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Exploring nonverbal synchrony in borderline personality disorder: A double-blind placebo-controlled study using oxytocin

Fabian Ramseyer[1], Andreas Ebert[2], Patrik Roser[3], Marc-Andreas Edel[4], Wolfgang Tschacher[5] and Martin Brüne[2]*

[1]Department of Clinical Psychology and Psychotherapy, Institute of Psychology, University of Bern, Switzerland
[2]Division of Social Neuropsychiatry and Evolutionary Medicine, Department of Psychiatry, Psychotherapy and Preventive Medicine, LWL University Hospital Bochum,Ruhr-University Bochum, Germany
[3]Centre for Addiction Disorders, Psychiatric Hospital Königsfelden, Psychiatric Services Aargau, Academic Hospital of the University of Zurich, Switzerland
[4]Fliedner Klinic, Gevelsberg, Germany
[5]Department of Experimental Psychology, University Hospital of Psychiatry and Psychotherapy, University of Bern, Switzerland

Objectives. Interpersonal dysfunction is a central feature of borderline personality disorder (BPD), and the neuropeptide oxytocin (OT) has been shown to impact patients' behaviour in numerous ways. Nonverbal signals such as the coordination of body movement (nonverbal synchrony) are associated with the success of interpersonal exchanges and could thus be influenced by features of BPD and by the administration of OT.

Design. We explored the effect of intranasal OT (inOT) on nonverbal synchrony in sixteen patients with BPD and fifteen healthy controls (CTL) randomly assigned to two double-blind clinical interviews under inOT and placebo (PL).

Methods. Nonverbal synchrony was assessed by automated video-analyses of subject's and interviewer's body movement. Lagged cross-correlations were used to objectively quantify coordination in dyads.

Results. Synchrony was higher than pseudosynchrony (= synchrony expected by chance), and there was a differential effect of inOT between groups: While healthy controls displayed increased synchrony under inOT, patients with BPD showed low levels of synchrony under inOT. Additionally, patient's synchrony was negatively associated with self-reported childhood trauma.

**Correspondence should be addressed to Martin Brüne, Division of Social Neuropsychiatry and Evolutionary Medicine, Department of Psychiatry, Psychotherapy and Preventive Medicine, LWL University Hospital, Ruhr-University Bochum, Alexandrinenstr. 1, D-44791 Bochum, Germany (email: martin.bruene@rub.de).*

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Conclusions. Nonverbal synchrony in clinical interviews is influenced by inOT, and this effect depends on subject's diagnosis. In line with previous research implying positive associations between nonverbal synchrony and relationship quality, inOT led to an increase of synchrony in healthy controls, but not in patients with BPD. Low levels of synchrony under inOT in patients and its association with childhood trauma suggest that additional mechanisms such as rejection sensitivity might mediate BPD patients' nonverbal behaviour.

Practitioner points

- Intranasal oxytocin (inOT) attenuated nonverbal synchrony – a proxy for relationship quality – in patients with borderline personality disorder (BPD), while it increased nonverbal synchrony in healthy controls (CTL).
- Available models (rejection sensitivity; social salience) suggest that inOT may alter the way patients with BPD assess social situations, and this alteration is expressed by changes in nonverbal coordination. Patients with BPD display low levels of synchrony which are even below expected pseudosynchrony based on chance.
- The association between self-reported childhood trauma and lower synchrony in BPD was most evident for patient's imitative behaviour: Under inOT, patients with high scores of childhood trauma refrained from imitating their interview partners.
- Study limitations include small sample sizes and limited data on the psychological impact of the clinical interviews.

Borderline personality disorder (BPD) is characterized by emotional dysregulation, impulsivity, risk-taking behaviour, instability of relationships, frantic efforts to avoid abandonment by others, self-injury, feelings of emptiness, dissociation, and, at times, paranoid ideation (Lieb, Zanarini, Schmahl, Linehan, & Bohus, 2004). Current conceptualizations of BPD have highlighted the interpersonal dimension of BPD (Stanley & Siever, 2010), and the analysis of observable interpersonal behaviours may provide important additional insights into how BPD patients form dyadic relationships (Lazarus, Cheavens, Festa, & Zachary Rosenthal, 2014). Nonverbal behaviour is one such readily observable factor, and numerous findings highlight its importance for interpersonal relationships (Gifford, 2010; Wilson, Stroud, & Durbin, 2017). The evaluation of social signals, in turn, is biased by individual differences in personality traits including rejection sensitivity (RS) – the susceptibility to interpret social cues as signs of rejection (Staebler, Helbing, Rosenbach, & Renneberg, 2011) – which is relevant for mental health in general, and for BPD in particular (Gao, Assink, Cipriani, & Lin, 2017). Put another way, individuals with BPD appear to process signals of social acceptance in deviant ways (Liebke *et al.*, 2018), and they perceive exclusion in a negatively biased way and feel more readily excluded than healthy controls (Renneberg *et al.*, 2012). The association between RS and BPD has been reported at a medium effect size (pooled $r = .413$) in a meta-analysis (Gao *et al.*, 2017), and a recent overview has shown that emotional abuse and neglect were linked to RS (Foxhall *et al.*, 2019). Aspects of social functioning – such as RS – can be assessed experimentally or by self-report, but their manifestation may also be revealed in nonverbal behaviour, which is much less under voluntary control than verbal report.

Nonverbal synchrony (Ramseyer & Tschacher, 2011) is a relatively new measure capturing the bidirectional influence in nonverbal (and other) signals arising in dyads and between interaction partners (De Jaegher, Peräkylä, & Stevanovic, 2016). Nonverbal synchrony has been identified as a relevant factor embodying the quality of relationships – higher synchrony is associated with higher relationship quality – and as a positive predictor for successful psychotherapy (Koole & Tschacher, 2016; Paulick, Deisenhofer *et al.*, 2018; Ramseyer & Tschacher, 2011). Such a behaviour-based measure could thus provide valuable information on the relationship dynamics of patients with BPD with their interaction partners, and furthermore, it could be susceptible to the intranasal administration of oxytocin (inOT; Brüne, 2016).

Nonverbal synchrony

Interactional synchrony – the coordination of behaviour between interacting humans – has been first described by Condon and Ogston (1966), and it has subsequently been associated with various positive aspects of interpersonal relationships (Chartrand & Lakin, 2013). Recent meta-analyses in the domain of social psychology found positive effects of synchrony on prosocial behaviour, social bonding, social cognition, and positive affect (Mogan, Fischer, & Bulbulia, 2017; Vicaria & Dickens, 2016). Previous work based on automatically quantified body movement using motion energy analysis (MEA; Ramseyer, 2019; www.psync.ch) has shown that in the context of psychotherapy, nonverbal synchrony was positively associated with favourable aspects such as high ratings of the quality of the therapeutic relationship and an overall favourable therapy outcome (Ramseyer & Tschacher, 2011). Taken together, these findings imply that synchrony may be viewed as a framework for the therapeutic alliance and – more broadly speaking – relationships in general (Koole & Tschacher, 2016).

Pacing and leading

In addition to a global synchrony measure, it is possible to measure the direction of synchrony, that is, pursuing the question who of the interactants moves first and therefore appears to set the timing for the interaction partner (Grammer, Kruck, & Magnusson, 1998; McGarva & Warner, 2003). This aspect of nonverbal coordination has previously been called ‘pacing’ and ‘leading’ (Bandler & Grinder, 1979; Ramseyer & Tschacher, 2011), or ‘imitation by . . .’ (Kupper, Ramseyer, Hoffmann, & Tschacher, 2015), because it takes into account whether an individual’s behaviour occurred first (= leading/the person is being imitated), or whether this interactant imitated the other person (= pacing/the individual imitates the other person). We identified how much a subject imitated the interviewer (= interviewer leader) by a lag of up to –3 s and how much the subjects were imitated by their interviewers (= subject leader) by a lag of up to +3 s. The differentiation regarding who was the leader thus provides indirect information whether, for example, the interviewer’s behaviour was characterized by more effort to attune to the partner (imitation, subject leader), or whether the interviewer’s behaviour was less influenced by the partner (= interviewer leader). Imitation scores are calculated by either summing negative and positive lags in cross-correlations; therefore, they are strongly associated with the overall level of synchrony ($r_{\text{pacing}} = .851$; $r_{\text{leading}} = .781$; in this sample) but less so with each other ($r = .336$; in this sample).

Oxytocin

In recent years, the initial enthusiasm that OT exerts unequivocally beneficial effects has given way to a more differentiated conceptualization of OT’s effect of on social behaviour (reviewed in Ebert & Brüne, 2017). Abundant evidence from non-clinical populations suggests that OT plays a central role in attachment-relevant behaviours (Feldman, 2012), as well as in the development of trauma-related disorders (Bakermans-Kranenburg & van

IJzendoorn, 2013). Studies in healthy humans have shown that the intranasal application of OT (inOT) increases empathic concern for others and improves mind-reading, trust, cooperation, and the experience of social reward (Domes, Heinrichs, Michel, Berger, & Herpertz, 2007; Kosfeld, Heinrichs, Zak, Fischbacher, & Fehr, 2005). However – in contrast to this list of positive effects – inOT was found to also potentiate negative emotions such as envy and schadenfreude (Shamay-Tsoory *et al.*, 2009), decrease the adherence to fairness norms (Radke & de Bruijn, 2012), promote defensive action (Striepens *et al.*, 2012), and increase aggression after provocation (Ne'eman *et al.*, 2016). These seemingly contradictory findings suggest that the outcome of inOT administration could depend much more on situational factors or individual trait- and state-like processes within the person.

OT in BPD

As regards studies of peripheral concentrations of OT, it seems that serum OT is reduced in BPD, whereby the experience of childhood trauma, particularly emotional abuse and neglect, symptom severity, and aggressiveness correlated inversely with OT levels (Bertsch, Schmidinger, Neumann, & Herpertz, 2013). Lower OT levels were also associated with fears of compassion, recalled troublesome parenting, and with unresolved attachment representations (Ebert, Edel, Gilbert, & Brüne, 2018; Jobst *et al.*, 2016). These findings are consistent with an association between lower OT levels in women reporting childhood abuse (Heim *et al.*, 2009), a condition often found in patients with BPD. When experimentally exposed to social stress in a virtual ball-tossing game imitating social exclusion, patients with BPD responded with more prolonged negative emotions and a decrease in serum OT level, whereby the speed of return to baseline OT correlated negatively with childhood trauma severity (Jobst *et al.*, 2014).

Experimental administration of intranasal OT has demonstrated an increase in stress tolerance in BPD and in non-clinical individuals with reduced emotion regulation abilities (Quirin, Kuhl, & Düsing, 2011; Simeon *et al.*, 2011). Studies conducting experimental application of inOT thus imply potential beneficial effects of inOT for patients with BPD. However, inOT has also been found to reduce interpersonal trust (Ebert *et al.*, 2013) and this reduction under inOT was more evident in BPD patients that reported higher childhood trauma in a self-report questionnaire (Ebert *et al.*, 2013). This is consistent with studies showing that inOT administration can exert even negative effects on social behaviour in non-clinical samples with adverse childhood experiences (Huffmeijer *et al.*, 2013). Together, OT may not always have beneficial effects in BPD (Bakermans-Kranenburg & van IJzendoorn, 2013; Brüne, 2016), which is potentially relevant for clinical, including psychotherapeutic, social interactions. One possible explanation for this apparent contradiction has been proposed in the social salience model (Shamay-Tsoory & Abu-Akel, 2016), which conceptualizes OT as an amplifier of social cues in a given social situation. Such an amplification could thus lead to increased activation of fearful or other negative emotions associated with relationships in patients suffering from BPD. These patients would thus be susceptible to an increase of social awareness/anxiety after administration of OT. A comparable effect has been documented with the concept of RS (Staebler *et al.*, 2011): The tendency to anxiously or angrily respond to social situations (Gao, Assink, Liu, Chan, & Ip, 2019) was moderately to strongly associated with BPD (Foxhall *et al.*, 2019; Gao *et al.*, 2017). Administering inOT in BPD could therefore lead to an (unwanted and detrimental) increase of socially aversive responses.

Joint assessment of nonverbal synchrony and OT

Several studies assessing parental bonding have found associations between interactional synchrony (measured by observable behaviour categories) and OT levels (Feldman, 2015), supporting the importance of the scientific study of nonverbal behaviour (display) during social interaction (Apter-Levi, Zagoory-Sharon, & Feldman, 2014). Reciprocal effects between increased OT levels after administration to fathers have been found in the children they interacted with (Weisman, Zagoory-Sharon, & Feldman, 2012), that is, a convergence of OT levels. Another study pointed out that there is a considerable overlap in brain regions for 'being imitated' and endogenous oxytocin secretion as well as regions active when OT is applied intranasally (Aoki *et al.*, 2014; Aoki & Yamasue, 2015; Delaveau, Arzounian, Rotgé, Nadel, & Fossati, 2015). The association between different forms of synchrony and OT has previously been studied in standardized movements (finger-tapping: Gebauer *et al.*, 2016; hand gestures and emotion expression: Spengler *et al.*, 2017) and in laboratory tasks (inter-brain synchrony: Mu, Guo, & Han, 2016). Positive associations between either the level of OT or administration of inOT and synchrony were reported in these studies. Two empirical studies conducted in a naturalistic context reported positive effects of inOT on a dyad's performance during a cooperative task (Arueti, Perach-Barzilay, Tsoory, Berger, Getter, & Shamay-Tsoory, 2013) and increased synchrony of movements between dance partners under inOT (Josef, Goldstein, Mayseless, Ayalon, & Shamay-Tsoory, 2019). The studies mentioned in this section thus suggest a potentially positive effect of inOT on the strength of different types of dyadic synchrony.

Study questions

First of all, we were interested in whether nonverbal synchrony – measured in the relatively natural social situation of a clinical interview – would differ between healthy controls and BPD patients. Secondly, we aimed to assess the effect of inOT on levels of nonverbal synchrony. Thirdly, we were seeking to explore associations between nonverbal synchrony and self-reported childhood trauma (CTQ).

The assessment of nonverbal synchrony was an extension to a previous investigation that applied an ethological coding system (Brüne, Kolb, Ebert, Roser, & Edel, 2015). This previous study concluded that inOT did not increase affiliative behaviour in BPD when compared to placebo (PL) administration, while it did so in healthy controls (only when inOT was given at the first timepoint of two interviews). On the other hand, inOT generally decreased nonverbal signals of flight in both groups. We were thus specifically interested whether a different quantification of nonverbal behaviour – using movement-based nonverbal synchrony – might provide additional insight into possible effects of inOT versus PL on the social interaction of patients with BPD or healthy controls. The study was a double-blind placebo-controlled investigation based on naturalistic interviews with healthy interview partners (clinical interviewers), and nonverbal synchrony was controlled for synchrony that would be expected by chance (pseudosynchrony; Ramseyer & Tschacher, 2010). We assumed that these short interviews (exploring current well-being and symptoms) would elicit a broad range of behaviours encompassing the relationship quality between interviewer and interviewee. This assumption was based on the fact that there is ample evidence documenting that brief behavioural samples are valid indicators of person- and situation-specific factors emerging in social interactions (Slepian, Bogart, & Ambady, 2014). We propose that the interviews used in this study would fall under this category. All interviewers were unacquainted to BPD patients or healthy controls prior to the first interview, and the focus on nonverbal synchrony was unknown to all participants and interviewers. In this particular setting, we aimed to explore whether and how inOT (relative to PL) administration would impact nonverbal synchrony in both groups.

Method

Design

The study was conducted as a randomized, double-blind experiment comparing intranasal oxytocin (inOT) with placebo (PL) in two clinical interviews (T1 and T2) 1 week apart.

Participants

Sixteen inpatients diagnosed with BPD (mean age 27.5 ± 7.3 years; six males) according to DSM-IV criteria and a Structured Clinical Interview for DSM-IV [SCID I and II; German version by Wittchen, Wunderlich, Gruschwitz, and Zaudig (1997)] and fifteen healthy controls (CTL; mean age 25.7 ± 6.5 years; four males) were enrolled in the study after giving full informed consent. The interviews took place within the first week of a 6- to 8-week dialectic behavioural therapy (DBT) programme at the University Hospital in Bochum, Germany, whereby the first treatment phase is characterized by psychoeducation, followed by a second phase comprising skills and mindfulness training. Healthy controls were recruited through advertisements. Exclusion criteria comprised excessive smoking, participation in another study within 30 days prior to screening, a history of substance dependence, pregnancy, or intention to become pregnant within 30 days of completing the study, current breastfeeding, prolactin level >200 ng/ml at baseline, clinically significant ECG abnormalities at screening, and any unstable medical condition such as cardiac arrhythmia. Due to mild to moderate depressive symptoms, 11 patients were on a stable dose of a serotonin reuptake inhibitor or a melatonergic antidepressant. None fulfilled the criteria for any other axis-I disorder. None of the participants in the healthy control group fulfilled criteria for any axis-I or axis-II disorder.

The study was approved by the Institutional Review Board of the Medical Faculty of the Ruhr-University Bochum, Germany and conducted in full accordance with the Declaration of Helsinki on ethical standards in medical research. Approval was also given by the German Federal Institute for Drugs and Medical Devices (Bundesinstitut für Arzneimittel und Medizinprodukte; BfArM). Demographic data are shown in Table 1.

Table 1. Demographic data and synchrony values of patients with BPD and controls

	Overall		BPD		Control		Comparison (groups)
	M	*SD*	*M*	*SD*	*M*	*SD*	*p*/*d*
Age	26.52	6.90	27.53	7.14	25.70	6.38	.420/.45
Female/Male	21/10		10/6		11/4		.519
Synchrony	0.282	0.865	0.171	0.955	0.404	0.750	.292/.27
Subject leading	0.437	1.007	0.339	1.040	0.546	0.976	.424/.21
Interviewer leading	0.059	0.856	−0.036	0.895	0.164	0.813	.363/.19
CTQ Emotional neglect (EN)	16.92	9.82	22.92	10.56	10.92	3.38	<.001/1.53
CTQ Emotional abuse (EA)	12.62	7.48	17.92	7.04	7.31	2.43	<.001/2.02
CTQ Physical abuse and neglect (PAN)	11.81	6.54	15.77	7.30	7.85	1.34	<.001/1.51

Note. CTQ = Childhood trauma questionnaire.

Movement assessment: Motion energy analysis (MEA)

All subjects participated in two videotaped interviews of approximately 10-min duration conducted 1 week apart. One was under inOT, the other under PL, whereby both subject and interviewer were blind to substance and order of administration (randomization of inOT/PL). Because of equipment malfunction in one of the 62 interviews, a total of $N = 61$ videotaped interviews were available for further analysis. The purpose of the interviews was (1) to gather information about the patients' current mood and motivation for the ongoing DBT-oriented treatment and (2) to provide naturalistic interactions for the ethological coding of nonverbal behaviour. Open-ended questions and an initial focus on patient's/subject's current psychological and medical condition resulted in relatively relaxed social exchanges. No information was given about how the interviews would be evaluated, except that anonymity was guaranteed. Nonverbal synchrony was retrospectively assessed after the completion of the study and unbeknown to both patients and healthy interviewers. We assessed subject's and interviewer's movement with an automated method called motion energy analysis (MEA: Ramseyer & Tschacher, 2011; Ramseyer, 2019; www.psync.ch). MEA tracks changes from one video frame to the next and stores the amount of change occurring in a defined region into a time-series representative of the movement that occurred in this region (see Figure 1). The MEA application is based on an image-differencing algorithm commonly used in the context of computer vision and delivers objective, valid, and quick assessments of movement avoiding most of the shortcomings inherent with human observers. MEA necessitates few technical requirements (e.g., no physical markers or special cameras), which recommends this method for analyses of a wide range of videotaped interactions, including archival material. The two basic requirements are a fixed camera shot and stable light conditions. In order to keep the conditions for movement for all interactions maximally stable, we selected a 7-min segment of the interview, starting at 60 s after the beginning of the recording. This temporal subsection limited factors external to the interview such as greeting, or arranging of seating positions. Recorded interviews were standardized to a resolution of 320 × 240 pixels with a frame rate of 25 frames per second, using the video codec h.264.

Regions of interest (ROIs), where movement should be quantified, were defined for the head region and the gesture region (see Figure 1). The definition of two ROIs per interactant therefore produced four continuous time-series measuring the amount of

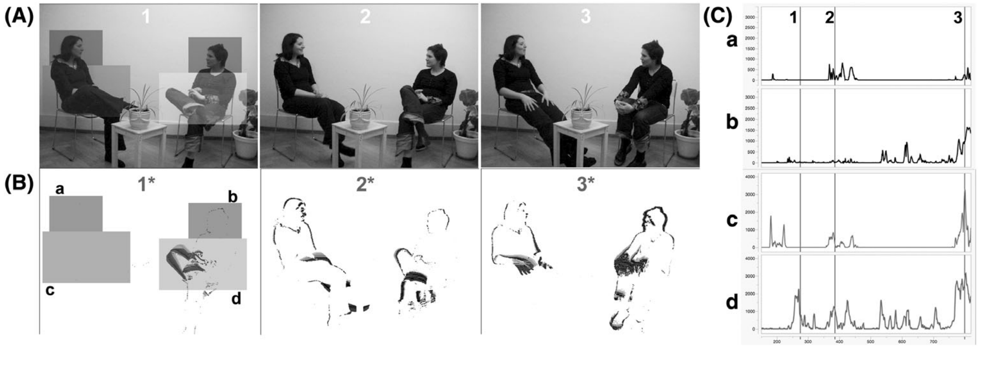

Figure 1. Motion energy analysis (MEA): Upper row (A) depicts the original video (1–3), middle row (B) pixels where movement occurred (1*–3*), and panel (C) time-series with raw amounts of movement for each region of interest (ROI: a, b, c, d). ROIs are shown as shaded areas in 1 and 1*, panels A and B.

movement in the head and gesture regions of patients/controls and healthy interaction partners. Further details and instructions for the usage of MEA are described in Ramseyer (2019). MEA provides a modern, fully automatic implementation of the manual frame-by-frame coding techniques initially used and described by Condon and Ogston (1966), who coined the term ‘interactional synchrony’. One important limitation of this kind of marker-free assessment of movement is the fact that MEA solely quantifies movement *dynamics*: It is blind to the direction and form of movement.

Quantification of nonverbal synchrony

Statistical calculations of movement percentages, synchrony, and pacing/leading were conducted in an *R*-package called rMEA (Kleinbub & Ramseyer, 2018) available for the statistical software *R* (R Core Team, 2014). ROIs of the head and body regions were summed up to one region per person, similar to another study using MEA (Ramseyer & Tschacher, 2011). We then standardized the values in relation to the size of a ROI (thus, the data are independent of the size of each individual’s ROI) and smoothed the data with a moving average of 0.4 s. A threshold for the separation of movement versus fluctuations in the signal was implemented directly in the MEA program (version 4.03), and we chose a value of 10, which led to an easily discernible segmentation into movement (values above zero) and no movement (zero).

The primary statistical analysis is based on a time-lagged cross-correlation algorithm (function *MEAccf* in rMEA) which quantifies the association of the two time-series in a range of ±3 s (*lagSec* = 3). This measure is computed segment-wise, that is, each 20 s (*winSec* = 20) of an interview is analysed separately to take into account time-dependent changes in the associations between patients and interviewers (thus allowing for the non-stationarity of the phenomenon). Segments are assessed with an overlap of 10 s (*incSec* = 10). The resulting correlation coefficients are charted in a colour-coded cell plot (see Figure 2) that shows the direction of associations for one member of the dyad. The matrix of correlation values may be considered an estimate of the total amount of structure in the sequence analysed (i.e., the quantity of coordination between the two partners). This measure of structure is simply the mean of all absolute values of the correlations of the graph. Additionally, we were interested in the direction of synchrony and thus considered whether the subject’s behaviour occurred first (= subject leader), or whether the subject imitated the interviewer (= interviewer leader). Therefore, nonverbal synchrony was calculated as (1) a global value, comprising all available cross-correlations of ±3 s ($N = 151$ cross-correlations, including the lag of zero) and (2) a subscore indicating how much each subject imitated the interviewer (lag −3, $n = 75$ cross-correlations), and (3) a subscore indicating how much the subject was imitated by the interviewer (lag + 3, $n = 75$ cross-correlations).

A final, quite important step in our analysis was to rule out that the detected synchrony could have occurred solely by chance: Comparing synchrony with so-called pseudosynchrony provides an estimate of the strength of the synchrony phenomenon (Moulder, Boker, Ramseyer, & Tschacher, 2018; Ramseyer & Tschacher, 2010). We therefore included a procedure that generated $N = 5{,}000$ surrogate datasets (out of a possible $N = 7{,}320$) by permuting the allocation of interviewers and subjects across all available dyads ($N = 31$) in a yoked control design. This strategy is different from another approach (Ramseyer & Tschacher, 2010), but provides more randomized pairings in situations with few patients and short observations (see Moulder *et al.*, 2018). Our choice of lags up to ±3 s was based on the empirical comparison of synchrony versus pseudosynchrony,

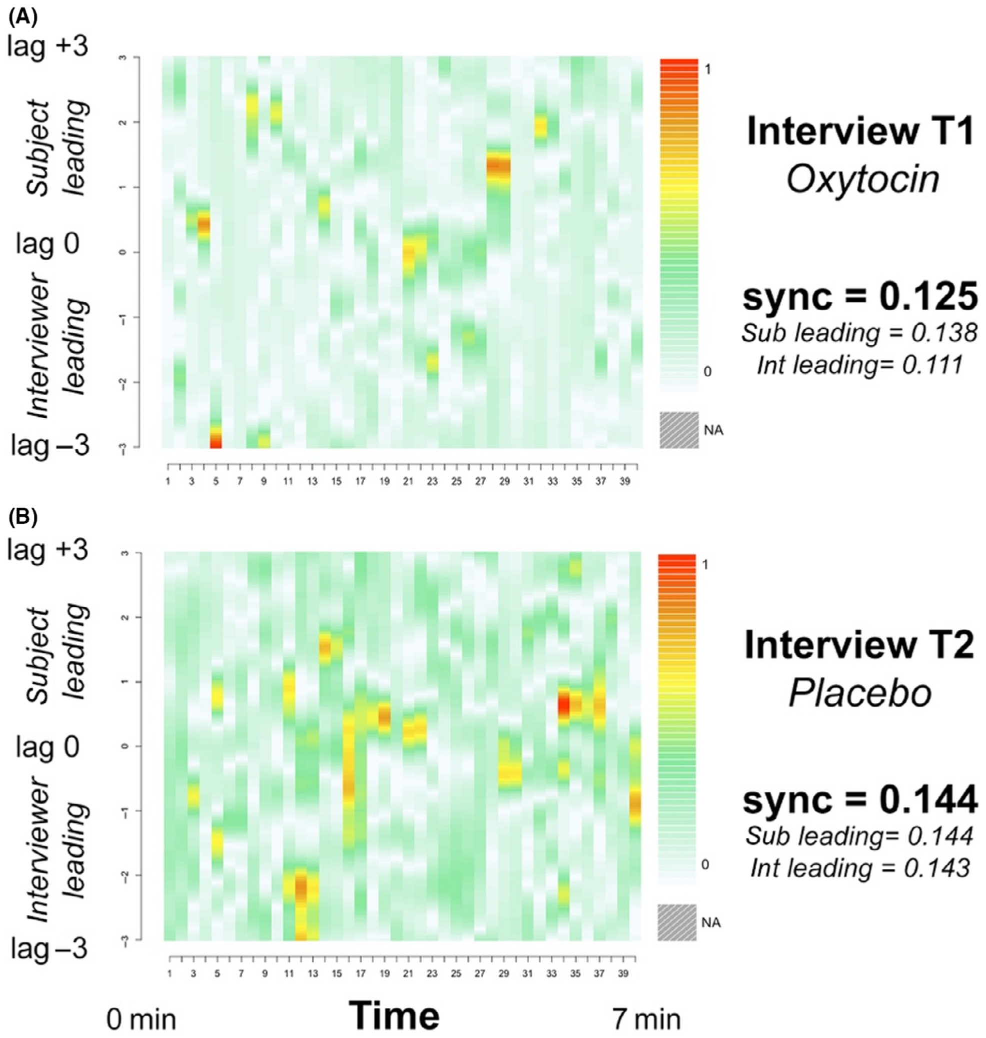

Figure 2. Cross-correlation plot (function *MEAheatmap* in rMEA) of one patient's two interviews under inOT at T1 (panel A) and at T2 under PL (panel B). sync = averaged absolute cross-correlations. X-axis: time; Y-axis: lagged cross-correlations (absolute values), values above the midline (lag 0) indicate subject (Sub) leading, and values below indicate interviewer (Int) leading. Higher amounts of synchrony are indicated by warmer colours.

namely the crossing points of genuine synchrony and pseudosynchrony (Tschacher, Ramseyer, & Koole, 2018). In order to convert nonverbal synchrony into a form comparable to an effect size, we followed the transformation suggested by Ramseyer and Tschacher (2011) and calculated a *z*-standardized synchrony score based on the following formula: synchrony – pseudosynchrony/ $SD_{\text{pseudosynchrony}}$. The resulting parameter is similar to Cohen's *d* and may be interpreted in an analogous way: Positive values of synchrony quantify the strength of the phenomenon (real synchrony vs. pseudosynchrony), while negative values stand for synchrony lower than one would expect by chance. A value of zero indicates that synchrony was not different from the cross-correlations found in pseudointeractions.

Oxytocin administration

The study was performed in a double-blind cross-over fashion. inOT was diluted from the original Syntocinon-Spray (Defiante Farmaceutica, Funchal, Portugal) by our hospital pharmacy in sodium chloride to ensure the application of the exact amount of the active substance. As a placebo, we used sodium chloride 0.9% (Ratiopharm, Ulm, Germany). All subjects attended three appointments consisting of a screening session and two experimental sessions in which either inOT or placebo was randomly given at T1 and the respective substance at T2. Administration of inOT and placebo was counterbalanced for the two timepoints. At screening, all subjects were physically examined. For safety reasons, an electrocardiogram (ECG) and laboratory testing (blood cell count, kidney function, electrolytes, prolactin, serum glucose, beta-HCG in female subjects) were carried out. On each experimental session, a urine analysis for drug consumption and (in female subjects) a pregnancy test were performed prior to testing. Subsequently, 24 IU of inOT or placebo were given intranasally. Following the recommendations of Guastella *et al.* (2013), the bottles were first primed and participants instructed how to administer the sprays. The second session took place between 5 and 7 days after the first session. Debriefing after completion of the study suggested that the participants were unaware of whether they had received inOT or placebo.

Childhood Trauma Questionnaire (CTQ)

The CTQ is a 25-item self-report questionnaire that retrospectively evaluates experiences of maltreatment during childhood (Bernstein *et al.*, 1994). In the present study, a validated four-factor model that allowed distinguishing between emotional neglect (EN), emotional abuse (EA), sexual abuse (SA), and physical abuse and neglect (PAN) was used (Wulff, 2006). The scale sexual abuse (SA) had a substantial higher rate of missing data (23.3%) than the other scales (16.7%) and was excluded from further analysis. CTQ scores differed significantly ($p < .001$) in all three factors between patients with BPD and healthy controls (see Table 1 for details).

Statistical analysis

As described in the section on study questions, the analysis reported here was conducted as an extension to observer-coded nonverbal behaviour reported elsewhere (****). The sample size had been determined in accordance with previous research on that subject matter and could thus not be adjusted for the present assessment of nonverbal synchrony. Statistical power was therefore assessed post hoc with G*Power (Faul, Erdfelder, Lang, & Buchner, 2007) and resulted in a value of $1 - \beta = 0.76$ for the main effect comparing OT/PL across the two groups. Direct comparisons between groups/substances were completed with simple *t*-tests and ANOVAs. Multilevel modelling using SAS JMP Pro 11 (SAS Institute, 2014) was used as the primary data analytic tool for the evaluation of global effects. The data were structured in two levels as follows: Interviews (T1/T2, Level 1) were nested within dyads (Level 2). Fixed effects were ‘inOT/PL’, ‘T1/T2’, ‘childhood trauma’, and ‘interaction effects’ of these variables. Random effects were ‘intercept’ and ‘dyad’, nested within each other. Dependent variables in multilevel models were synchrony, ‘subject leading’, and ‘interviewer leading’. Various multilevel models were thus constructed to explore the effects of inOT/PL, time, and self-reported childhood trauma (CTQ) on synchrony. Models were compared according to their corrected Akaike information criteria (AICc). Degrees of freedom were calculated using the Satterthwaite method (Littell *et al.*, 2007). In the Results section, type-3 tests of fixed effects are presented, along with significant fixed-effects parameter estimates and their 95% confidence intervals. Because we standardized synchrony with pseudosynchrony, parameter estimates may be interpreted as effect sizes of synchrony.

Results

Synchrony versus pseudosynchrony, inOT/PL, T1/T2, subject/interviewer leading

Nonverbal synchrony was significantly higher than pseudosynchrony [$t(60) = 2.45$; $p = .017$; $d = .27$] in all interviews assessed (two per subject). Synchrony did not differ significantly in the two conditions of inOT versus PL [$t(29) = 1.01$; $p = .322$; $d = .26$], and it was higher at T2 compared to T1, but only at the level of a trend [$t(29) = 1.92$; $p = .059$; $d = .49$]. Subject leading was significantly higher than interviewer leading [$t(60) = 2.72$; $p = .009$; $d = .41$], that is, subjects were more imitated by their interviewers than vice versa. Considering the effect of inOT and the role of leading, subject leading was (non-significantly) lower under inOT [$t(29) = 1.32$; $p = .192$; $d = .34$] and interviewer leading did show no relevant difference between substances [$t(29) = 0.27$; $p = .790$; $d = .07$] (see Table 2 for further details and comparisons across groups).

BPD versus CTL, gender combinations, associations with childhood trauma

The multilevel evaluation revealed the following differences: For synchrony, the best-fitting model (AICc) contained the fixed effects of inOT/PL and the group combination. The interaction of 'group × substance' was highly significant [$F(1,33.7) = 8.25$, $p = .007$]. This was due to patients with BPD showing lower synchrony under inOT [$t(52.9) = -2.86$; $p = .006$; CI 95 [−0.869 −0.153]]. While this effect was found in both subject leading [$F(1,30.3) = 6.89$, $p = .014$] and interviewer leading [$F(1,38.1) = 4.90$, $p = .033$], it was stronger in subject leading (see Figure 3 for illustration). Associations between synchrony and self-reported childhood trauma were again assessed with mixed models first. The best fit was found in models containing the interaction effect of 'group × substance'. In overall synchrony, the sole significant predictor was this interaction [$t(24.3) = -2.558$; $p = .018$; CI 95 [−0.547 −0.058]]. In subject leading, again the significant predictor was the interaction of group × substance [$t(22.8) = -2.28$; $p = .032$; CI 95 [−0.523 −0.026]], while in interviewer leading, the significant predictor was emotional neglect [$t(22.5) = -2.28$; $p = .032$; CI 95 [−0.053 −0.003]]. Additionally, we explored these associations with Pearson's correlations (for Spearman's correlations, see supporting information Table S1), revealing that during the first encounter (T1), patients who reported emotional abuse (CTQ_EA) displayed lower synchrony [$r(24) = -.402$; $p = .047$], an association that was no longer present at the second interview [T2: $r(24) = .003$; $p = .989$; see Table 3]. The association between childhood trauma and synchrony was even more pronounced when substance was considered: Under inOT, all three scales (emotional neglect, physical abuse, and emotional abuse) correlated negatively with synchrony [$r(24) = -.443$ to $-.456$; all $p < .05$]. These associations were not found under PL [$r(25) = .054$ to $.206$]. Considering the role of leading, associations in the complete sample indicated that interviewer leading – under inOT – was more strongly associated with childhood trauma ($r = -.408$ to $-.460$; $p < .05$) than subject leading ($r = -.272$ to $-.317$; p = ns; see Table 3, for details). Differentiating the sample into group and substance categories resulted in very small

Table 2. Synchrony (standardized) of all dyads [*M* (*SD*)] for different groups [*inOT/PL*]

	BPD		*CTL*			
	inOT (16)	*PL* (16)	*inOT* (14)	*PL* (15)	*p*	*d* inOT/PL
Synchrony	−0.216 (0.763)	0.558 (0.992)	0.603 (0.770)	0.223 (0.710)	.026	−1.07/.65
Subject leading	−0.062 (0.914)	0.740 (1.028)	0.641 (0.853)	0.458 (1.101)	.111	−.80/.26
Interviewer leading	−0.316 (0.769)	0.243 (0.948)	0.423 (0.931)	−0.077 (0.620)	.077	−1.06/.40

Note. *p*-values are based on one-way analyses of variance. Effect sizes (Cohen's *d*) are based on the direct comparison across groups, within substance (e.g., BPD-inOT vs. CTL-inOT).

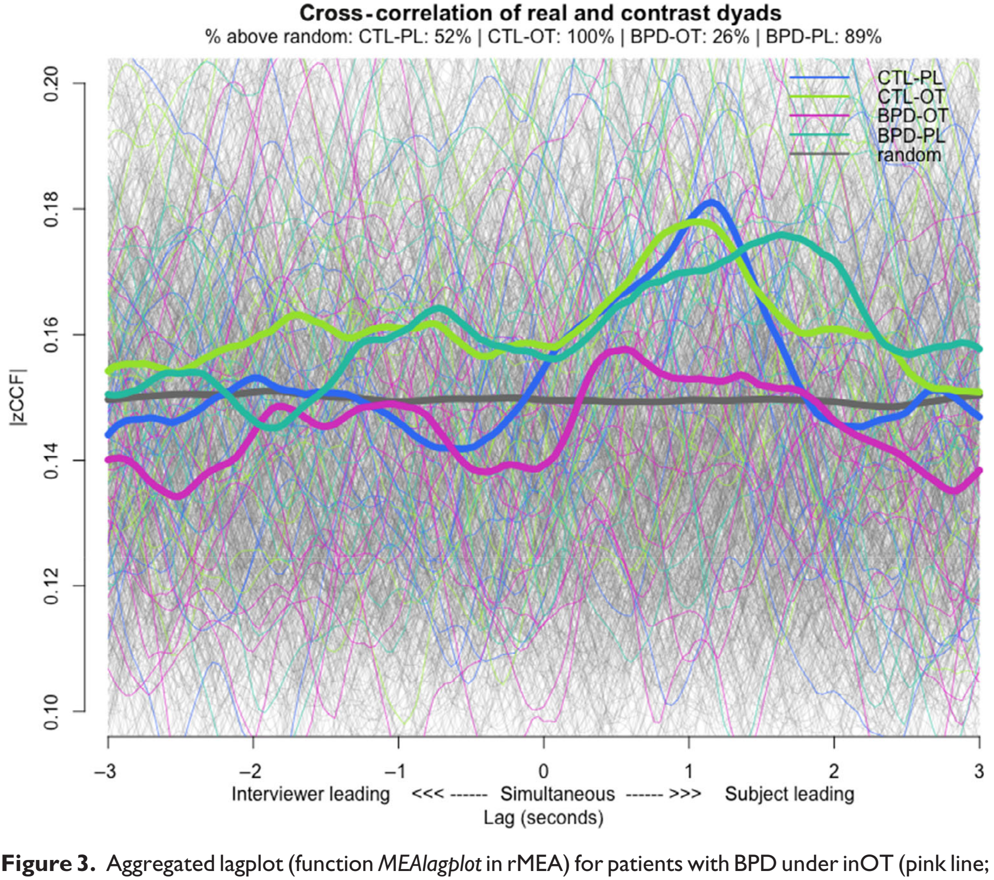

Figure 3. Aggregated lagplot (function *MEAlagplot* in rMEA) for patients with BPD under inOT (pink line; BPD-OT) and PL (turquoise line; BPD-PL), and controls under inOT (green line; CTL-OT) and PL (blue line; CTL-PL). Pseudosynchrony (random, grey line) derived from bootstrapping procedure with *N* = 5000 artificial dyads (= *pseudointeractions*). X-axis: lagged cross-correlations up to ±3 s: Negative lags represent *interviewer leading*, and positive lags represent *subject leading*. Y-axis: averaged absolute cross-correlations.

subgroups (n = 12, n = 13) which mandated careful interpretation. The trend in these small groups showed that the effect mentioned above was primarily due to the group of patients with BPD, who showed strong negative associations between interviewer

Table 3. Correlation coefficients (Pearson's *r*) of 16 patients and 15 healthy controls (*subj*) interacting with an interviewer (*int*)

	Substance						Time					
	inOT (n = 25)			PL (n = 26)			T1 (n = 25)			T2 (n = 25)		
Self-report	Sync inOT	Leading subj inOT	Leading int inOT	Sync PL	Leading subj PL	Leading int PL	Sync T1	Leading subj T1	Leading int T1	Sync T2	Leading subj T2	Leading int T2
CTQ (EN)	−.445*	−.317	−.408*	.054	.152	−.103	−.402*	−.270	−.417*	.003	.095	−.124
CTQ (EA)	−.456*	−.284	−.460*	.206	.220	.098	−.154	−.030	−.233	−.086	.015	−.173
CTQ (PAN)	−.433*	−.272	−.432*	.202	.306	−.026	−.207	−.055	−.296	−.012	.126	−.194

Note. Missing data in various groups; available measures are indicated after groups.
CTQ (EN) = Childhood Trauma Questionnaire, emotional neglect; CTQ (EA) = Childhood Trauma Questionnaire, *emotional abuse*; CTQ (PAN) = Childhood Trauma Questionnaire, *physical abuse and neglect*. Scale CTQ *sexual abuse* not included because of additional missing data.
*p < .05.

leading and CTQ ($r = -.461$ to $-.588$), which was not the case for subject leading and CTQ ($r = -.119$ to .081; see Table 4 and Figure S1, for details). In the control group, associations were generally lower and similar for interviewer leading ($r = .285$ to .363) as well as subject leading ($r = .208$ to .240), with a notable exception for physical abuse: CTQ physical abuse in the control group showed high positive correlations with all three synchrony scores ($r = .506$ to .750). However, it should be noted that seven out of 12 subjects had the lowest score possible on this scale, that is, no physical abuse. Visual inspection of scatterplots confirmed that these high positive correlations should be treated with utmost care. Taking these results together, we can state that a lack of synchrony in traumatized patients appeared to be primarily due to their inability to imitate the interviewer (see Table 4 for details, and Figure 3, left part with negative lags, i.e., interviewer leading).

For the factor 'time', we found a trend that synchrony was higher during the second interview [$t(35.5) = 1.90, p = .066$; CI 95 [−0.028 0.862]], a significant effect for subject leading [$t(40.6) = 2.19$, $p = .034$; CI 95 [0.037 0.926]], and no effect for interviewer leading [$t(33.8) = 1.07, p = .290$; CI 95 [−0.228 0.739]], that is, the increase of synchrony across interviews was more due to interviewers imitating subjects upon second encounter (T2).

Discussion

The present study explored, for the first time, nonverbal synchrony in clinical interviews of patients with BPD and healthy controls. Moreover, we were interested in the specific effect of inOT on nonverbal synchrony. Considering the existence of the phenomenon, nonverbal synchrony was detected in both groups, with a small effect size. It was differentially affected by the intranasal application of OT: While subjects in the healthy control group displayed a tendency to increase synchrony after inOT, the opposite was true for patients with BPD: Their synchrony under inOT was at a low level clearly inferior to pseudosynchrony ($d = -.216$), which is graphically visible in Figure 3: The pink line of BPD-OT falls below the grey line of pseudosynchrony (= random). A similar pattern of differential effects by inOT in BPD has been found, for example, *trust* and *cooperation* (Bartz *et al.*, 2011; Ebert *et al.*, 2013), while another study in a non-clinical sample documented detrimental effects of inOT on mood only in subjects with early life abuse, while inOT had beneficial effects on mood in subjects without abuse (Walsh *et al.*, 2018). It is conceivable that the pattern reported here matches these previous findings insofar as inOT may have triggered a range of negative emotions and fears in patients with BPD, which was not the case in healthy controls. Healthy controls showed an increase of synchronized body movement under inOT, which has also recently been reported in healthy pairs dancing together (Josef *et al.*, 2019). The level of synchrony in our healthy controls under inOT was highest among all subgroups ($d = .60$) and at a comparable level to the one observed in student dyads ($d = .56$ to 1.11; Tschacher, Rees, & Ramseyer, 2014) or psychotherapy dyads ($d = .50$–.59; Ramseyer & Tschacher, 2011). The finding of relatively similar levels of synchrony for BPD patients under PL and controls under inOT suggests that a reversed social effect from inOT may shape BPD patients' nonverbal behaviour: InOT appears to alter patients' (but not healthy controls') perception of the social situation in ways that lead patients to perceive the situation as more threatening (Shamay-Tsoory & Abu-Akel, 2016), which hence may trigger fears of rejection (Foxhall *et al.*, 2019). Accordingly, BPD patients are more cautious and display fewer prosocial

Table 4. Correlation coefficients (Pearson's *r*) of 16 patients and 15 healthy controls (*subj*) interacting with an interviewer (*int*) under inOT versus PL

	BPD						CTL					
	inOT (n = 13)			PL (n = 13)			inOT (n = 12)			PL (n = 13)		
Self-report	Sync inOT	Leading subj inOT	Leading int inOT	Sync PL	Leading subj PL	Leading int PL	Sync inOT	Leading subj inOT	Leading int inOT	Sync PL	Leading subj PL	Leading int PL
CTQ (EN)	−.357	−.119	−.461	−.183	.034	−.379	.351	.240	.285	.358	.367	.055
CTQ (EA)	−.310	.081	−.588*	.178	.306	−.013	.385	.208	.363	−.107	.030	−.296
CTQ (PAN)†	−.367	−.058	−.537***	.125	.366	−.176	.750**	.506***	.604*	.190	.448 ‡	−.447

Note. Missing data in various groups; available measures are indicated after groups.
CTQ (EN) = Childhood Trauma Questionnaire, emotional neglect; CTQ (EA) = Childhood Trauma Questionnaire, *emotional abuse*; CTQ (PAN) = Childhood Trauma Questionnaire, *physical abuse* and neglect. Scale CTQ *sexual abuse* not included because of additional missing data.
†In healthy controls, high percentage (58%) of subjects with no physical abuse reported [CTQ (PAN) = 5].; ‡One outlier detected in scatterplot: $r(10) = -.061$ with outlier excluded from analysis.; $**p < .01$; $*p < .05$; $***p < .10$.

behavioural signals. Less engagement – in the sense of fewer social interactions – has been documented in a diary study of everyday social interaction, where patients with BPD not only reported a lower number of interactions, but also fewer positive interactions (Stepp, Pilkonis, Yaggi, Morse & Feske, 2009). We assume that most of these processes occur outside of conscious control, and subtle cues such as facial emotional display, which are negatively biased in BPD (Daros, Uliaszek, & Ruocco, 2014), contribute to this pattern. It seems that our sensitive measure of nonverbal synchrony is able to pick up one facet of these small changes in the domain of coordinated movement.

Associations between synchrony and self-reported childhood trauma suggested an influence of trauma on synchrony, namely a suppression of imitation by the subject (strongest correlation between CTQ scores and interviewer leading). This association was most prominent under inOT, and it fits the reported relationship between childhood experience and RS (Foxhall *et al.*, 2019). The fact that such an association was primarily present under inOT lends further support to the above-mentioned model of social salience (Shamay-Tsoory & Abu-Akel, 2016): inOT influenced patients' perception of the interview situation, leading to an inability or refrainment from imitating the interviewer.

Some of the existing literature on nonverbal synchrony suggests that an increase of synchrony is associated with better relationship quality (Ramseyer & Tschacher, 2011), positive affect (Tschacher *et al.*, 2014), and appears to be linked with dyads characterized by high affiliative complementarity (Lozza *et al.*, 2018). Other studies failed to find clear associations with affect (Paxton & Dale, 2013) or indicated that an optimal level of synchrony would lie somewhere in between the extremes of low versus high synchrony (Paulick, Deisenhofer *et al.*, 2018), and that synchrony was dependent on patient's diagnosis (Paulick, Rubel *et al.*, 2018). In the present sample, synchrony was importantly influenced by inOT/PL, diagnosis, and self-reported childhood trauma. The correlation between childhood trauma and synchrony is noteworthy insofar as multiple factors appeared to influence this connection: Firstly, inOT increased the association; secondly, the effects were more notable in 'interviewer leading', that is, traumatized patients under inOT unconsciously avoided imitating their interview partners. This behaviour is consistent with ethologically observed nonverbal behaviour in this sample (see Brüne et al., 2015): Healthy controls (but not BPD) showed more affiliative nonverbal behaviour under inOT when administered at T1 (Brüne et al., 2015). Not imitating an interview partner could thus imply that BPD patients under inOT may perceive this situation as potentially more threatening than under PL, which results in a more reserved or cautious way to interact. This is compatible with studies reporting that BPD patients rely more on nonverbal signals than verbal cues when asked to judge the valence of emotional states, particularly due to difficulties to acknowledge positive verbal cues as trustworthy (Brück *et al.*, 2017).

Taken together, our findings corroborate interpretations suggesting that inOT may increase the salience of social stimuli, and act differentially on behaviours related to approach and avoidance (Shamay-Tsoory & Abu-Akel, 2016). We believe that future studies should seek to include the analysis of synchrony and attachment measures, as the pattern found in our study could, very tentatively interpreted, support the idea that inOT increases the social salience for patients with BPD in ways that mistrustful inner working models may be enhanced by inOT.

The present study has several limitations. First, the sample size was relatively small, yet not uncommon for a double-blind placebo-controlled study. Second, attachment style and relationship outcome after the interview were not systematically examined. One could imagine that even though the questions asked in the interviews did not differ between groups, the patient group could have been more negatively activated by questions regarding their current well-being. Third, although studies like this one implicitly assume that OT reaches the central nervous system when given intranasally, there was no objective measure of OT availability in the brain (for a discussion of this potential shortcoming, see Van IJzendoorn & Bakermans-Kranenburg, 2012). Fourth, since some patients received antidepressant medication, it cannot be ruled out that these substances interfered with the inOT administration. Finally, the specificity of findings for BPD is unknown, as no clinical control group was included.

Conclusions

Patients with BPD show a decrease of nonverbal synchrony under inOT, which seem to support previous reports suggesting disruptive effects of OT on social interaction in BPD. The apparent detrimental effect of inOT on nonverbal synchrony could be explained by RS and the social salience model, which may be altered in BPD under the influence of inOT. With regard to the clinical relevance, these findings suggest a potentially important factor in encounters with BPD patients. Their alertness in social situations may hinder them to fully engage nonverbally, and this alertness is even more pronounced when social stimuli are more salient. Moreover, patients with BPD seem to experience and seek fewer social interactions, which also deprives them of possible training opportunities. Clinicians may thus not only seek to establish a safe environment for the development of a secure relationship, but may also focus on both the quality and the quantity of social interactions when dealing with BPD patients. The application of inOT appears detrimental to this aim, and established techniques fostering good relationships (e.g., Bateman & Fonagy, 2010) should be implemented as the first line of treatment.

Future studies into the mechanisms driving nonverbal behaviours and their associations with endocrinological variables are warranted and ideally pursued in larger samples.

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Supporting Information

The following supporting information may be found in the online edition of the article:

Table S1. Correlation coefficients (Spearman's *rho*) of 16 patients and 15 healthy controls (*subj*) interacting with an interviewer (*int*) under inOT versus PL. Missing data in various groups; available measures are indicated after groups.

Figure S1. Scatterplot for "interviewer leading" and childhood trauma questionnaire "emotional abuse" for patients with BPD under inOT (pink line, dots; BPD-OT,) and PL (turquoise line., stars; BPD-PL), and healthy controls under inOT (green line, squares; CTL-OT) and PL (blue line, triangles; CTL-PL). Linear Fit for entire group (grey, dashed line).