

Neuronal correlates of social cognition in borderline personality disorder

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Patients with borderline personality disorder (BPD) have severe problems in social interactions that might be caused by deficits in social cognition. Since the findings about social-cognitive abilities in BPD are inhomogeneous, ranging from deficits to superior abilities, we aimed to investigate the neuronal basis of social cognition in BPD. We applied a paradigm with three social cognition tasks, differing in their complexity: basal processing of faces with a neutral expression, recognition of emotions, and attribution of emotional intentions (affective ToM). A total of 13 patients with BPD and 13 healthy matched controls (HCs) were included in a functional magnet resonance imaging study. BPD patients showed no deficits in social cognition on the behavioral level. However, while HCs showed increasing activation in areas of the mirror neuron system with increasing complexity in the social-cognitive task, BPD patients had hypoactivation in these areas and hyperactivation in the amygdala which were not modulated by task complexity. This activation pattern seems to reflect an enhanced emotional approach in the processing of social stimuli in BPD that allows good performance in standardized social-cognitive tasks, but might be the basis of social-cognitive deficits in real-life social interactions.

Keywords: borderline personality disorder; social cognition; functional magnetic resonance imaging; mirror neuron system; amygdala

INTRODUCTION

Borderline personality disorder (BPD) is a psychiatric disorder characterized by prominent deficits in affect regulation (Putnam and Silk, 2005) and social functioning (Skodol *et al.*, 2002; Hill *et al.*, 2008). Patients with BPD and persons with BPD traits distinguish themselves from individuals without BPD-traits by negative perception (Benjamin and Wonderlich, 1994; Meyer *et al.*, 2004) and expectations of others (Barnow *et al.*, 2009). These impairments in social settings might be conceptualized as deficits in the domain of social cognition.

The term social cognition refers to the processing of all information that culminates in the perception of the intentions and dispositions of an individual (Brothers, 1990). According to Brothers (1990), social cognition comprises different processing stages that are all related to social interactions, starting from the perception of an interaction partner, via the recognition of emotions, to the recognition of intentions. In light of this model, one might ask whether the impairments of BPD patients observed during social interactions can be linked to dysfunctions in one particular processing stage or occur at all levels, in terms of a generalized alteration in the processing of social information.

Although studies on emotion recognition constitute the main area of research in social cognition in BPD their number is still small and their results are heterogeneous, ranging from findings of deficits (Levine *et al.*, 1997; Bland *et al.*, 2004; Guitart-Masip *et al.*, 2009; Unoka *et al.*, 2011), comparable performance with healthy controls (HCs; Minzenberg *et al.*, 2006; Domes *et al.*, 2008; Dyck *et al.*, 2009) to increased sensitivity (Lynch *et al.*, 2006). Results from studies on the attribution of emotion to neutral or ambiguous facial expressions range from no deficit (Levine *et al.*, 1997; Bland *et al.*, 2004;) to

a tendency to attribute negative emotions to neutral faces or ambiguous emotional expressions (Wagner and Linehan, 1999; Domes *et al.*, 2008; Dyck *et al.*, 2009).

The ability to recognize mental states, such as intentions, wishes, and desires of oneself and of others can be conceptualized as theory of mind (ToM; Premack and Woodruff, 1978). A concept very close to ToM is mentalizing: the capacity to implicitly and explicitly understand oneself and others through subjective states and mental processes (Fonagy and Bateman, 2008). It is supposed that in BPD the ability to mentalize develops insufficiently due to an insecure attachment style and an insufficiently marked mirroring of the emotional state by the caretaker during the early development of the patients (Fonagy and Bateman, 2008). However, studies on ToM in BPD point towards no deficit (Murphy, 2006; Harari *et al.*, 2010), or only a subtle one (Preissler *et al.*, 2011), or even a superiority in BPD (Arntz *et al.*, 2009; Fertuck *et al.*, 2009; Franzen *et al.*, 2011). Especially, interesting is a study, by Harari *et al.* (2010), showing that patients with BPD are superior in affective ToM (the ability to recognize affective mental states), while showing equal performance in cognitive ToM (the ability to recognize mental states without the aid of emotional information).

From a neurobiological perspective, several brain structures have been discussed as being substantially involved in social cognition. While the perception of faces in general is mainly based on the inferior occipital lobe, the fusiform gyrus and the superior temporal sulcus (STS), emotion recognition additionally recruits the amygdala and the insula (Haxby *et al.*, 2000; Fusar-Poli *et al.*, 2009). If the recognition of intentions is required as in ToM, prefrontal areas, such as the anterior cingulate and the inferior prefrontal gyrus are recruited for task solving (Gallese and Goldman, 1998; Frith and Frith, 2006). One network that seems to be especially important for the recognition of intentions is the mirror neuron system (MNS). The MNS is the place where the matching of one's own motor representation and the motor representation of others seem to coincide by a simulation mechanism (Gallese and Goldman, 1998). Areas that belong to the human MNS are the inferior prefrontal gyrus, specifically Brodmann area

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44 (BA 44), the inferior parietal lobe and associated the superior temporal sulcus (STS) (Iacoboni *et al.*, 2001; Rizzolatti and Craighero, 2004). However, it was demonstrated recently that neurons with mirror properties can also be found outside of these areas, such as in the medial temporal lobe, in the somatosensory cortices, and in the anterior cingulate cortex (Keysers and Gazzola, 2010; Keysers *et al.*, 2010; Mukamel *et al.*, 2010). In addition, if intentions are linked to affective states, as in affective ToM, intention recognition also seems to be associated with an activation in the amygdala (Baron-Cohen *et al.*, 1999; Castelli *et al.*, 2000; Gallagher and Frith, 2004) that exceeds the already observed activation during emotion recognition (Mier *et al.*, 2010).

Several brain imaging studies concordantly point to a particular importance of the amygdala for social-cognitive deficits in BPD. Hyperactivation in the amygdala in BPD was found during the presentation of negative scenes (Herpertz *et al.*, 2001; Koenigsberg *et al.*, 2009a, 2009b) as well as during the processing of neutral and emotional facial expressions (Donegan *et al.*, 2003; Minzenberg *et al.*, 2007). To the best of our knowledge, there are no studies investigating the neuronal bases of ToM in BPD, until now. However, there are some studies giving evidence for alterations in BPD in the MNS. Koenigsberg *et al.* (2009a) found increased STS-response to negative pictures in BPD, Dziobek *et al.* (2011) reported decreased STS-activation in BPD associated with cognitive empathy, and Juengling *et al.* (2003) investigating metabolism during resting-state demonstrated decreased inferior prefrontal glucose consumption.

Taken together, while the results about social cognition in BPD on the behavioral level are rather inconclusive, functional imaging studies point more homogeneously to a hyperactivation of the amygdala in response to social stimuli. Thereby alterations are reported on different stages of social cognition. However, in none of the studies, different stages of social cognition were investigated together in one paradigm and, in none of these studies, ToM was assessed. As a first attempt to study neural correlates of ToM in BPD, we applied a paradigm, including affective ToM-, emotion recognition-, and basal face processing-tasks (Mier *et al.*, 2010a, b). This enabled us to investigate whether possible alterations in affective ToM are specific to the intention recognition process or rather based on a global deficit in the processing of social stimuli. Based on the literature, we did not assume finding performance deficits in BPD, but alterations in the neuronal activation associated with the tested social-cognitive tasks. We hypothesized that patients with BPD show hyperactivation in the amygdala already at the lowest stage of processing i.e. the processing of neutral faces without the necessity to attribute an emotional state. In addition, it was hypothesized that the more complex social cognition processes, i.e. emotion recognition and affective ToM, are associated with additional aberrations in cortical structures. Especially, we were interested in alterations regarding structures linked to the simulation of intentions, namely areas of the MNS, such as the STS and BA 44 (Rizzolatti and Craighero, 2004; Iacoboni *et al.*, 2005; Mier *et al.*, 2010a).

MATERIALS AND METHODS

Sample

The sample consisted of 13 patients with BPD and 13 healthy control subjects. Both groups were matched by gender, age and education (Table 1). To avoid inclusion of control subjects with current or life-time psychiatric diagnosis, control subjects were screened with the Mini-DIPS (Margraf, 1994) and included only if they had no first relatives with any history of psychiatric disorders.

Exclusion criteria for BPD-patients were comorbid schizophrenia, and alcohol or drug-addiction, other than nicotine or cannabis.

Table 1 Sociodemographic variables for both groups

	Borderline patients	Healthy controls	Significance
Gender	9 f, 4 m/f	8 f, 5 m	Chi, $P=0.50$, <i>n.s.</i>
Age	28.15 years (s.d. = 7.06)	30.46 years (s.d. = 4.29)	$P=0.33$, <i>n.s.</i>
School education	10.23 years (s.d. = 1.30)	10.85 years (s.d. = 1.68)	$P=0.31$, <i>n.s.</i>

Diagnoses of BPD were made by an experienced psychiatrist. All patients met criteria for a DSM-IV diagnosis of BPD. All, except one, of the BPD patients were inpatients. A total of 12 of the patients were medicated (10 received anti-depressants, 7 received anti-psychotics, 2 received anti-epileptics and 1 received a hypnotic). To assess depressive symptoms the Becks Depression Inventory (BDI) was used (Beck *et al.*, 1996). All patients had clinical relevant symptoms of a depressive episode [mean BDI = 28.9, s.d. = 8.6 (cut-off = 18)]. Comorbidities were: nine recurring depressions with acute episode, two substance misuses, two substance addictions, one acute depressive episode, one general anxiety disorder, one post-traumatic stress disorder, one adjustment disorder and one mixed disorder of conduct and emotion.

None of the subjects had a history of neurological disease and all were right-handed. Participants gave their written informed consent prior to participating in the study. The study was approved by the local ethic commission of the Justus Liebig-University of Giessen Medical School.

Procedure

The experimental design is described in detail elsewhere (Mier *et al.*, 2010b). In brief, face stimuli were used with a neutral expression, or an expression of joy, anger, or fear. Three conditions were implemented in an event-related functional magnetic resonance imaging (fMRI) design, each introduced by a different statement, either concerning an emotional intention (affective ToM), an emotional state (emotion recognition), or a physical feature (neutral face processing) of the depicted person. Each trial started with the display of the particular statement, followed by one of the face stimuli. Stimuli in the affective ToM and in the emotion recognition task were identical. The stimuli in the neutral condition consisted of the same persons, but only stimuli with neutral facial expressions were used. Subjects had to indicate by button press whether the statement matched the picture of the person (Figure 1, for experimental design). The experiment was implemented in the Presentation software, version 9.50 (Neurobehavioral Systems, Albany, CA, USA).

Data acquisition and data analysis

fMRI data were collected with a 1.5 T General Electrics (Milwaukee, IL, USA) whole-body scanner. A total of 185 volumes were collected in an interleaved order with an axial T_2^* -weighted echo-planar sequence (30 slices, slice thickness 5 mm, TR 3000, TE 50, alpha 90°, FoV 220, 64 × 64 matrix). Slices were adjusted to AC-PC.

As behavioral dependent variables accuracy of task solving (percentage of correct responses) and reaction times (RT) were measured. RTs and performance data were analyzed separately with 2 × 3 factorial ANOVAs with the independent factor 'group' (BPD vs healthy control) and the repeated measurement factor 'condition' (affective ToM vs emotion recognition vs neutral task). In addition, Pearson product moment correlations were calculated to investigate the relationship between affective ToM and emotion recognition performance. These analyses were done with SPSS v15 (SPSS Inc., Chicago, IL, USA).

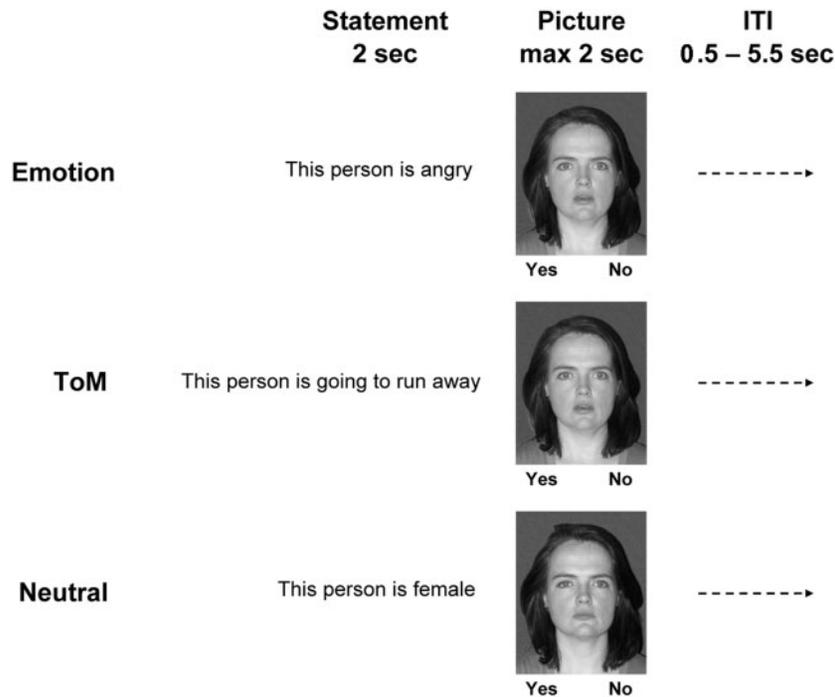


Fig. 1 Experimental conditions and procedure, exemplarily shown for a single trial per condition.

Functional imaging data were pre-processed and analyzed using SPM5 (Wellcome Department of Cognitive Neuroscience, London). Pre-processing consisted of realignment, slice time correction, normalization and smoothing (8 mm full width at half maximum, Gaussian isotropic kernel).

For the statistical analysis, a fixed effects general linear model was calculated for each person separately. Using an event-related approach, the regressors were convolved with a hemodynamic response function. The onsets of all trials with correct responses were used as predictors separately for each condition. Furthermore, one regressor was defined with all trials with incorrect responses across the three conditions. Realignment parameters were used as covariates. To further control for noise in the data, time series from white matter and cerebrospinal fluid were extracted and used as covariates. A high-pass filter with 128 s was applied. After model estimation, linear contrasts were applied to explain activation in the three experimental conditions. Those linear contrasts were used in a second-level full factorial design using a random effects model. For group comparison, region of interest analyses (ROIs) were conducted for the amygdala, the STS and BA 44. The masks for amygdala and BA 44 were taken from the Brodmann atlas, as implemented in the automatic anatomical labeling atlas (AAL; Tzourio-Mazoyer *et al.*, 2002) and edited with a 3D dilation kernel of one with the Wake Forest University (WFU)-Pickatlas (<http://www.fmri.wfubmc.edu/cms/software>). The mask for the STS was taken from a previous study with a similar design (Mier *et al.*, 2010a) and edited with MARINA (Walter *et al.*, 2003). Whole-brain activations for the group comparisons are reported at a significance level of $P < 0.001$ uncorrected. ROI-analyses were conducted, applying a lowered significance level of $P < 0.01$ uncorrected, but from all supra-threshold clusters only those with a peak voxel significantly activated at $P < 0.05$ small volume corrected are reported. Results from the single groups are reported at a significance level of $P < 0.001$ uncorrected and can be found in the Supplementary Tables S1–S4.

RESULTS

Behavioral results

There was no main effect of group or interaction by group and condition, neither for performance nor for reaction times (all $ps > 0.05$; Supplementary Figure S1). Correlation analyses revealed a significant correlation between affective ToM and emotion recognition performance in the healthy controls ($r = 0.618$; $P = 0.024$), replicating earlier findings (Mier *et al.*, 2010a,b), and on a trend level in the BPD patients ($r = 0.506$; $P = 0.078$), too.

Functional brain-imaging data

Main effect of group

HCs showed a significantly stronger activation of the right inferior prefrontal gyrus and thalamus, and in the left visual association cortex and cerebellum compared to BPD patients (Table 2). ROI-analyses revealed significantly higher activation in the HCs than in the BPD patients for BA 44 bilaterally (left: peak voxel $-57\ 12\ 6$, cluster size 19, $T = 3.37$, $P = 0.041$, small volume corrected; right: peak voxel $48\ 12\ 15$, cluster size 45, $T = 3.60$, $P = 0.019$, small volume corrected).

BPD patients, on the other hand, showed stronger activations than the HCs in the left amygdala and somatosensory, and primary motor cortex, and in the right visual association cortex (Table 2; Figures 2 and 3A). ROI-analyses confirmed the hyperactivation of the left amygdala in the BPD patients (peak voxel: $-33\ -3\ -18$, cluster size = 8, $T = 3.45$, $P = 0.019$, small volume corrected).

Group \times condition interactions

Whole-brain analysis revealed no regions showing a significant interaction between groups and task condition. However, a group difference that was modulated by the to be solved task could be observed in ROI-analyses for the left BA 44 (peak voxel $-51\ 15\ 9$, cluster size 32, $T = 3.57$, $P = 0.025$, small volume corrected) and left STS

Table 2 Main effect of group

Area	BA	Cluster	MNI			T-value
			x	y	z	
<i>Healthy controls > Borderline patients</i>						
Cerebellum		21	33	-69	-42	4.50
Middle Occipital Gyrus	19	16	-33	-81	21	3.81
Cuneus	19		-30	-81	30	3.55
Inferior Prefrontal Gyrus	44	9	48	12	15	3.60
Thalamus		7	9	-3	6	3.47
<i>Borderline patients > Healthy controls</i>						
Cuneus	19	8	24	-90	36	4.00
Post-central Gyrus	1	16	-66	-15	27	3.64
Pre-central Gyrus	4		-60	-15	33	3.57
Amygdala		5	-33	-3	-18	3.45

Note: Results are reported with a significance threshold of $P < 0.001$, uncorrected.

(peak voxel -51 60 21, cluster size 47, $T = 3.64$, $P = 0.027$, small volume corrected), resulting from increasing activation from the neutral task to the affective ToM task in the healthy control group, but not in the BPD group (Figure 3B and C).

We additionally tested for group differences at the single social cognitive stages. These results are reported in the Supplementary Materials (Supplementary Text and Tables S5–S8).

Relationship to depressive symptomatology

To explore potential influences of the comorbid depression in the BPD-group, simple regression analyses between BDI sum score and brain activation in the ROIs were conducted, using SPM. In none of the tasks a significant relationship was found.

DISCUSSION

Based on Brothers (1990) model of social cognition, the aim of this study was to investigate affective ToM, as well as more basic stages of social cognition, i.e. face processing, and emotion recognition in BPD. It was assumed that patients show hyperactivation in the amygdala independent of the specific social-cognitive process, and with increasing complexity of the social-cognitive task have aberrations in brain activation in areas of the MNS, too.

Patients with BPD had no alterations on the behavioral level in any of the tested stages of social cognition. However, as hypothesized, they showed alterations in brain activation. We found evidence for general aberrations in the processing of social stimuli, as well as aberrations that were linked to the complexity of the social-cognitive task: patients with BPD showed hypoactivation in areas of the MNS and hyperactivation in the amygdala. While a hypoactivation of BA44 in BPD was found across all tasks, this difference between groups increased over the three stages of social cognition, with the most marked difference occurring during the attribution of intentions. In addition, only during affective ToM a hypoactivation of right STS was found (Supplementary Results). These data reflect that in healthy subjects, the recruitment of cerebral areas, which are assumed to be part of the MNS, was boosted with increasing demands on social-cognitive processes, as reported before (Mier et al., 2010a). In contrast, a comparable activation pattern could not be found in BPD patients. The hypoactivation of the STS is in agreement with a recent study by Dziobek et al. (2011) who found reduced STS-activation in BPD during cognitive empathy. Furthermore, and again in agreement with the literature (Herpertz et al., 2001; Minzenberg et al., 2007; Koenigsberg et al., 2009b), our data clearly point to a hyperactivation

of the amygdala in BPD that was not modulated by task. Activation neither in areas of the MNS nor in the amygdala varied with the task-demands in the BPD-group. However, since we applied only social stimuli (faces) in this paradigm, it is not clear whether this activation pattern can be linked to the processing of social information or whether it is caused by a more basal perceptual aberration that would be evident with non-social material, too.

In addition, to these activation differences between groups in the pre-defined ROIs (amygdala, BA44 and STS), hyper- as well as hypo-activations could be shown in several others brain regions. Additionally, to the hyperactivation in the amygdala, we found a task-independent hyperactivation in the somatosensory cortex in the BPD group. Both the amygdala as well as the somatosensory cortex seem to be involved in emotional simulation processes (Adolphs and Spezio, 2006; Decety et al., 2008; Hooker et al., 2008). On the other hand, in addition to the described task modulated effect in BA44 and STS, we found a general hypoactivation in the thalamus and inferior prefrontal gyrus. These areas are associated with the conscious representation and simulation of actions and intentions (Coricelli, 2005; Iacoboni et al., 2005). It is supposed that the amygdala conveys information about emotional aspects of facial expressions via the insula to the inferior prefrontal cortex where action representation and the recognition of intentions take place (Carr et al., 2003; Pfeifer et al., 2008). Our data suggest that BPD patients and HCs achieve a comparable performance in their social-cognitive functions by a differential usage of a network of brain areas that were recently found to be involved in emotion simulation (Carr et al., 2003; Pfeifer et al., 2008) and affective ToM: BA44, STS, amygdala and somatosensory cortex (Mier et al., 2010a). While BPD patients show enhanced demands on areas associated with an emotional simulation process (Adolphs and Spezio, 2006; Decety et al., 2008; Hooker et al., 2008), HCs have enhanced demands on areas associated with the conscious representation of intentions with increasing complexity of the social-cognitive task (Coricelli, 2005). Thus, the results give evidence not only for general alterations in the processing of social stimuli (amygdala-hyperactivation) but also for alterations that are associated with the specific social-cognitive task (hypoactivation in areas of the MNS that was pronounced for affective ToM). This pattern of activation could represent a more rigid affect dominated processing of social stimuli in BPD that is not adaptive to the specific requirements of the particular social-cognitive task. This interpretation is in agreement with the clinical picture of BPD patients that is marked by high emotionality and a prominent emotion regulation deficit (Putnam and Silk, 2005). A recent study showed, indeed, that hyperactivation in the amygdala while viewing negative pictures was associated with deficits in emotion regulation in BPD (Niedtfeld et al., 2010).

Such an affect dominated processing of social stimuli in BPD could lead to mis-identification of intentions if there are indeed no affective aspects to be considered. Based on heightened amygdala activation, patients with BPD might have an increased sensitivity for negative emotions and intentions (Lynch et al., 2006) and are thus prone to search for negative intentions resulting in a negative bias (Wagner and Linehan, 1999; Dyck et al., 2009). On the other hand, deficits in intention recognition could also occur if intentions must be identified in situations that are highly emotional and self-relevant (Fonagy and Bateman, 2006; Domes et al., 2009). One might speculate that the increased usage of this more 'emotional network' for the identification of intentions, in combination with a reduction in prefrontal control mechanisms (Ruchow et al., 2008; Koenigsberg et al., 2009a) interferes with the processing of the actual emotional content and thus result in false attribution of intentions in BPD patients. Domes et al. (2009) conclude that BPD patients' emotional arousal interferes with the cognitive processing of emotions which is mirrored in a limbic

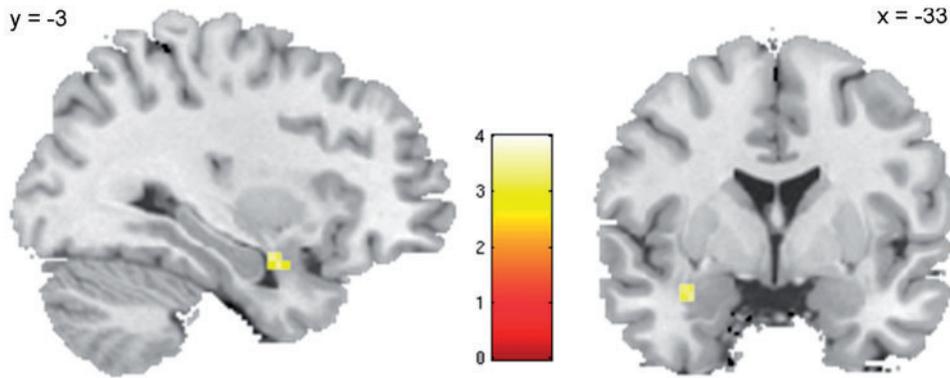


Fig. 2 Main effect of group. Displayed is the significantly increased left amygdala activation in the borderline patients compared to the healthy controls. Threshold for display: $P < 0.005$ uncorrected.

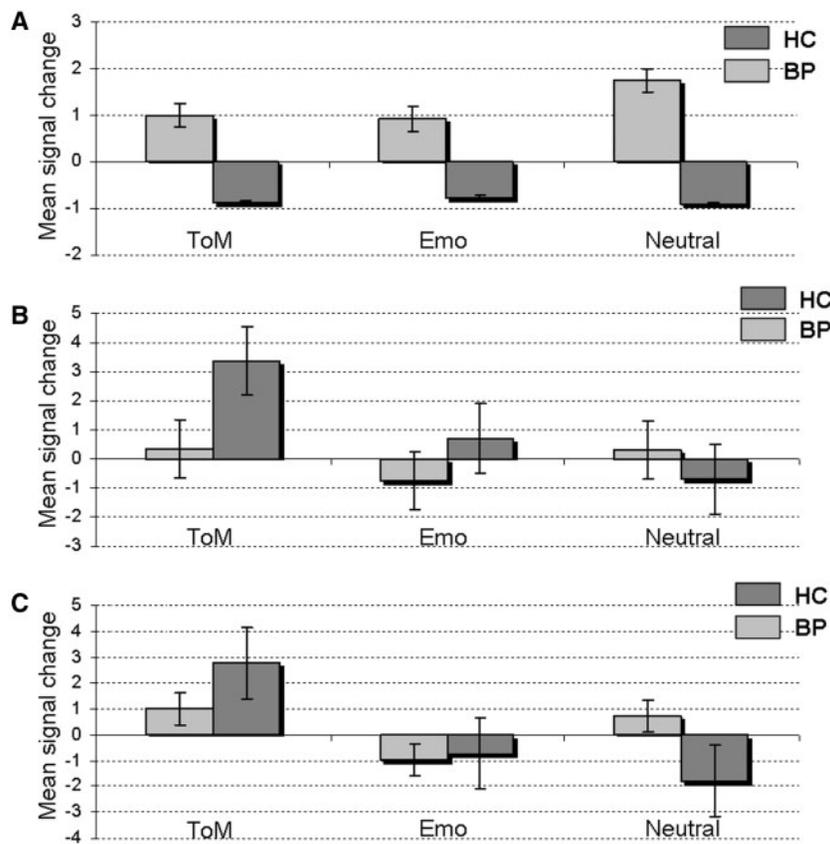


Fig. 3 Mean signal change for both groups in the three conditions. (A) Signal change in the left amygdala. (B) Signal change in the right BA 44. (C) Signal change in the right STS. Note: BP = Borderline Patients, HC = Healthy Controls, ToM = affective ToM, Emo = Emotion recognition, Neutral = Neutral facial processing.

hyperactivation and a hypoactivation in frontal areas. Fonagy and Bateman (2008) assume that mentalizing deficits in BPD lead to a reduced ability to differentiate between the feelings of one and of others. Hence, one could imagine that a hyperactive amygdala, along with reduced prefrontal activation in BPD-patients during social interactions results in a feeling of threat that is directly transferred into the perception of the other person and results in the negative expectations of others.

However, since we could not observe any performance alterations or deficits in the BPD group, this emotional processing of social stimuli, i.e. face stimuli, seems to allow appropriate functioning at least for affective ToM tasks that are not presented in an emotional context.

This assumption is in line with the findings from Harari *et al.* (2010), showing even enhanced abilities in affective ToM, but reduced abilities in cognitive ToM and with the results of the study by Fertuck *et al.* (2009) and our own data (Franzen *et al.*, 2011) showing enhanced ability to recognize affect-related mental states in BPD. It might be that the amygdala hyperactivation in BPD cannot only be seen as a disadvantage that leads to emotion regulation problems and deficits in social interactions but under certain circumstances also as an advantage; i.e. that this amygdala hyperactivation helps overcoming deficits caused by an hypoactive MNS, and thereby supporting emotional interpersonal abilities. Although, it cannot be ruled out that deficits in ToM occur also in a standardized laboratory setting when

more subtle methods are used to assess ToM-abilities (Preissler *et al.*, 2011).

From a developmental point of view, one could speculate whether the hypoactivation in areas of the MNS and the hyperactivation in the amygdala seen in BPD might result from a reduced emotional validation of the BPD patients during childhood (Dziobek *et al.*, 2011), what is a core assumption about the etiology of BPD (Linehan, 1993). The MNS is a network of brain areas that are used early in ontogeny and are inherent of plasticity. Even infants, as young as 6–12 month, show activation in areas of the MNS when predicting actions (Falck-Ytter *et al.*, 2006; Southgate *et al.*, 2009). Beyond this early development of the cerebral system, its activation adapts according to environmental demands, i.e. it can be re-organized and has plasticity (Pierro *et al.*, 2009). Fonagy and Bateman (2008) assume that in BPD, the ability to mentalize develops only partially based on reduced mirroring of the emotional state of the child by the caretaker. Ghiassi *et al.* (2010) could indeed show that the quality of parental care is correlated with mentalizing abilities in patients with BPD. While healthy persons seem to learn understanding their own feelings and predicting actions of their caregiver by a mirroring process, this is refused to children who grow up in an invalidating environment and might lead to a more intuitive emotional assessment. This deviating processing strategy might be reflected in an activation pattern characterized by an amygdala hyperactivation and a MNS hypoactivation as observed in this study.

However, there are several shortcomings that have to be mentioned. The sample size was rather small, what results in a reduced power to detect group differences. It could be shown that the extent of clinical relevant depressive symptoms did not affect brain activation alterations in amygdala, BA 44 and STS. However, patients had various comorbidities and medication that might have influenced the neural processing of the social stimuli. Although all patients had a clinical diagnosis of BPD, the diagnosis and the diagnoses of comorbidities were not further confirmed by a diagnostic interview or clinical scales. Hence, we investigated a relatively heterogeneous sample of BPD patients, varying in gender, medication and occurrence of comorbidities. While this can be regarded as a representative sample of BPD patients (Zanarini *et al.*, 1998; Zimmerman and Mattia, 1999), it holds the disadvantage that the contribution of specific symptom domains upon the investigated social cognition stages remains uncertain. Further studies with larger sample sizes are needed to investigate how different symptom expressions, the various comorbidities, and the medication might contribute to the observed alterations in brain activation during social cognition. Furthermore, it would be interesting for future studies to explore behavioral and neural differences between groups, depending on the valence of the emotional intentions.

In conclusion, to our knowledge, the study reported here is the first study in which the neuronal correlates of affective ToM were investigated in BPD. Our data suggest that BPD patients achieve comparable performance as HCs, not only in affective ToM but also in more basic social cognitions, such as basal face processing and emotion recognition with a differential recruitment of task-relevant brain areas. Patients with BPD had alterations in brain activation that were independent of the specific social-cognitive task (hyperactivation in the amygdala) that point to a deviant processing of social stimuli, in general, as well as to changes in brain activation that got augmented with increasing complexity of the social-cognitive task and point to alterations in more complex social cognitions, such as affective ToM (hypoactivation in areas of the MNS). This pattern of increased amygdala activation and decreased activation in areas of the MNS may reflect a more affect dominated processing of social stimuli that can be appropriate for task solving in affective ToM tasks but results in

deficits in social situations that afford a less emotional and more cognitive interaction style.

SUPPLEMENTARY DATA

Supplementary data are available at SCAN online.

Conflict of Interest

None declared.

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