Depersonalization/ Derealization Disorder: A Neglected Disease in Psychiatry

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Depersonalization/ derealization disorder is an overlooked, common, and debilitating dissociative condition. Core features include persistent or recurrent depersonalization and/or derealization (i.e., profound sensations of unreality and detachment). The disorder affects both sexes equally and usually begins in adolescence. Etiological factors include illicit drug use, emotional abuse, and prolonged stress. Neural substrates include ventrolateral-prefrontal dysfunction, anomalies in the parietal and temporal lobes, and dysregulated serotonergic neurotransmission. The disorder has been deemed refractory to medication; however, tricyclic antidepressants, anticonvulsants, and opioid antagonists have helped some patients. Repetitive transcranial magnetic stimulation, cognitive behavioral therapy, and mindfulness-related exercises have shown promise. More research is required to further the efficacy of treatment and to raise awareness of the disorder in both clinical and public settings.

Depersonalization/ derealization disorder, a dissociative disorder, is estimated to affect up to 2.8% of the world's population (American Psychiatric Association [APA], 2013). Accordingly, it represents a condition that is more common than schizophrenia and anorexia nervosa combined, two conditions that are well established (Carlson, 2013; Comer, 2011). Despite this fact, "most psychiatrists are still trained to believe that [it] is extremely rare or non-existent" (Sierra, 2009, p. 3), a flawed conviction that has led to many misdiagnoses and treatment attempts designed for entirely irrelevant conditions (Medford, Sierra, Baker, & David, 2005). The intent of this article is to prevent these problems. A review of the disorder is prefaced with a discussion on dissociation for better interpretation.

Dissociation

Dissociation is a hardwired, adaptive mechanism elicited during periods of overwhelming stress or trauma (Steinberg & Schnall, 2001). It is a "disruption of and/or discontinuity in the normal integration of consciousness, memory, identity, emotion, perception, body representation, motor control, and behavior" (APA, 2013, p. 291). In some cases, dissociation does not function as a defense mechanism. Indeed, there are many expressions of dissociation, which can be conceptualized as fragments on a spectrum that correspond with pathology and severity. For example, the continuum begins with absorption (i.e., a narrowed state of focus that diminishes awareness of outside stimuli) and ends with dissociative identity disorder (Seligman & Kirmayer, 2008). Thus, a normal and non-invasive manifestation of dissociation is present on one side, while a pathological and incapacitating

one is present on the other. Somewhere amidst these extremes are two dissociative presentations called depersonalization and derealization.

Depersonalization. Depersonalization is a subjective experience of unreality and detachment felt with respect to one's self, mental processes, sensations, and agency (e.g., speech and movements). Depersonalization gives rise to disturbing sensations, which include a sense of not existing; acting without control; and being outside of the body. Additionally, depersonalization is accompanied by physical and/or emotional numbing (APA, 2013).

Derealization. The term 'derealization' has similar components but refers to feelings of unreality and detachment towards the world. That is, one's surroundings appear distant and unreal. Derealization engenders feelings of unfamiliarity, which make family, friends, and familiar places seem foreign (Steinberg & Schnall, 2001). Many liken derealization to a dream state, yet those who experience derealization are fully awake (Mayer-Gross, 1935).

Relevance to dissociation. Depersonalization and derealization appear to be coping strategies intended to assuage intense emotional reactions and remove unpleasant stimuli from consciousness. If a traumatic event did not seem real, for example, one could be spared from significant distress. However, depersonalization and derealization seem to be non-selective mechanisms. That is, feelings of unreality and detachment do not become circumscribed to specific events but instead infiltrate the perception of everything. Depersonalization and derealization are also not always warranted responses. Thus, depersonalization and derealization can manifest as both useful coping mechanisms and terrifying intrusions.

Prevalence, triggers, and duration. Depersonalization and derealization are common as transitory phenomena in the general population (Giesbrecht, Jongen, Smulders, & Merckelbach, 2006; Hunter, Sierra, & David, 2004; Seth, Suzuki, & Critchley, 2012) and usually arise in the contexts of life-threatening danger, emotional stress, and

illicit drug use. In addition, depersonalization and derealization manifest as symptoms in certain psychiatric and medical conditions (see subsequent references). In most cases, depersonalization and derealization are fleeting phenomena; however, as Seth et al. (2012) note, depersonalization and derealization can become unremitting disturbances and lead to depersonalization/ derealization disorder, a chronic, disabling condition.

Depersonalization/ Derealization Disorder

The core features of depersonalization/ derealization disorder are persistent or recurrent episodes of depersonalization and/or derealization (APA, 2013). Additional features include unrestrained existential thinking and philosophical inquiries, which lead to significant distress (Neziroglu & Donnelly, 2010); micropsia and macropsia, two phenomena related to distorted size perception (Simeon & Abugel, 2006); and impairments in visual memory (Sierra, 2009).

Depersonalization/ derealization disorder affects men and women equally (Simeon & Abugel, 2006) and appears to arise in adolescence, with an average age onset of 16 years (Simeon et al., 1997). The disorder usually takes a chronic course (Simeon & Abugel, 2006), which, in extreme cases, has lasted decades (APA, 2013; Schilder, 1939). To be diagnosed with depersonalization/ derealization disorder, one must have persistent or recurrent episodes of depersonalization, derealization, or both; show impairment in important areas of functioning; and have intact reality testing. Additionally, the disturbance must not be attributable to a substance or medication, or the symptoms of a psychiatric or medical condition (APA, 2013).

History

The delayed awareness of depersonalization/ derealization disorder is perplexing when considering how chronic cases of depersonalization and derealization have been documented in medical literature (Sierra, 2009) and personal diaries (Simeon & Abugel, 2006) since the

1800's. It has taken until 1946 for such phenomena to become well recognized (Sierra, 2009). Toward the end of the 20th century, research programs became established and "more has been learned about the condition in the last 10 years than the previous 100 years" (Sierra, 2009, p. 3). Nevertheless, the same problems that were addressed nearly 80 years ago still remain today: "Textbooks give [depersonalization/ derealization disorder] scant attention [and] special papers on the topic deal with a small number of cases" (Mayer-Gross, 1935, p. 103).

A Look in the DSM. When the American Psychiatric Association published its first edition of the DSM in 1952, it viewed depersonalization as a symptom of a dissociative response but not as a disorder, and not one word was written about derealization. In its second edition (1968), the American Psychiatric Association acknowledged the phenomenon of chronic depersonalization and called it "depersonalization syndrome." However, it wrote only three short sentences about it. In its next edition (1980), the name was changed from "depersonalization syndrome" to "depersonalization disorder" and listed among the dissociative disorders. In its current edition (2013), the name was changed to "depersonalization/ derealization disorder," to include derealization, which is now recognized as a frequent associated feature of the disorder.

Although depersonalization/ derealization disorder has an extensive history, it is clearly a novelty in modern psychiatry. It may be safe to say that the disorder is officially established. The next step, then, is raising awareness and contributing to the literature. The remainder of this article reviews research relevant to the etiology, physiology, neurobiology, and treatment of the disorder.

Precipitants

Depersonalization and derealization can occur in the context of neurological disorders such as migraine (Cahill & Murphy, 2004), temporal lobe epilepsy (Medford et al., 2005), brain lesions (Sierra, Lopera, Lambert, Phillips, & David, 2002),

and vestibular disease (Sang, Jáuregui-Renaud, Green, Bronstein, & Gresty., 2006). In addition, the two symptoms can occur as side effects of pharmaceutical drugs, namely Minocycline (Cohen, 2004), and recreational and illicit drugs such as marijuana, hallucinogens, ketamine, and ecstasy (Favrat et al., 2005; Medford et al., 2003; Simeon, Knutelska, Nelson, & Guralnik, 2003). Depersonalization and derealization can also arise during sleep deprivation (Medford et al., 2006); in panic disorder, borderline personality disorder, and acute stress disorder (APA, 2013); and during and/or after emotional, physical, and sexual abuse (Simeon & Abugel, 2006).

Although the precipitants above can activate episodes of depersonalization and derealization, the pathological presence of depersonalization and derealization (i.e., depersonalization/ derealization disorder) has been thought to follow trauma or abuse (Steinberg & Schnall, 2001), with emotional abuse being the greatest predictor (Simeon, Guralnik, Schmeidler, Sirof, & Knutelska, 2001). However, studies have shown that the full criteria for the disorder can still be met in the absence of traumatic and abuse-related antecedents (Baker et al., 2003; Simeon, Knutelska, Nelson, & Guralnik, 2003). Simeon and Abugel (2006) report cases of people who have developed the disorder after a divorce, a stressor of similar severity, or illicit drug use. Thus, what triggers a temporary reaction for some may induce an ongoing disorder for others.

Autonomic Arousal

The paradox of depersonalization/ derealization disorder is that many patients feel anxious but show blunted physiology in response to anxiety provoking stimuli. Kelly and Walter (1968) note that "in physiological terms, anxiety is experienced but is not translated into defense reaction arousal," (as quoted by Sierra, 2009, p. 133). Indeed, people with depersonalization/ derealization disorder and people with anxiety disorders have shown similar ratings of anxiety but different skin conductance levels (SCL), with the latter group

displaying greater levels of arousal (Sierra, Senior, Phillips, & David, 2006). SCL are frequently used in research to measure physiological arousal.

Scientists have also observed a discriminatory effect on arousal in depersonalization/ derealization disorder. For example, Sierra, Senior, et al. (2002) found that patients had attenuated SCL in response to unpleasant imagery but not pleasant or neutral imagery, a finding that supports the view that depersonalization/ derealization disorder functions to inhibit emotional responses to unpleasant stimuli.

In addition, many people with depersonalization/ derealization disorder report emotional numbness but show normal emotional motor expressions and present themselves as emotional individuals (Sierra, 2009), which may be explained by a "disruption of the process which allows emotions to gain conscious representation" (Sierra, 2009, p. 144). Michal et al. (2013) found that people with depersonalization/ derealization disorder showed normal autonomic activity but reported low levels of arousal. Thus, emotions seem to be dissociated from awareness, which presents an illusion that emotions do not exist.

In light of the studies, not all people with depersonalization/ derealization disorder show normal or blunted physiology. Indeed, Schoenberg, Sierra, and David (2012) found that people with the disorder had greater resting SCL in comparison to healthy volunteers. Similar differences have been observed in cortisol studies. Giesbrecht, Smeets, Merckelbach, and Jelicic (2007) found higher cortisol levels in people with depersonalization and derealization, while others found lower levels (Sierra, 2009). Thus, since cortisol levels reflect arousal, these studies support the observation that levels of arousal are not homogenous among patients. Disparities may reflect the severity of patients' symptoms. For example, Sierra, Medford, Wyatt, and David (2012) found comorbid anxiety in depersonalization/ derealization disorder but only in patients who reported low levels of dissociation. In line with this finding, levels of norepinephrine, which are important in arousal (Simeon & Abugel,

2006), have been found to be inversely correlated with dissociative severity (Simeon, Guralnik, Knutelska, Yehuda, & Schmeidler, 2003). Thus, levels of arousal vary among patients and may be contingent on the degree of patients' symptoms. Additionally, overt emotional expressions may hide subjective numbness and contribute to the lack of attention this disorder has received.

Neurobiology

Certain neurological disorders have been used as models to map the neural substrates of depersonalization/ derealization disorder. Visual hypoemotionality and asomatognosia have been particularly used, as the former is related to a lesion in the temporal lobe and derealization, and the latter is associated with a lesion in the right parietal lobe and depersonalization (Sierra, Lopera, et al., 2002). There is some evidence that suggests a relation between these two sites of the brain and depersonalization and derealization. Neurosurgeon Wilder Penfield produced phenomena redolent of depersonalization and derealization in patients when he stimulated their middle and superior temporal gyri (as cited in Simeon & Abugel, 2006), as did De Ridder, Van Laere, Dupont, Menovsky, & Van de Heyning (2007) when they stimulated a patient's right superior temporal gyrus. There seems to be a particular association between depersonalization and the parietal areas, namely the inferior parietal lobule and its substructure: the angular gyrus. Tumors in the angular gyrus, and stimulation to this area, have been implicated in depersonalization (Simeon & Abugel, 2006). Moreover, a PET study showed a positive correlation between activity in parietal areas and depersonalization intensity (Simeon et al., 2000).

In addition, scientists have considered separate facets of the disorder and their relevance to different brain systems. For example, reduced arousal has been proposed to follow hyperactivity in the prefrontal cortex (Sierra & Berrios, 1998), which increases frontal-limbic inhibitory regulation and relays inhibitory signals to structures involved

in emotion (Jay, Sierra, Van den Eynde, Rothwell, & David, 2014). Astoundingly, when Jay et al. (2014) used transcranial magnetic stimulation to inhibit activity in patients' ventrolateral prefrontal cortices, patients showed increased SCL and reported reduced emotional numbness.

A dysregulated serotonergic system has also been suspected because of the obsessive properties in the disorder (i.e., excessive philosophizing) and because of drugs that have acted on this system and precipitated dissociative phenomena. For example, chronic depersonalization and derealization have followed LSD (Medford et al., 2003), a drug that increases serotonergic input at 5-HT2A and 5-HT2C receptors (Simeon & Abugel, 2006). In addition, Psilocybin, a potent 5-HT2A agonist, has also led to dissociation (see Sierra, 2009), as has m-CPP, another serotonin agonist (Simeon et al., 1995). Thus, specific serotonin receptors may receive too much serotonin in depersonalization/ derealization disorder and treatment may therefore lie in balancing this system. (For a complete review of the neurobiology of depersonalization/ derealization disorder see Abugel, 2010; Sierra, 2009; Simeon & Abugel, 2006.)

Pharmacological Efficacy

The efficacy of medicine in treating depersonalization/ derealization disorder has been inconsistent and unreliable. Sierra et al. (2001) found that some patients improved while taking Lamotrigine, an anticonvulsant, but a follow-up study did not replicate these findings (Sierra, Phillips, Glynis, Krystal, & David, 2003). Lamotrigine has been deemed overall ineffective when used alone; however, combining it with SSRIs has helped patients (Rosagro-Escámez, Gutiérrez-Fernández, Gómez-Merino, de la Vega, & Carrasco, 2011; Sierra, Baker, et al., 2006).

Naloxone and Naltrexone, two opioid antagonists, have benefited some, but not all, patients (Nuller, Morozova, Kushnir, & Hamper, 2001; Simeon & Knutelska, 2005). SSRIs, such as Fluoxetine, have been ineffective when used alone

(Simeon, Guralnik, Schmeidler, & Knutelska, 2004). Inconsistent with this finding, however, are trials with Clomipramine, a tricyclic antidepressant with potent SSRI properties. In a very small sample (n = 4), Clomipramine led to significant improvement, where in one case, near complete remission lasted for years with continuous use (Simeon, Stein, & Hollander, 1998).

Although depersonalization/ derealization disorder does not reflect psychosis (Hunter, Phillips, Chalder, Sierra, & David, 2003), atypical antipsychotic Aripiprazole has shown promise. Uguz and Sahingoz (2014) report three patients who have been treated successfully with Aripiprazole, and Janjua, Rapport, and Ferrara (2010) present a case of a patient who showed complete remission after 4 months of using Aripiprazole as an augmenting medication with Clomipramine and Diazepam. Aripiprazole may be effective because of its function as a 5-HT2A receptor antagonist (Celik, Tahiroglu, Firat, & Avci, 2011), which may restore balance in the serotonergic system. Claiming efficacy or inefficacy of any of these drugs, however, is premature, as such findings represent few cases. The dearth of treatment trials and participants in studies merit further investigation.

Other Treatment Avenues

It has been proposed that depersonalization/ derealization disorder is the corollary of a "catastrophic appraisal of the normally transient symptoms of [depersonalization and derealization]" (Hunter et al., 2003, p. 1451). That is, individuals blow dissociative episodes out of proportion and develop causal attributions that perpetuate the disturbance (e.g., permanent brain damage). Hunter et al. (2003) devised a CBT treatment plan, which functions to resolve causal attributions, among other things (see Hunter et al., 2003). This model has been used in 13 sessions with 21 patients and showed efficacy, where at 6-month follow-up, 29% of the sample no longer met the criteria for the disorder (Hunter, Baker, Phillips, Sierra, & David, 2005).
Recent research has transcended the parameters

of conventional psychotherapy. Michal et al. (2007) found an inverse relation between patients' symptoms and mindfulness (i.e., present moment awareness). Michal et al. (2013) demonstrated immediate symptom reduction and attachment restoration with a mindful breathing exercise in patients with depersonalization/ derealization disorder. Repetitive transcranial magnetic stimulation (rTMS) has also been used in recent treatment trials and shows promise (Christopeit et al., 2014; Jay et al., 2014; Mantovani et al., 2011). Thus, although depersonalization/ derealization disorder has been viewed in the past as a refractory condition (Simeon et al., 1997), it is clearly "far from being the unassailable rock early writers led us to believe" (Sierra, 2009, p. 130).

Discussion

Depersonalization/ derealization disorder affects a considerable proportion of the population and is nothing new. Extant medical literature, outmoded diary entries, and early publications show an extensive history. It can be extrapolated from these documents that the disorder has been an ever-present human affliction, and the now established prevalence rate may have always been the same.

The disorder is neglected but not entirely abandoned in that research teams in various pockets of the world have been studying it. However, investigations have been blatantly overshadowed by superfluous interest in well-established disorders, which has resulted in both poor circulation of basic information about the disorder and important findings. Thus, although recent research has shown promise with respect to treatment, discoveries unlikely seep into mainstream psychiatry and are applied. The neglect may exist for many reasons. Foremost, the disorder cannot be objectively studied. For example, a psychiatrist can observe delusional ideation and low mood but cannot see dissociation. Second, there are discrepancies between what a patient reports and displays. That is, a patient reports emotional numbness but presents

emotions; loss of control but shows autonomy. To a psychiatrist, incongruities may strongly invalidate patients' complaints and, theoretically, the disorder. Third, psychiatrists may have difficulty relating to dissociative phenomena and are at odds with its validity. Further, the disorder is belittled by overpublicized literature on other disorders; descriptions, such as feeling like an automaton, confuse most psychiatrists and are interpreted differently; and serious psychopathology is masked by lucidity and normal appearance, which gives a false impression that the disorder is not serious, or even non-existent.

As previously discussed, people with depersonalization/ derealization disorder often receive false diagnoses (Medford et al., 2005). Misdiagnoses may arise from the belief that the disorder is nonexistent but may also follow patients' descriptions, which could be mistaken as delusions (e.g., "feeling out-of-body"). Likewise, the dissonance between description and demonstration may lead to the assumption of psychosis. In addition, misdiagnoses may follow anxious and distressed presentations, which are assumed to reflect anxiety disorders, when they are merely reactions to the effects of the disorder. Proper diagnoses will therefore follow when it is understood that 1) patients' descriptions reflect feelings and not beliefs; 2) discord between what is described and displayed is normal and expected; 3) overt anxiety is a reaction to the effects of the condition; and, above all, 4) the disorder is a legitimate and common condition. To get this far, however, existing literature must be more adequately investigated.

Indeed, more literature will convey a message that the disorder is prevalent and deserves attention. However, it is challenging to accomplish this goal with only a small population of scientists. Thus, more scientists must involve themselves in the research enterprise. More research will not merely stimulate awareness but also generate more findings, advancing what is known about the disorder. In addition, it will fill holes in

current research. Many studies involve as little as 6-15 participants (Giesbrecht, Merckelbach, van Oorsouw, & Simeon, 2010; Lemche et al., 2007; Medford et al., 2006; Phillips et al., 2001; Sierra, Senior, et al., 2002; Simeon, Guralnik, et al., 2003), which makes it difficult to extrapolate patterns and make conclusions about the larger population. Thus, it is critical to replicate both studies that have shown and not shown promise in the lab and get more patients involved.

While the neural substrates of the disorder seem established, medicine seems unreliable. A starting point for medicinal treatment trials is reassessing drugs that have helped some patients (i.e., Aripiprazole, Clomipramine, Lamotrigine, Naloxone, and Naltrexone). In addition, those well versed in medicine may consider testing drugs that heighten awareness. Research in the future should give attention to CBT, rTMS, and mindfulness-related exercises, which have all helped patients. Mindfulness should be particularly investigated in that symptoms of the disorder are contingent on low levels of awareness. That is, mindfulness could be used as an invaluable tool to restore normal levels of awareness and, therefore, relieve symptoms.

Depersonalization/ derealization disorder affects millions and is more common than bipolar disorder (Comer, 2011). In addition, current estimates indicate that there may be more cases of the disorder than cases of autism spectrum disorder and obsessive-compulsive disorder combined, and the disorder may be equally as common as generalized anxiety disorder and panic disorder (APA, 2013). Depersonalization/ derealization disorder is both among the most common and, paradoxically, the most neglected. Its subjectivity makes outside detection difficult and detecting dissociative phenomena will likely remain challenging. While we may never be able to visualize the condition, we can strive to understand it. By recognizing its legitimacy, concealed nature, distressing properties, and prevalence, we may just end what Jeffrey Abugel (2010) calls "the hidden epidemic."

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