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Dysregulation between emotion and theory of mind networks in borderline personality disorder

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ABSTRACT

Individuals with borderline personality disorder (BPD) commonly display deficits in emotion regulation, but findings in the area of social cognitive (e.g., theory of mind, ToM) capacities have been heterogeneous. The aims of the current study were to investigate differences between patients with BPD and controls in functional connectivity (1) between the emotion and ToM network and (2) in the default mode network (DMN). Functional magnetic resonance imaging was used to investigate 19 healthy controls and 17 patients with BPD at rest and during ToM processing. Functional coupling was analysed. Significantly decreased functional connectivity was found for patients compared with controls between anterior cingulate cortex and three brain areas involved in ToM processes: the left superior temporal lobe, right supramarginal/inferior parietal lobes, and right middle cingulate cortex. Increased functional connectivity was found in patients compared with controls between the precuneus as the DMN seed and the left inferior frontal lobe, left precentral/middle frontal, and left middle occipital/superior parietal lobes during rest. Reduced functional coupling between the emotional and the ToM network during ToM processing is in line with emotion-regulation dysfunctions in BPD. The increased connectivity between precuneus and frontal regions during rest might be related to extensive processing of internal thoughts and self-referential information in BPD.

1. Introduction

Current theories of borderline personality disorder (BPD) propose that the experience of early life trauma (e.g., childhood abuse or maternal separation), genetics, neurobiological alterations, or a combination of the above may play crucial roles in the development of the disorder (Goodman et al., 2004; Steele and Siever, 2010). In recent years, the spotlight has increasingly been focused on neurobiological abnormalities revealed using in vivo neuroimaging techniques. This focus has resulted in a growing body of evidence supporting the existence of functional neurobiological disturbances in BPD (Goodman et al., 2004; Foti et al., 2011). The majority of previous functional magnetic resonance imaging (fMRI) studies in BPD have looked at activation abnormalities in regions understood to be involved in the regulation of stress responses, emotion and affect, amongst others. The most common finding amongst these studies is that of hyperactivity in the amygdala and insula of BPD patients as well as decreased frontal activity, e.g., in the anterior cingulate cortex (ACC), compared with controls during tasks that involve the processing of emotionally aversive stimuli (Donegan et al., 2003; Minzenberg et al., 2007; O'Neill and Frodl, 2012; Krause-Utz et al., 2014).

Social cognitive aspects like mentalization and theory of mind (ToM), although relevant to BPD and its therapy, have thus far only been explored at a rudimentary level in BPD research. *ToM* describes the ability an individual has to understand and appreciate that others can have mental states (wants, needs, beliefs, knowledge, emotions, etc.) different from one's own, and to understand that these can be used to explain and predict the behaviours of others (Saxe and Kanwisher, 2003). *Mentalization* is the process by which we implicitly and explicitly interpret the actions of ourselves and others as meaningful on the basis of intentional mental states (Bateman and Fonagy, 2004), and thus mentalization shares similarities with the concept of ToM. A deficit in this ability is found in a number of psychiatric and neurodevelopmental disorders, BPD being no exception (Bouchard et al., 2010). Amongst individuals with BPD, researchers have suggested that a deficit in cognitive empathy may contribute to the

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interpersonal dysfunction typically observed (Harari et al., 2010). Franzen et al. (2011) used the trust game to analyse processes of mentalising in a simulated social interaction situation. BPD patients adjusted their investment to the fairness of their partner. In contrast, healthy controls disregarded the trustees' fairness in the presence of emotional facial expressions. Both groups performed equally in an emotion-recognition task and assessed the trustees' fairness comparably (Franzen et al., 2011). When the unfair trustee provided emotional cues, BPD patients assessed their own behaviour as more fair, while the lack of cues led patients to assess their own behaviour as unfair. The authors thus concluded that BPD patients are superior in the attribution of mental states to interaction partners when emotional cues are present (Franzen et al., 2011).

With regard to functional neuroimaging studies, no pure ToM tasks have yet been used. Studies on social cognition in BPD, which involve aspects of ToM, but also have wider implications on encoding, storage, retrieval, and processing of information about other individuals, have found ambiguous results. At present there are two studies in patients with BPD addressing the issue of altered social cognition processing during fMRI. Using the Multifaceted Empathy Test (MET), one study found evidence suggesting deficits in both emotional and cognitive empathy in BPD (Dziobek et al., 2011). Since subjects are required to infer the mental states of the individuals shown in the photographs by selecting one of four mental state descriptors, this task involves some aspects of ToM. Applying the fMRI version of the MET, the authors found that during emotional empathy, the right mid-insula was more activated in individuals with BPD than in non-clinical controls (Dziobek et al., 2011). During cognitive empathy processing, however, the BPD sample displayed decreased activation in both left superior temporal sulcus (STS) and gyrus (STG) (Dziobek et al., 2011). The insula is thought to be related to self-oriented emotion processing (Wicker et al., 2003; Jabbi et al., 2007; Craig, 2009; Singer et al., 2009), and the STS and STG are related to the ability to infer the mental states of others (Saxe and Wexler, 2005; Dodell-Feder et al., 2011).

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) – was applied in the other study. BPD patients showed no deficits in social cognition on the behavioural level. However, while the control participants showed increasing activation in areas of the social brain with increasing complexity in the social-cognitive task, BPD patients had *hypo*activation in these areas and *hyper*activation in the amygdala, effects that were not modulated by task complexity. From this activation pattern, the authors concluded that there is an enhanced emotional approach in the processing of social stimuli in BPD that allows good performance in standardised social-cognitive tasks, but might be the basis of social-cognitive deficits in real-life social interactions (Mier et al., 2013).

While there are no studies in BPD using ToM tasks, ToM was investigated in healthy participants. With fMRI, findings in 12 participants who performed the classic attribution task (McArthur, 1972) showed that the left medial prefrontal cortex (MPFC) played a significant role in ToM (Harris et al., 2005). However, this finding has not proved to be consistent. Saxe and Wexler (2005) found that enhanced activation in the right temporo-parietal junction was selective to the attribution of mental states, and was not recruited by processing other socially relevant facts about a person. Further, right temporo-parietal junction activity was enhanced when the protagonist of a story professed a belief or desire that was inconsistent with the subject's expectations, based on the protagonist's background (Saxe and Wexler, 2005). These results are consistent with neuropsychological deficits in patients with selective forms of brain damage. Damage to the right temporo-parietal junction is associated with a selective impairment of ToM, whereas damage to the medial prefrontal cortex is not (Saxe and Wexler, 2005). A within-subject comparison of reorienting and ToM paradigms revealed that both paradigms activated very similar temporo-parietal junction regions (Mitchell, 2008) implying that the temporo-parietal junction is also involved in non-social mental processes. Interestingly, another study suggested that there are neighbouring but distinct regions within the right temporo-parietal junction implicated in ToM and orienting attention (Scholz et al., 2009).

One option when investigating ToM processes is to use humorous material based on false beliefs of others. It has recently been shown that ToM cartoons (which require additional mentalising skills in order to be understood – the ability to recognise that one character portrayed in the cartoon has a false belief – require more involvement of so-called 'mentalising areas' [e.g., medial prefrontal cortex, temporo-parietal junction (TPJ)] in contrast to cartoons that can be understood without taking the characters' false beliefs into account (Samson et al., 2008, 2009). While there is a good understanding on which regions are activated during ToM processes, no study has investigated the functional connectivity during ToM processing in BPD patients compared with controls.

Work considering "functional connectivity" amongst neural networks is also less common in the BPD literature. As we use the term here, functional connectivity describes the relationship between different brain regions and within particular networks by assessing the correlation of their neuronal activity (Nierhaus et al., 2012). Regions within one particular neural network, the default mode network (DMN), have been found to display their greatest levels of activity when at rest, and decreased activity in some DMN sub-regions during task-based stimulation (Sheline et al., 2010; Zhang and Li, 2012b). During these periods of "active rest", the DMN is thought to be involved in internal processes such as self-referential processing, inner speech, emotional control, episodic memory, and ToM processes (Spreng et al., 2009; Wolf et al., 2011). Research has shown the constituent regions of the DMN to include the medial temporal lobe, the medial prefrontal cortex, the posterior cingulate cortex, the precuneus, and the medial, lateral, and inferior parietal cortex (Broyd et al., 2009; Spreng et al., 2009; Wolf et al., 2011). Surprisingly, though interest in the DMN is on the rise generally, and given the correspondence between the DMN functional roles and the dysfunction observed in BPD, there remains a dearth of research investigating abnormalities in DMN functioning in BPD. Of the research that exists, one study explored alterations in the functional connectivity of the DMN in patients with BPD during pain processing. This particular study observed less integration of the left retrosplenial cortex and left superior frontal gyrus into the DMN in the BPD group than in the controls during pain appraisal (Kluetsch et al., 2012). An earlier study explored prefrontal and limbic resting state networks in BPD patients without any external stimulus. To our knowledge, it is the only study thus far to explicitly examine DMN connectivity in BPD, yielding results that showed an increase in functional connectivity in the left inferior frontal gyrus (IFG) and the left insula, and decreased connectivity in the left cuneus in the BPD group (Wolf et al., 2011). The researchers opine that, with regard to the increased connectivity observed in the IFG, these findings may have implications for the processing of internal thoughts, self-referential information, and interpersonal interactions, and may in the future be found to be a potential biological marker for the disorder (Wolf et al., 2011). Regarding the increased connectivity with the insula, the researchers suggest that abnormal connectivity may be related to both dissociative symptoms and decreased pain sensitivity observed in BPD patients (Wolf et al., 2011).