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Research report

The neurobiology and clinical significance of depersonalization in mood and anxiety disorders: A critical reappraisal

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Abstract

Depersonalization and derealization occur on a continuum of situations, from healthy individuals to a severely debilitating disorder where the symptoms can persist chronically. Since 1960s, different neurobiological models have been hypothesized and they have been associated with the temporal lobes. Recent advances in the functioning of the limbic system and the application of Geschwind's concept of disconnection in the cortico-limbic networks, pointed the role of the amygdala and its connections with medial prefrontal cortex and anterior cingulate cortex, the same structures that are strictly interlinked with the neurobiology of emotions and affective disorders.

In this paper, we hypothesize that depersonalization may represent a clinical index of disease severity, poorer response to treatment and high level of comorbidity, in mood and anxiety disorders, discussing the neurobiology of depersonalization and the available clinical evidence.

Keywords: Depersonalization; Derealization; Amygdala; Bipolar disorder; Major depression; Panic disorder

1. Introduction

Depersonalization (DP) is defined as an experience in which the individuals feel a sense of unreality and detachment from themselves. Symptoms often include dreamy state and a sense of detachment. There may be a sensation of being an outside observer of one's mental processes, one's body, or parts of one's body. Various types of sensory anesthesia, lack of affective response, and a sensation of lacking control of one's actions, including speech are often present. These experiences are not delusional in nature since the sufferer retains insight that these are subjective phenomena rather than objective reality. DP is often associated with derealization in which the external environment also appears unfamiliar. The term derealization was coined during the early 20th century, but, in this paper, unless specifically indicated, DP will be used as the generic term for both aspects, as there is no conclusive evidence that derealization is an independent phenomenon (Sierra and Berrios, 2001).

DP occurs on a continuum of situations, from healthy individuals (lasting only a few moments), often under conditions of stress, fatigue, or drug use, to a number of neuropsychiatric conditions such as epilepsy, migraine, anxiety disorders (especially panic disorder), major depression and schizophrenia. DP may also present as a

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severely debilitating disorder where the symptoms can persist chronically and unremittingly for decades. DP disorder is classified with four essential criteria as one of the dissociative disorders in the DSM-IV (American Psychiatric Association, 1994) (Table 1).

Although the interest in the phenomenology and epidemiology of the dissociative disorders has flourished over the last decades with the accumulation of a large literature, most of the studies have several limitations: the utilization of different methods in the assessment, data collection and diagnostic criteria. Transient symptoms of DP in the general population are common with a lifetime prevalence rate ranging between 26% and 74% (Hunter et al., 2004). Community surveys using standardized diagnostic interviews reveal rates of 1.6%–1.9% for 1-month prevalence in two UK samples (Bebbington et al., 1981, 1997) and 2.4% in a Canadian study (Ross et al., 1991). Prevalence rates in clinical samples of specific psychiatric disorders vary between 30% of subjects with post-traumatic stress disorder (Davidson et al., 1990), 60% of inpatients with unipolar depression (Noyes and Kletti, 1977) and 80% in patients with panic disorder. Interestingly, a Japanese study (Mizobe et al., 1992) reported a relatively low prevalence in patients with panic disorder (ranging between 9% and 25%) that may be due to methodological differences or truly national or ethnic variations in dissociative symptoms.

In this paper we hypothesize that DP may represent an index of severity in mood and anxiety disorders discussing the neurobiology of DP and the available clinical evidence.

2. The neurobiology of depersonalization

The neurobiology of DP seems to be partly interlinked with that of affective disorders, overlapping in several aspects and differentiating in others. Thus, two main models are relevant for the understanding of the biological basis of DP: the neurobiology of emotional processing and the view that DP may represent a vestigial brain-response to life-threatening situations (Roth and Argyle, 1988).

Table 1
DSM-IV diagnostic criteria for depersonalization disorder

A. Persistent or recurrent experiences of feeling detached from, and as if one is an outside observer of, one's mental processes or body (e.g. feeling like one is in a dream).
B. During the depersonalization experience, reality testing remains intact.
C. The depersonalization causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.
E. The depersonalization experience does not occur exclusively during the course of another mental disorder, such as schizophrenia, panic disorder, acute stress disorder, or another dissociative disorder, and is not due to the direct physiological effects of substance (e.g. a drug of abuse), a medication or a general medical condition (e.g. temporal lobe epilepsy).

2.1. Depersonalization and the neurobiology of emotions

The neurobiology of emotional processing is still not completely clear but converging evidence suggests that the amygdala, the anterior cingulated cortex (ACC) and the medial prefrontal cortex (MPC) are salient structures of parallel networks that integrate emotional responses. In animals and humans, the amygdala is implicated in processing threat and fear stimuli (Adolphs et al., 1994; Buchel et al., 1998; Hamann et al., 1996; LeDoux et al., 1988) and in assigning emotional and cognitive significance giving a strong feeling of reality and personal relevance (Gloor, 1990). Moreover, neuroimaging studies also showed activation of the amygdala during recall of emotionally charged memories (Cahill et al., 1996) and emotional visual imagery (Shin et al., 1997). Thus, increased amygdala function appears to be clearly linked to phobic disorders (Stein et al., 2002). The central amygdala nucleus seems to play a crucial role in the generation of autonomic arousal responses to threat stimuli (LeDoux et al., 1988) and correlates with evoked sympathetic arousal (Buchel et al., 1998; Morris et al., 1997).

The ACC activates during some of the same emotional states, but also in the emotional assessment of pain, generation of motivated behavior and attentional processes, suggesting that this region probably represents the main output center for all the autonomic responses due to amygdala activation in emotional processing. Moreover, recent studies demonstrated that the ACC mediates context-driven modulation of bodily arousal states (Critchley et al., 2003). However, this process has not been completely defined, explaining the contrasting results of studies investigating the role of stress hormones in patients with DP disorder, particularly the hypothalamic–pituitary–adrenal (HPA) axis (Stanton et al., 2001; Simeon et al., 2001) and the norepinephrine system (Simeon et al., 2003a,b). Stanton et al. (2001) found that patients with DP disorder have lower basal cortisol levels than subjects with major depression, supporting the view that DP pathophysiology, as reflected in the functioning of the HPA axis, is distinct from depression. Moreover, DP disorder seems to involve a pattern of HPA axis dysregulation which differs also from PTSD, being the former associated to a