CASE REPORT

Depersonalization Disorder: Effects of Caffeine and Response to Pharmacotherapy

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Introduction

The symptoms of depersonalization and derealization have been reported across a wide spectrum of psychiatric disorders. These include schizophrenia (Lehmann and Cancro 1985), borderline personality disorder (Cowdry et al. 1985; Chopra and Beatson 1986), panic disorder (Boulenger et al. 1986; Stein and Uhde 1989), and of course, the dissociative disorders, such as multiple personality disorder (Putnam et al. 1986). As an isolated disorder, the syndrome of chronic depersonalization and derealization is believed to be rare (Nemiah 1985). DSM-IIIR refers to this syndrome as "depersonalization disorder" and has placed it under the classification of "dissociative disorders."

Although very little is known about the course of depersonalization disorder, it is believed to start most commonly in adolescence or early adulthood, to begin abruptly, to become chronic in the majority of cases, and to be resistant to treatment (Nemiah 1985). Though intrapsychic processes have been most frequently implicated as a mechanism for depersonalization (Levy and Wachtel 1978), biological factors may also be important, but have been relatively unexplored to date (Noyes et al. 1987). Depersonalization can occur as a symptom of temporal lobe dysfunction (Gloor et al. 1982; Ghadirian et al. 1986) or as an adverse effect of various medications, such as indomethacin (Schwartz and Moura 1983). Depersonalization may also occur following marijuana use (Moran 1986) and may become chronic in some of these cases (Szymansky 1981; Keshaven and Lishman 1986). There is thus ample rationale to explore the role of biological factors in this disorder.

In this article, we describe a detailed psychobiological investigation of a single patient with depersonalization disorder. The patient participated in single-blind therapeutic trials of carbamazepine and clonazepam and also took part in a caffeine challenge paradigm. The latter was conducted to explore our hypothesis that depersonalization disorder might share a common pathophysiology with panic disorder, a syndrome known to be exacerbated by caffeine administration (Boulenger et al. 1984; Charney et al. 1985; Uhde and Boulenger 1988).

Case Report

The patient studied was a 28-year-old married woman with a 6-year history of chronic depersonalization and derealization. Her symptoms began abruptly one morning while

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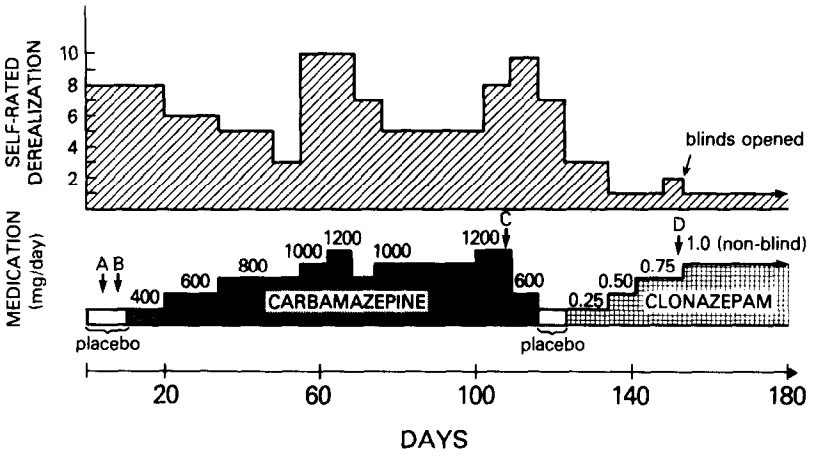

Figure 1. Course of treatment of a patient with depersonalization disorder (A) Placebo administered; (B) 240 mg caffeine administered while on placebo; (C) 240 mg caffeine administered while on 1200 mg of carbamazepine/day; (D) 240 mg caffeine administered while on 0.75 mg of clonazepam per day.

she was a senior in college at age 22 and under no readily identifiable stressor. Her symptoms consisted of the constant feeling "like I'm looking in on a conversation and not participating," accompanied by the feeling of being in a "fog" and associated with the symptom of "dizziness." The patient also complained of chronic problems with her concentration and memory, which she attributed to feeling "out of touch" with her surroundings. She described a pattern of diurnal variation to her symptoms, being typically more severe in the morning.

Historically, the patient described a happy childhood and denied any experiences of physical or sexual abuse. She had always been a social, outgoing individual, without any evidence of overt premorbid psychopathology. At the time of assessment, she had been married for 3 years, and had a 10-month-old daughter; interestingly, she reported a postpartum exacerbation of her symptoms. Also of interest, the patient's mother was currently in treatment with another psychiatrist for panic disorder and was reportedly doing well on a combination of amitriptyline and clonazepam.

The patient was assessed using a semistructured interview derived from the Schedule for Affective Disorders and Schizophrenia–Lifetime version (SADS-L) to allow the formulation of DSM-IIIR lifetime diagnoses. She met current diagnostic criteria for depersonalization disorder and had no other lifetime psychiatric diagnosis, including any affective, anxiety, or other dissociative disorder. Laboratory testing revealed a normal complete blood count (CBC), SMA-20, and thyroid function indices. A sleep-deprived electroencephalogram (EEG) with nasopharyngeal leads was normal, as were a computerized tomogram of the cerebrum and magnetic resonance image (MRI) of the posterior fossa (in view of the complaint of dizziness).

The patient's clinical response to single-blind trials of carbamazepine and clonazepam is shown in Figure 1. Although a transient initial response to carbamazepine could be seen in the patient's global self-rating of depersonalization/derealization symptoms, this was not sustained, despite increases in dosage to 1200 mg/day (with carbamazepine blood level of 6.2 μg/ml). Interestingly, however, the patient experienced an exacerbation of symptoms when her carbamazepine dose was abruptly reduced from 1200 to 600 mg/day,

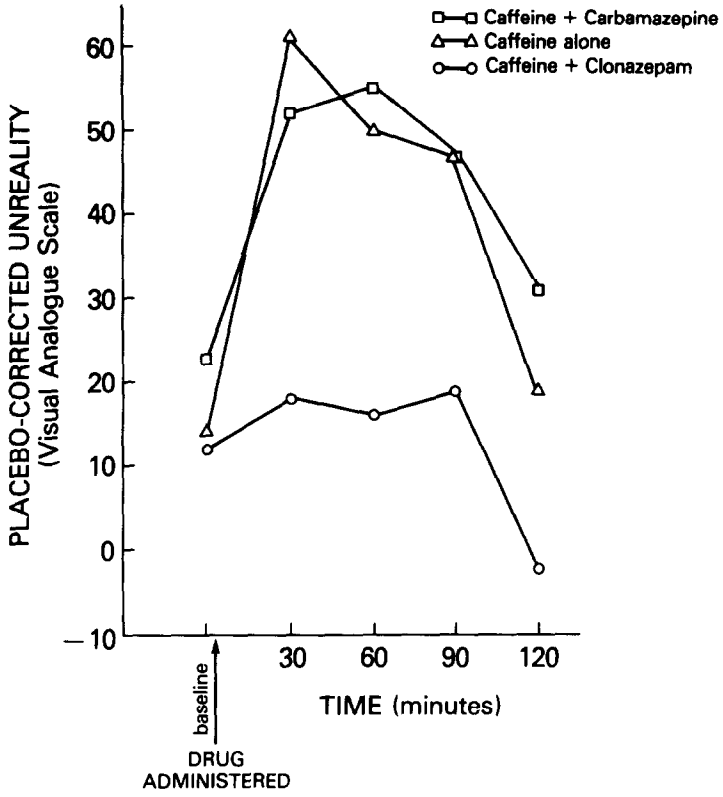

Figure 2. The increase in derealization in response to caffeine administration (240 mg) is attenuated by clonazepam but not by carbamazepine.

and she had two spontaneous panic attacks (which she had never experienced before). When clonazepam was instituted, a prompt reduction in symptoms occurred. For the first time in nearly 6 years, the patient described feeling nearly free of her depersonalization/derealization symptoms.

The patient also gave her informed, written consent to the blind administration of oral caffeine (240 mg) and/or placebo as part of a challenge paradigm to study her symptoms in our laboratory. These challenges were conducted at various phases in her treatment, as indicated in Figure 1. It can be seen that caffeine resulted in a robust increase in self-rated derealization (as measured by visual analog scale), which was significantly attenuated by chronic clonazepam treatment, but not by chronic carbamazepine treatment (Figure 2).

Discussion

In this report, we have illustrated the case of an individual with depersonalization disorder whose symptoms were exacerbated by caffeine administration and responded to pharmacological therapy. Although the findings from a single case must be interpreted cautiously, we believe that some interesting hypotheses may be generated from these observations.

The relatively limited literature to date on depersonalization disorder has focused

primarily on psychotherapeutic approaches to treatment (Torch 1987). It has recently been suggested that the tricyclic antidepressant desipramine may be a possible treatment for depersonalization disorder (Noyes et al. 1987). Our experience in the treatment of the patient we have described suggests that the benzodiazepine anticonvulsant clonazepam may have a role to play in this disorder. Although we initially chose the anticonvulsants carbamazepine and clonazepam as potential treatments because of the clinical links between the experience of depersonalization/derealization and temporal lobe epilepsy (Gloor et al. 1982), it is intriguing to note that clonazepam proved effective, whereas carbamazepine did not. This parallels our experience and that of others in the treatment of panic disorder, where potent benzodiazepines are efficacious (Spier et al. 1986; Ballenger et al. 1988), and carbamazepine is considerably less efficacious in most patients (Uhde et al. 1988). Of interest, this might suggest the preferential importance of central-type benzodiazepine receptors over peripheral-type benzodiazepine receptors (Weiss et al. 1985) in the pathogenesis and treatment of depersonalization disorder. However, in view of this being a single case report, these speculations remain tentative.

We believe that our observations suggest that depersonalization disorder, or perhaps a subset of this disorder, may more rightfully belong in the class of "anxiety disorders," rather than "dissociative disorders." Several factors point us toward this conclusion.

First, the symptoms of depersonalization and derealization are extremely common as prominant complaints in patients with panic disorder (Uhde et al. 1985; Boulenger et al. 1986; Stein and Uhde 1989). In fact, Sir Martin Roth originally referred to it as the "phobic anxiety–depersonalization syndrome" (Roth 1959). Second, the suggestion that some cases of depersonalization disorder may respond to treatment with tricyclics or high-potency benzodiazepines is consistent with the response pattern for panic disorder. Third, our patient's symptom exacerbation in response to caffeine is consistent with the experience of patients with panic disorder (Boulenger et al. 1984; Charney et al. 1985; Uhde and Boulenger 1988). This response to caffeine, however, has not been well studied in other psychiatric disorders, and therefore, may not be specific for panic or anxiety disorders. The response of subjects with depersonalization disorder to lactate administration, a known anxiogenic stimulus in panic disorder (Liebowitz et al. 1983), would be of great theoretical interest in this regard. Fourth, our patient's first-degree family history of panic disorder (her mother) and response to clonazepam suggest that a shared heritability for panic and depersonalization may exist; again, this remains as an intriguing supposition at the present time.

Other authors (Obendorf 1950; Brauer et al. 1970; Noyes et al. 1987) have also posited a close relationship between anxiety and depersonalization disorder. Others (Ross and Anderson 1988) have recently noted an overlap in phenomena between obsessive-compulsive disorder and multiple personality disorder, thereby reinforcing our impression that a close relationship between the dissociative disorders and the anxiety disorders may exist in some cases.

This report is not intended to suggest that intrapsychic or psychosocial factors are unimportant in depersonalization disorder. On the contrary, stressful life situations have been associated with the exacerbation of panic disorder (Roy-Byrne et al. 1986a,b), and events such as work pressures were clearly seen to cause a worsening of the patient's symptomatology in the case described here. Nonetheless, our observations allow us to propose that biological factors, heretofore relatively neglected in the literature, may also play an important role in this disorder. In some individuals, there may exist a physiological predisposition to the so-called "dissociative" experience of depersonalization/

derealization. This is a hypothesis deserving of additional consideration and study. Furthermore, controlled drug trials should be undertaken for the treatment of this chronic, often disabling, disorder.

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