Depersonalization disorder

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Purpose of review

There is increasing interest in depersonalization disorder, in part because of the increased community awareness of the condition via the Internet. The disorder may be more prevalent than schizophrenia but is often misdiagnosed; hence, an update is timely.

Recent findings

Recent research has included characterization of the nosology and phenomenology of the disorder, whereas emerging evidence demonstrates a neurophysiological dampening down in addition to psychological dampening in the face of emotional stimulation.

Summary

Greater understanding of the clinical characteristics of this disorder will improve the reliability of diagnosis and aid the development of neurobiological and psychological models for empirical testing. Although response to current treatments has been disappointing, recent research has identified the basis for the development of new pharmacological and psychological treatments

Keywords

depersonalization, depersonalization disorder, dissociation

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Introduction

Fleeting experiences of depersonalization, such as feeling detached from the self, are common, with an annual prevalence of 46–74% in the general population and a lifetime prevalence of 26–70% [1]. In some people, these feelings become chronic and reach the threshold for diagnosis of depersonalization disorder (DPD) when the experience interferes with the ability to form close relationships or fulfil their social roles. The availability of support groups and self-diagnosis websites on the Internet has resulted in increased lay interest. Professional interest is also increasing, and an update is, therefore, timely.

The Diagnostic and Statistical Manual, Fourth Edition, Text Revision (DSM-IV-TR) diagnostic criteria for 300.6 Depersonalization Disorder [2] are as follows:

(1) 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).
(2) During the depersonalization experience, reality testing remains intact.
(3) The depersonalization causes clinically significant distress or impairments in social, occupational or other important areas of functioning.
(4) 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 a substance (e.g. a drug of abuse, a medication) or a general medical condition (e.g. temporal lobe epilepsy).

The International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10) diagnostic criteria for F48.1 Depersonalization–Derealization Syndrome [3] are as follows:

Either or both of (1) and (2), plus (3) and (4):

(1) Depersonalization symptoms, that is, the individual feels that his or her own feelings and/or experiences are detached, distant, not his own, lost, and so on.
(2) Derealization symptoms, that is, objects, people and/or surroundings seem unreal, distant, artificial, colourless, lifeless, and so on.
(3) An acceptance that this is a subjective and spontaneous change, not imposed by outside forces or other people (i.e. insight).
(4) A clear sensorium and absence of toxic confusional state or epilepsy.

For this review, Medline and Embase searches were conducted using the search terms 'depersonalization disorder'. References in individual articles were hand-searched for relevant articles. As depersonalization may be a feature of many psychiatric disorders, this article focuses on the disorder and not the symptom.

Epidemiology and clinical features

DPD may be more common than is generally believed. Community and population studies reveal a period prevalence of about 1–2% for DPD [1], compared with a period prevalence of 3.3/1000 for schizophrenia [4].

The main clinical features of depersonalization represent a schism within a person's previously integrated sense of self. Sensory and emotional experiences are disconnected from motor aspects and conscious awareness, resulting in patients' self-descriptions as follows: feeling like a robot, detachment from one's emotions, image in the mirror feeling 'strange' and detachment from body movements or speech. Those with DPD also complain of poor attention, concentration and memory. Neuropsychological testing has confirmed difficulties with attention as well as speed of information processing and immediate visual and verbal recall [5].

Depersonalization frequently coexists with other psychiatric disorders. One study noted that symptoms of derealization (the feeling of being detached from one's surroundings) were reported in 73% of patients with DPD [6]. A study of dissociation in borderline personality disorder found 19% of patients had comorbid DPD [7••]. Anxiety and depression coexist in the majority of cases. Of the anxiety disorders, a study of 117 patients found 64% with lifetime comorbid anxiety disorders, which included social phobia, obsessive compulsive disorder (OCD) and generalized anxiety disorder. Seventy-three percent had a lifetime comorbid unipolar mood disorder, whereas only 11% had no lifetime history of either unipolar mood disorder or anxiety disorder [8]. Baker *et al.* [6] found similarly high rates of psychiatric comorbidity. Fifty percent of patients had a previous psychiatric diagnosis, with depression (62%) and anxiety disorders the most common. Only about 10% did not have depression or anxiety.

The high rate of comorbidity with other psychiatric disorders impels the question whether depersonalization is a distinct disorder or an atypical presentation of anxiety and depression. The nosology of the disorder may have been hampered by current diagnostic criteria. DPD is classified as a dissociative disorder in DSM-IV-TR [2], but with mood and anxiety disorders in ICD-10 [3]. Some researchers have pointed out that the current definitions reduce depersonalization to 'feelings of unreality' [9], that is, a single symptom. Using the Cambridge Depersonalization Scale (CDS), two separate research groups have derived remarkably similar symptom groups on factor analysis. Sierra *et al.* [9] described four groups – 'anomalous body experience', such as lack of agency; 'emotional numbing'; 'anomalous subjective recall' or memory of personal experiences; and 'alienation from surroundings' – which correspond closely to clusters described by Simeon *et al.* [10•] as 'numbing', 'unreality of self', 'perceptual alterations', 'unreality of surroundings' and 'temporal dissociation'. Taken together, these studies bolster the argument that DPD is a distinct syndrome comprising clusters of symptoms rather than a single symptom entity of detachment from one's surroundings.

DPD generally starts in adolescence or young adulthood. In one study, the mean age of onset was 15.9 years with less than 20% having an onset later than 20 years [8], whereas, in another, the mean age of onset was about 23 years, with a wide range of ages at onset (4–69) noted [6]. Onset can be *de novo*, after illicit drugs or during a stressful period of life [6,8]. The course varies from an abrupt commencement of unrelenting course to discrete episodes of depersonalization lasting from hours to months, which over time become chronic. The intensity of symptoms may fluctuate depending on individual exacerbating and relieving factors such as psychological stress, fatigue or exercise [6,8].

Diagnosis

The diagnosis of DPD is clinical, and a number of scales have been developed to aid diagnosis and differentiate it from other dissociative disorders. The Structured Clinical Interview for DSM-IV Dissociative Disorders (SCID-D) [11] is extensive but requires training and takes at least 30 min to administer.

The Dissociative Experiences Scale (DES) [12] has been widely used as it is quick to self-administer, but has only a few items on depersonalization. The diagnosis of DPD has been aided by the development of the CDS [13], a 29-item scale, which captures the frequency and duration of depersonalization symptoms. More recently, the Structured Clinical Interview for Depersonalization–Derealization Spectrum (SCI-DER) has been developed with the aim of assessing depersonalization symptoms across an individual's lifespan and in the context of other psychiatric diagnoses [14••] rather than diagnosing DPD *per se*, based on the premise that the presence and severity of depersonalization symptoms in other psychiatric disorders is of prognostic importance [15].

Cause

Symptoms of depersonalization can occur during medication use [16] or intoxication by illicit drugs, and in

neurological conditions, particularly epilepsy and migraine [17,18]. In epilepsy, the preponderance of cases occurred in those with partial seizures [18]. A history of migraine was described in 13% of those with DPD surveyed in one study [8] and in 31% of patients in another study [6]. Indeed, the relationship between migraine and DPD is long recognized, with Shorvon *et al.* [19] reporting that 38% of patients with DPD in a case series had a history of migraine. A careful history is required to differentiate between primary DPD and symptoms secondary to migrainous aura, particularly as the aura can last for days [17].

Primary DPD may be triggered by drug use, with symptoms continuing even after cessation of the illicit substance. Marijuana, hallucinogens, ketamine and 3,4-methylenedioxymethamphetamine (MDMA or ecstasy) have all been implicated [20]. Two studies [20,21•] have found no differences in phenomenology between drug-induced and nondrug-induced DPD. One study found greater improvement in the drug-induced DPD group, but no greater severity of symptoms [21•], whereas the other noted higher frequency of symptoms [20]. Both studies found a substantial number of patients had the onset of their disorder after their first use of the illicit drug. Simeon *et al.* [21•] reported 87% had experienced a 'bad trip' in the intoxication leading to DPD, whereas Medford *et al.* [20] found a strong personal history of anxiety disorder, suggesting an interaction between psychological and neurobiological factors.

Inducement of depersonalization by marijuana, lysergic acid diethylamide (LSD) and ecstasy suggests serotonergic mechanisms may be involved in the pathophysiology of DPD. The serotonergic agonist metachlorophenylpiperazine has been used to induce depersonalization in healthy individuals [22]. Glutaminergic pathways may potentially be involved, as ketamine, a dissociative anaesthetic, can trigger the onset of DPD and has been shown to blunt the emotional response to visual stimuli [23]. Ketamine administered in subanaesthetic doses blocks *N*-methyl-D-aspartate (NMDA) receptors, which in turn stimulates glutamate release resulting in subsequent increased glutaminergic stimulation of non-NMDA receptors [24]. Lamotrigine has been shown to block ketamine-induced effects on cognition probably through glutaminergic inhibition [25].

The depersonalization-inducing effects of illicit drug intoxication have been utilized to investigate the neurobiological correlates of depersonalization in healthy people. Mathew *et al.* [26] found increased right frontal and anterior cingulate blood flow in a PET study of marijuana-induced depersonalization. Abel *et al.* [23] examined ketamine's effects on brain activation, demonstrating that the normal response to aversive visual stimuli activated the left amygdala, both visual processing regions and the cerebellum. Ketamine administration resulted in only the visual processing region being activated during aversive stimuli, suggesting that the limbic response was abolished.

Amygdala hypoactivity was also demonstrated in an fMRI study of pain perception in hypnosis-induced depersonalization. Relative signal decreases occurred in the amygdala ipsilateral to the stimulus, as well as the contralateral somatosensory and motor cortices [27].

There are a small but growing number of neuroimaging studies on patient groups.

Phillips *et al.* [28] used fMRI to compare patients with DPD, OCD and healthy controls in their response to emotional stimuli. Unlike the healthy and OCD groups, those with DPD did not demonstrate activation of the insula when confronted with aversive stimuli, but showed increased activation of the right ventral prefrontal cortex. Insula activation occurred only when confronted with neutral stimuli. DPD patients also demonstrated decreased activation of the middle and superior temporal gyrus and inferior parietal lobe in response to aversive stimuli. Simeon *et al.* [29] found similar areas of relative hypoactivity in the right superior and middle temporal gyri in a PET study of patients with DPD, whereas greater activity was seen in right temporal, parietal and left occipital association areas subserving the integration of sensory material.

Medford *et al.* [30] used fMRI to investigate emotional memory in patients with DPD. Compared with controls, the patients with DPD showed decreased activation in the anterior cingulate, hippocampus and amygdaloid complex. Unlike controls, patients with DPD showed little difference in their response to neutral and aversive stimuli during an encoding task, but showed increased activation in response to recognition of words in neutral compared with emotional contexts. Another fMRI study of patients with DPD shown different facial expressions found decreasing signal intensity in the hypothalamus and amygdala as emotional intensity increased, in contrast to controls, who demonstrated the opposite trend. In addition, there was a negative correlation between autonomic responses to emotional stimuli and signal intensity in the dorsolateral prefrontal cortex [31]. Although patients with DPD demonstrated these abnormalities in response to both happy and sad faces, it is interesting that a recent study demonstrated impairments in recognition of expressions of anger but not fear, disgust, happiness, sadness or surprise in 13 patients with DPD [32].

The findings of neuroimaging studies are difficult to compare as different aspects of DPD have been studied,

for example response to aversive visual stimuli and emotional memory, and some have induced depersonalization symptoms in normal individuals rather than study patients with the disorder. Despite this, there appear to be a number of trends. Overall, decreased activity in limbic and paralimbic areas has been noted in patients with depersonalization, suggesting a dysfunction in the processing of emotion and its integration with cognition and sensation.

More widespread or increased activation in response to neutral compared with emotional stimuli has been documented in several studies of patients with DPD [28,30,31,33•] and in normal individuals in a state of depersonalization [23], suggesting a damping down of emotional response in the face of emotionally aversive stimuli. A study of skin conductance responses in patients with DPD is supportive of this theory. Patients with DPD were compared with patients with anxiety disorders and normal controls. The DPD and anxiety disorder groups had similar anxiety measures, but the autonomic response of the DPD group was similar to that of healthy controls, suggesting that the autonomic response was blunted [34].

Observations of hypoemotionality are consistent with a psychodynamic conceptualization, which proposes that depersonalization serves as a form of mental escape from reality and may be utilized by children facing trauma [35]. Support for this theory was shown in a study of 49 patients with DPD and 26 controls in which Simeon *et al.* [36] found childhood interpersonal trauma and, particularly, emotional abuse to be predictive of DPD diagnosis and severity. Interestingly, it appears that those with DPD are not more fantasy prone than nonsufferers [37], suggesting that they are not using imagination-based coping resources. Patients with DPD have also been shown to score more highly than controls and patients with post-traumatic stress disorder (PTSD) on scores of alexithymia [38••]. Whether alexithymia is causal in the development of DPD or a result of chronic DPD remains to be elicited [38••].

Hunter *et al.* [39] have proposed that DPD develops in susceptible individuals who misinterpret normal, transient feelings of depersonalization as something more serious. This results in anxiety and subsequent behavioural changes such as avoidance, which, along with cognitive biases, serve to exacerbate and maintain the symptoms that eventually become chronic. Baker *et al.* [40] have found some support for this model, finding an association between severity of the disorder and cognitive features of psychological illness attributions and strong illness identity.

Other lines of investigation into the pathophysiology of DPD include examinations of the hypothalamic–pituitary axis and norepinephrine. Studies examining cortisol have produced conflicting results, with one finding increased plasma cortisol [41] and another [42] reporting decreased salivary cortisol in patients with DPD. A more recent study examining salivary cortisol response to depersonalization symptoms in healthy students found increased salivary cortisol during acute stress [43]. A preliminary study of 24 h urine norepinephrine found a strong inverse correlation ($r = -0.88$) with depersonalization severity, supporting the theory of autonomic hypoarousal [44].

Sierra and Berrios [45] have suggested a 'corticolimbic disconnection hypothesis' for depersonalization, with prefrontal activation resulting in inhibition of the anterior cingulate and amygdala, and consequent hypoemotionality, attentional difficulties, autonomic blunting and indifference to pain. Limbic and paralimbic inhibition [28,30,31] have been demonstrated in some neuroimaging studies, and concomitant prefrontal activation [28,31] reported, but further studies are required to determine whether these findings are consistent. Additionally, it is noteworthy that hypoactivity of posterior cortical structures involving somatosensory integration and processing has been demonstrated [28,29], suggesting dysfunction in a circuit comprising prefrontal cortex, limbic and paralimbic structures and somatosensory association areas. Stein and Simeon [46•] suggest that circuits involving sensory and somatic processing may mediate symptoms, whereas circuits involving prefrontal and limbic areas may mediate emotional and cognitive features.

Treatment

To date, there is no effective treatment for DPD, with individuals generally advised to avoid triggers that may exacerbate their condition.

Conventional pharmacological treatment of DPD has been disappointing. Despite case reports [47,48] and small studies [49,50] indicating that serotonin-specific reuptake inhibitors (SSRIs; including clomipramine) may be helpful, a larger placebo-controlled trial of fluoxetine did not show any benefit [51]. Lamotrigine, which affects ketamine-induced NMDA blockade, has been trialled. A placebo-controlled trial of lamotrigine as a sole agent in patients with DPD failed to show any benefit [52]. Two small open label trials of lamotrigine added to a preexisting antidepressant regime have shown some benefit [53,54]. In one study, combination treatment resulted in a greater than 30% improvement in CDS scores in 56% of the 32 patients with a trend for greater improvement in patients taking the SSRI–lamotrigine combination compared with those taking a combination of tricyclic antidepressants and lamotrigine [54].

The nonspecific opioid receptor antagonists naloxone and naltrexone have been shown to diminish stress-associated analgesia in those with PTSD [55] and dissociative symptoms in borderline personality disorder in one study [56] but not another [57]. In DPD, two small open label trials of opioid antagonists have been conducted with promising results. A 6–10-week trial of naltrexone 100–250 mg/day resulted in a diminution of symptoms by at least 70% in three of 12 patients, with four patients symptomatically unchanged and only one symptomatically worse [58]. A more profound result was noted with the single administration of intravenous naloxone in 11 patients with DPD. Seven patients demonstrated marked improvement and three had a total remission of their symptoms [59]. Of interest, the κ-opioid receptor agonist enadoline has been shown to induce feelings of depersonalization [60], suggesting that the development of κ-opioid receptor antagonists may have potential therapeutic applicability.

Clonazepam has been trialled successfully in some patients, usually in combination with an SSRI [61]; however, no controlled studies have been conducted. It is likely that improvements are due to the anxiolytic effect of benzodiazepines.

For a more extensive overview of the pharmacotherapy of DPD, the reader is directed to a recent review by Sierra [62••].

Psychotherapy is useful for persons with DPD, particularly because of the significant rate of trauma and childhood abuse. Although Cattell and Cattell [63] cautioned against traditional psychoanalysis, warning that the lack of visual contact with the therapist may aggravate feelings of unreality, other forms of psychodynamic therapy may be useful to help the patient understand and come to terms with any antecedent trauma.

Based on their theory that DPD arises from catastrophic misinterpretations of initially normal, fleeting feelings of depersonalization [39], Hunter *et al.* [64] trialled the use of individualized cognitive behavioural therapy (CBT) for a maximum of 20 sessions in 21 patients. They found improvements in symptomatology and general functioning that were sustained at 6-month follow-up. Although the improvements were primarily due to the reduction in mood and anxiety symptoms, dissociative symptoms improved and 29% no longer met criteria for DPD [64].

General psychotherapeutic techniques may also benefit those with DPD. Simeon [65] suggested the use of strategies to modulate the individual's level of arousal, grounding techniques and the use of a diary to monitor symptom intensity.

Conclusion

DPD is a complex chronic disorder which affects young people, who often tend to suffer in isolation because of lack of knowledge about the disorder among mental health professionals as well as the laity. Despite DPD being more common than schizophrenia, it is poorly recognized, researched and resourced. Recent publications suggest that many different lines of research into the cause and treatment of this disorder are underway, and it is likely that this will yield improvements in the quality of life for sufferers.

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Papers of particular interest, published within the annual period of review, have been highlighted as:

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Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 297).

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