEE scales "emotional warmth" (paternal/maternal) led to non-significant results (all $p > 0.05$); those scales were correlated with each other (all $p < 0.05$).

**Oxytocin levels, compassion and uprising in controls**

*Oxytocin levels and compassion/uprising*

We also performed the same correlation analyses for the control group; again Spearman's rho correlation coefficient was uses for these analyses. In contrast to the BPD group, there were no correlations between oxytocin plasma levels, the FOC or the FEE scales (all $p > 0.05$).

## Discussion

The present study focused on the possible relationships between oxytocin and compassion as well as the recalled upbringing by their parents in patients suffering from Borderline Personality Disorder compared to non-clincial a control group. BPD had significantly higher fears and resistances to all forms of compassion compared to the control group. Also, BPD patients had less favorable memories about the behavior of their parents during their upbringing. In addition we found that BPD patients had lower oxytocin plasma levels than controls, in line with previous research (Bertsch et al., 2013). This offers further support the hypothesis of alterations in the endogenous oxytocin system in BPD (Stone & Stone, 2013). Second, oxytocin levels were

negatively correlated fears of compassion form others. This is an important finding because it may indicate that these individuals need specific help in learning to trust and be open to the helpfulness and support of others; indeed one of the main elements of CFT is to focus on is blocked resistances (Gilbert and MON in press). and positively with experiences of emotional warmth by parents of both sexes during childhood.

Regarding compassion, this points towards a prosocial and beneficial influence of oxytocin on the ability to accept compassion offered by others. This contributes to the knowledge about the impact of oxytocin on social cognition, especially as oxytocin effects have been found to be complex and sometimes even undesirable lately – in particular in the context of BPD (see introduction; e.g. Bartz et al., 2011; Ebert et al., 2013). This is of special interest because there is a paucity of literature on the connection of oxytocin with compassion and the available studies focus on the influence of intranasally administered oxytocin (Rockcliff et al., 2011; Palgi et al., 2015 and 2016). Therefore our results indicate that also endogenous oxytocin might foster compassion, at least some aspects of it. In addition, the importance of compassion is rapidly increasing in the context of psychotherapy, both as the central element of Compassion focused therapy (Gilbert, 2009; see introduction) and as an important part of mindfulness-based or –associated psychotherapeutic approaches such as Mindful self-compassion (MSC; Neff and Germer, 2013) or Acceptance and commitment therapy (ACT; Hayes et al., 1999).

As decreased oxytocin levels in the cerebrospinal fluid have been described in subjects with traumatic experiences during childhood (Heim et al., 2009), early life experiences might influence and modify the oxytocin system (Alves et al., 2015). In this context, oxytocin levels in the plasma and saliva of parents have been linked to their attachment to their own parents as well as their children (Feldman et al., 2011). Therefore the association of memories of parental emotional warmth during childhood with increased oxytocin plasma levels in our BPD cohort

might fit in the picture: The lack of experienced emotional warmth could have the same effects as a mild trauma on the oxytocin system of children with vulnerability to develop Borderline-associated symptoms in their adulthood. On the other end of the spectrum, a parental style incorporating high levels of experienced emotional warmth by children could be considered protective in connection with the development of a "normal" oxytocin system. However, as this is to our knowledge the first study to examine these connections and no causal relationship can be concluded because of the mere correlational results, there has to be a lot more research done until these findings may have specific implications, e.g. for an individualized choice of the psychotherapeutic approach for BPD patients.

There are also other limitations which have to be considered. On the one hand, there is a discussion, whether oxytocin levels in blood samples may be used for neuropsychiatric studies in general. Although this has been done widely (e.g. Goldman et al, 2008; Hoge et al., 2012; Jobst et al., 2014), there is some doubt to which degree plasma levels of oxytocin may be linked to oxytocin concentrations in the central nervous system (Kagerbauer et al., 2013; Dal Monte et al., 2014). On the other hand, we also cannot explain why the correlation analyses delivered highly significant results in the BPD group concerning the links between oxytocin, compassion and emotional warmth of the parents, but such connections were not found in the control group. One might assume that compassion is only influenced by oxytocin levels in the context of other factors related to BPD, but this remains speculative to date. Another point to consider might be medication effects on the outcome. Moreover, we cannot exclude influences of the menstrual cycle of our female subjects on oxytocin levels, as variation of oxytocin levels depending on the cycle have been shown before (Salonia et al., 2005).

In conclusion, our findings underpin the close but nevertheless complex relationship between an altered oxytocin system in patients suffering from Borderline Personality Disorder and its links

with compassion and childhood experiences. Further investigation might result in better and possibly more specific psychotherapeutic approaches for individuals with BPD.

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**Table 1** Details of oxytocin plasma levels and scores of the Compassion Evaluation Scale (CES) and the Questionnaire of Recalled Parental Rearing Beavior/Fragebogen zum erinnerten elterlichen Erziehungsverhalten (FEE)

| | **BPS Patients** | **Healthy Controls** |
|---|---|---|
| **Oxytocin plasma levels [pg/ml]** | (2.09; SD ± 0.9) | (2.45; SD ± 0.9) |
| **CES** | | |
| Scale 1: Fear of compassion for others | (23.7; SD ± 8.1) | (11.7; SD ± 7.1) |
| Scale 2: Fear of compassion from others | (28.5; SD ± 11.5) | (6.30; SD ± 7.4) |
| Scale 3: Fear of self compassion | (37.8; SD ± 13.8) | (24.6; SD ± 19.1) |
| **FEE** | | |
| Scale 1: emotional warmth (father) | (15.8; SD ± 7.1) | (24.0; SD ± 6.1) |
| Scale 2: emotional warmth (mother) | (16.5; SD ± 7.0) | (26.1; SD ± 6.4) |
| Scale 3: rejection and punishing (father) | (14.2; SD ± 7.1) | (9.0; SD ± 2.0) |
| Scale 4: rejection and punishing (mother) | (16.5; SD ± 7.2) | (9.2; SD ± 2.9) |
| Scale 5: control and over-protective behavior (father) | (15.8; SD ± 5.0) | (11.4; SD ± 3.1) |
| Scale 6: control and over-protective behavior (mother) | (17.6; SD ± 5.8) | (13.3; SD ± 4.3) |

The values given are mean values (with standard deviation; SD).