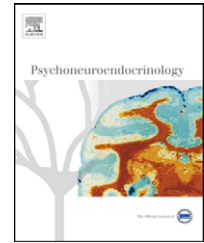




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Neural correlates of the individual emotional Stroop in borderline personality disorder

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Received 18 June 2008; received in revised form 22 October 2008; accepted 22 October 2008

KEYWORDS

Borderline personality disorder;
fMRI;
Stroop task;
Stress;
Emotion;
Cingulum

Abstract

Objective: Emotional dysregulation is a key feature of borderline personality disorder (BPD) with altered inhibitory functions having suggested as being crucial. The anterior cingulate cortex and further prefrontal brain regions are crucial for response inhibition. The regulation of emotions is ensured via inhibitory control over the amygdala. The present study aimed to investigate neural correlates of response inhibition in BPD by using an emotional Stroop paradigm extending the task to word stimuli which were related to stressful life events.

Methods: Twenty BPD patients and 20 healthy controls underwent functional magnetic resonance imaging (fMRI) while performing the individual emotional Stroop task. A block design was used with the following word type conditions: neutral words, general negative words, and individual negative words. The individual negative words were recruited from a prior interview conducted with each participant.

Results: While BPD patients had overall slower reaction times in the Stroop task compared to healthy controls, there was no increased slowing with emotional interference. Controls exhibited significant fMRI blood oxygenation level-dependent signal increases in the anterior cingulate cortex as well as in frontal cortex contrasting generally negative vs. neutral and individual negative vs. neutral conditions, respectively. BPD patients did not show equivalent signal changes.

Conclusions: These results provide further evidence for a dysfunctional network of brain areas in BPD, including the ACC and frontal brain regions. These areas are crucial for the regulation of stress and emotions, the core problems of BPD patients.

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1. Introduction

Borderline personality disorder (BPD) is characterized by a pervasive pattern of instability of interpersonal relationships, self-image, affects and marked impulsivity. Affective dysregulation has been emphasized as a core difficulty in patients with a diagnosis of BPD and is evident in interpersonal relationships and stressful situations (Posner et al., 2003; Lieb et al., 2004). Indeed, stressful life events, daily hassles and (early) trauma are frequent in BPD and seem to have an important impact on onset and course of illness (Pagano et al., 2004; Jovev and Jackson, 2006; Zanarini et al., 2006). Moreover, enhanced endocrine responses to psychosocial stress have been reported, especially for BPD patients with high dissociation scores, further reflecting problems of these patients handling stressful situations successfully (Simeon et al., 2007). It has been shown that patients with high impulsivity are characterized by a strong intensity of affective responses (Herpertz et al., 1997) and that negative emotions as anger are not only stronger, but also more prolonged (Jacob et al., 2008). On the other hand there is also evidence that these observations are not specific for BPD, but are also seen in other personality disorders or depression (Koenigsberg et al., 2002; Renneberg et al., 2005). Several studies investigating physiological correlates of affective responses to emotional stimuli measured the startle response. Some (Ebner-Priemer et al., 2005), but not all (Herpertz et al., 1999, 2000, 2001b) psychophysiological investigations in BPD demonstrated an exaggerated startle reflex. This finding was interpreted in the context of an amygdala hyperresponsivity. Different methods may account for the conflicting results: while Ebner-Priemer et al. used an acoustic startle paradigm, Herpertz et al. used emotional pictures. Interestingly, only BPD patients with low dissociation were characterized by an enhanced startle reaction (Ebner-Priemer et al., 2005), which is in line with the study of Simeon et al. (2003). These data suggest subgroups of BPD patients with different psychophysiological reactions. Other studies investigating hypothalamic-pituitary adrenal functioning in BPD confirm these findings (Rinne et al., 2002; Wingenfeld et al., 2007a,b).

Neuroimaging studies found an increased responsiveness of the amygdala in response to negatively valenced pictures or to facial expressions of emotion (Herpertz et al., 2001a; Donegan et al., 2003). Beside the amygdala itself, a fronto-limbic dysfunction has been emphasized to be crucial emotional dysregulation in BPD (Schmahl and Bremner, 2006). Most brain imaging studies in BPD focused on major negative autobiographical memories. Two positron emission tomography (PET) studies analyzed memories of abandonment and traumatic events, respectively (Schmahl et al., 2003, 2004b). Relative to a psychiatric control groups, BPD patients showed altered brain activation mainly in the orbitofrontal and in the anterior cingulate cortex. A fMRI study of our group compared autobiographical memories of unresolved vs. resolved life events in BPD relative to controls (Beblo et al., 2006). Patients showed increased bilateral activation of the frontal cortex including parts of the insula and of the orbitofrontal cortex as well as temporal activation including the amygdala.

These findings suggest altered brain functioning during the retrieval of negative autobiographical events in BPD. In sum, most (but not all) studies suggest a decreased activation and responsiveness of the ACC (Donegan et al., 2003; Schmahl et al., 2003, 2004b), the hippocampus (Juengling et al., 2003), the medial and orbitofrontal cortex (Soloff et al., 2003; Schmahl et al., 2004b) and the dorsolateral prefrontal cortex (Schmahl et al., 2003, 2004b). On the other hand the amygdala seems to be characterized by increased activity (Herpertz et al., 2001a; Donegan et al., 2003). Accordingly, one hypothesis to explain emotional dysregulation in BPD is a failure of the ACC and of prefrontal brain areas to inhibit the amygdala.

Inhibition has been suggested to be one principal mechanism of emotional regulation and inhibitory dysfunctions have been hypothesized to play an important role in BPD patients (Domes et al., 2006; Fertuck et al., 2006). A widely used method for investigating inhibition of interference is the emotional Stroop task. In this test subjects have to name the colors in which words are printed. Cohen et al. (1990) generally proposed that this "Stroop effect" or "Stroop interference" might be due to an inherent property of parallel distributed processing systems, e.g. neural circuits for reading and color-naming. The strength of an interfering neural circuit, or pathway, depends on an individual's prior practice and learning, on emotional impact, and on personal relevance. Thus, interference grows in proportion to the strength of these parallel stimulated processing routines. Summarizing neuroimaging results on the Stroop task, most studies found activation in the following brain regions: the ACC (Carter et al., 1995; Bush et al., 1998; Whalen et al., 1998; Peterson et al., 1999), parietal lobe (Carter et al., 1995; Taylor et al., 1997; Peterson et al., 1999) and lateral prefrontal cortex (Carter et al., 1995; Taylor et al., 1997). Further, activation of the middle frontal gyrus and the inferior frontal gyrus has been reported (Taylor et al., 1997). The ACC is an important component of parallel distributed attentional networks and is involved in several emotional and cognitive processes, as integrating input from various sources (Bush et al., 2000). In our context, the inhibitory role of medial prefrontal structures with respect to regions involved in emotional responses, e.g. fear, as the amygdala has to be emphasized (Morgan et al., 1993; Morgan and LeDoux, 1995). In sum, the Stroop task seems to be a reliable tool to investigate neural correlates of the inhibitory control of emotional stimuli.

Reduced inhibition has been shown in several clinical populations, especially when emotional stimuli are specifically related to the core psychopathology (Williams et al., 1996). For example, when presenting trauma-related words in the Stroop test, patients with posttraumatic stress disorder (PTSD) showed remarkably slower reaction times and more interference to these words, interpreted as an attentional bias to trauma-related stimuli (Foa et al., 1991; Cassidy et al., 1992; McNally et al., 1993; Kaspi et al., 1995). Noteworthy, these stimuli are not only related to psychopathology but also to highly stressful events. Interestingly, research has shown that enhanced interference could also be evoked in a non-clinical sample, but predominantly to words which were related to stressful life events, and, thus are characterized by personally relevance (Wingenfeld et al.,

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