

Neuroimaging in borderline personality disorder

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Abstract

Neuroimaging has become one of the most important methods in the investigation of the neurobiological underpinnings of borderline personality disorder. Structural and functional imaging studies have revealed dysfunction in different brain regions which seem to contribute to borderline symptomatology. This review presents relevant studies using different methodologies: volumetry of limbic and prefrontal regions, investigations of brain metabolism under resting conditions, studies of serotonergic neurotransmission, and challenge studies using emotional, stressful, and sensory stimuli. Dysfunction in a frontolimbic network is suggested to mediate much, if not all of the borderline symptomatology.

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1. Introduction

The past few years have seen a rapidly growing body of research in the field of neurobiological correlates of borderline personality disorder (BPD) (Lieb et al., 2004; Schmahl et al., 2002; Skodol et al., 2002). In addition to research on the genetic basis of the disorder (Jang et al., 1996; Torgersen et al., 2000), psychopharmacological treatment (Soloff, 2000), and neuroendocrinology (Rinne et al., 2002), progress in neuroimaging has been fruitful in the elucidation of the underlying neurobiology of this severe and chronic disorder.

Affective dysregulation has been suggested to represent the core of borderline symptomatology and to underlie most if not all of the characteristic features of the disorder, such as instable self image, disturbed interpersonal relationships, and self-injurious behavior. Ani-

mal studies as well as investigations in healthy human subjects suggest that limbic as well as prefrontal regions play a decisive role in emotion regulation (Davidson and Irwin, 1999). Thus, it can be hypothesized that frontolimbic dysfunction underlies affective dysregulation as well as other closely connected symptoms of BPD. Consequently, structural as well as functional neuroimaging investigations have focussed on alterations in these brain regions.

This review on neuroimaging in BPD is arranged according to the different imaging methods used. It will start with studies using volumetrics and spectroscopy of different brain regions, such as hippocampus, amygdala, and prefrontal regions. An overview of functional neuroimaging will begin with studies of brain metabolism under resting conditions using FDG-PET. Imaging of the serotonergic neurotransmission system using serotonergic agents will then be reviewed, followed by challenge studies that investigate reactivity of brain areas to stimuli such as emotional pictures, stressful memories, or sensory challenges with the aid of PET or

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functional MRI. Finally, conclusions from the literature reviewed will be drawn and an outlook on future studies will be given.

2. Volumetrics and spectroscopy

Neuroimaging research in the field of BPD began in the early 1980s with the use of computed tomography (CT). Similar to research on brain alterations in schizophrenic patients, whole brain volumes and ventricle sizes were investigated. In contrast to findings in schizophrenia, studies in BPD did not show ventricular enlargement (Schulz et al., 1983; Snyder et al., 1983), or changes in ventricle–brain ratio (Lucas et al., 1989) in patients with BPD. With the advent of Magnetic Resonance Imaging, Lyoo reported a marginally significant reduction of overall frontal lobe volumes in BPD (Lyoo, 1998), although this finding has been criticized for technical reasons such as low spatial resolution and lack of correction for head tilt.

BPD has been suggested to be part of a trauma-related psychiatric spectrum of psychiatric disorders (Bremner, 2002), with posttraumatic stress disorder (PTSD) as the core of the spectrum, but also including BPD, depression and dissociative disorders. A major neurobiological finding of the last decade is a reduction in hippocampal volume as assessed by MR-based volumetry in combat-related (Bremner et al., 1995; Gilbertson et al., 2002; Gurvits et al., 1996) as well as abuse-related PTSD (Bremner et al., 1997; Bremner et al., 2003; Stein et al., 1997). There is an ongoing debate as to whether this volume reduction is due to an elevated activity of stress-associated neurobiological systems, such as the HPA axis or is genetically determined (Gilbertson et al., 2002). In contrast to the finding of reduced hippocampal volume, all published studies investigating amygdala volumes in patients with PTSD did not find any significant amygdala volume difference compared to controls (Bonne et al., 2001; Bremner et al., 1997; De Bellis et al., 1999; Gilbertson et al., 2002; Gurvits et al., 1996).

The first investigation of MRI-based volume of hippocampus and amygdala (Driessen et al., 2000) found 16% smaller volumes of the hippocampus and 8% smaller volumes of the amygdala in women with BPD compared to healthy controls. Tebartz van Elst et al. (2003) found an even more pronounced volume difference between patients with BPD and controls with 20.5% smaller hippocampal and 24% smaller amygdala volume. In addition, they found a highly significant volume-reduction of the left orbitofrontal cortex and of the right anterior cingulate cortex. Our own investigation revealed a reduction of 13% for hippocampus and 21% for amygdala (Schmahl et al., 2003a). A fourth study (Brambilla et al., 2004) also found volume reduction of hippocam-

pus and amygdala, however these reductions did not reach significance. The authors also explored structural brain changes in BPD in relation to childhood abuse. Compared to 20 healthy controls, the ten unmedicated (abuse: $n = 6$, no abuse: $n = 4$) BPD patients, male and female, had significantly smaller right and left hippocampal volumes and significantly increased right and left putamen volumes. There were still significant differences in hippocampal volume when BPD patients with history of childhood abuse were compared to healthy controls. This significance disappeared when comparing healthy controls to BPD patients without childhood abuse. No significant differences between groups were found for caudate, amygdala, temporal lobes, dorsolateral prefrontal cortex and total brain volumes. The authors conclude that early traumatic experiences may play a role in hippocampal atrophy.

Taken together, these findings suggest that, in contrast to PTSD, not only hippocampus but also amygdala volumes seem to be reduced in patients with BPD. In a study using voxel-based morphometry, grey matter volume loss was found in the left amygdala without differences in grey or white matter volume or density anywhere else in the brain (Ruesch et al., 2003).

A different approach to assess neuronal dysfunction is Magnetic Resonance Spectroscopy, which measures concentration of neurochemical metabolites such as *N*-acetylaspartate (NAA), choline, or lactate in specified brain regions. Tebartz van Elst et al. (2001) found a significant 19% reduction of NAA concentration in the dorsolateral prefrontal cortex in patients with BPD compared to controls, suggesting neuropathology in this area of the brain. More studies are needed in this area to draw definite conclusions about disturbed brain metabolism in BPD.

3. Brain metabolism under resting conditions assessed with FDG-PET

[¹⁸F]Deoxyglucose positron emission tomography (FDG-PET) can be used to assess baseline brain metabolism under resting conditions. The first study using FDG-PET in BPD was conducted by Goyer and coworkers (1994). Their investigation comprised 17 patients with DSM III-R personality disorders, six of which (four women and two men) were clinically diagnosed with BPD. However, the average score on the diagnostic interview for borderlines (DIB; Zanarini et al., 1989) in the BPD group was only 3.7, which is only about half of the usual cut-off score of 7. Thus, the results have to be interpreted with caution. In the group of six BPD patients, the authors found decreased metabolism in upper bilateral prefrontal cortex as well as increased metabolism in lower left and right prefrontal areas. Since the spatial resolution of the analysis is

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