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CLINICAL CORRESPONDENCE

Migraine and depersonalization disorder

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In a recent study of 204 patients with depersonalization disorder attending a specialist psychiatric clinic, Baker et al. (1) reported that 31% had a self-reported history of migraine and, of these, one third believed that their headaches and depersonalization were connected. Depersonalization disorder is classified as a dissociative disorder in the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV), and is defined as '*persistent or recurrent experiences of feeling detached from, and as if one is an outside observer of, one's mental processes or body*' (2). Other criteria necessary for diagnosis include that reality testing remain intact, and that the experience cause '*significant distress or impairment in social, occupational, or other important areas of functioning*'. Depersonalization is often accompanied by derealization, which is defined as an '*alteration in perception or experience of the world so that it seems unreal*'. It is currently unclear whether derealization represents a distinct disorder or is a subtype of Depersonalization. Depersonalization and/or derealization may occur in the context of organic disorders such as head injury, epilepsy or migraine (3). In such circumstances, a DSM-IV diagnosis of Depersonalization disorder is not permissible. Other exclusions to diagnosis include symptoms occurring exclusively during the course of another mental disorder, or secondary to the effects of a substance (drug of abuse or medication).

The precise nature of the association between migraine and depersonalization/derealization is currently unknown. Such symptoms may occur as a component of migraine aura. A particularly dramatic example occurs in the so-called Alice in Wonderland syndrome, most common in children, where the aura is characterized by a variety of paroxysmal body schema disturbances, which may co-occur with depersonalization, derealization, visual illusions and disorders in the perception of time (4). In addition, Blau (5) has reported that migraineurs commonly experience a feeling of being '*unusually removed from reality*' in the interval between termination of aura and the onset of headache, although patients do not often spontaneously volunteer this information. Observation by Baker et al. (1) that patients who described sudden onset of depersonalization/derealization (i.e. 38%) were significantly more likely to experience seeing flashes of light, may represent onset in association with visual aspects of migraine aura. Although 31% of their patients reported episodic symptomatology, the majority (64%) reported a pattern of chronic depersonalization with little or no fluctuation. A chronic pattern may not, however, completely exclude migraine as a possible aetiological factor in this subgroup of patients. Aura symptoms are usually fully reversible and individually last no longer than 60 min. However, the International Headache Society (IHS) also describes categories of migraine with prolonged aura (one or more aura symptom lasts > 60 min and ≤7 days, neuroimaging is normal) and migrainous infarction (aura symptoms persist for > 7 days and/or neuroimaging demonstrates an infarction) (6). The term migraine aura status (not included within the IHS classification system) is used to refer to the repeated occurrence of large numbers of consecutive auras, often in the absence of headache. Thus, depersonalization/derealization occurring in the context of migrainous aura could uncommonly follow a protracted course. In support of this, Ogunyemi (7) has described a case in which prolonged migraine aura was associated with depersonalization.

The observed association between migraine and depersonalization/derealization could also reflect a shared underlying pathophysiology. Dysregulation of serotonergic neurotransmission has been implicated in the pathophysiology of both migraine and depersonalization (8, 9). In addition, glutamate hyperactivity may be relevant to the neurobiology of both disorders. Glutamate been implicated in the

development of cortical spreading depression, trigeminovascular activation and central sensitization in migraine (10). Lamotrigine inhibits the neuronal release of glutamate and has demonstrated efficacy for the treatment of migraine aura in open pilot trials (11, 12). There are also reports of lamotrigine response in cases of prolonged migraine aura (13). Clinical studies suggest that NMDA receptor antagonists such as ketamine may transiently stimulate glutamate release and produce symptoms resembling depersonalization in humans (14), and lamotrigine has been shown to significantly decrease ketamine-induced perceptual abnormalities (15). Sierra et al. (16), in a double-blind, placebo-controlled, cross-over design, found no benefit from 12 weeks of lamotrigine over placebo in the treatment of depersonalization. However, only nine patients completed the trial and the presence or absence of migraine was not considered. It is currently unknown whether depersonalization occurring in association with migraine might preferentially respond to lamotrigine or other specific anti-aura treatments. It is also possible that the association between migraine and depersonalization observed by Baker et al. (1) may have arisen as a result of studying a highly selective population in a clinical setting (Berkson's bias), or occurred due to the high prevalence of anxiety and depressive disorders in those suffering from migraine, which may themselves be associated with secondary symptoms of depersonalization.

The relationship between migraine and depersonalization/derealization is under-recognized by both psychiatrists and neurologists. A diagnosis of migraine should be considered in all patients presenting primarily with symptoms of depersonalization/derealization. Indeed, as previously mentioned, DSM-IV diagnostic criteria for depersonalization disorder insist that symptoms should not occur as a direct result of a general medical condition. In addition, given the generally unpleasant and disabling nature of depersonalization/derealization, such symptoms should be sought in patients who present with migraine. Many psychiatrists are unfamiliar with the IHS classification system, in particular the concepts of migraine aura without headache, migraine with prolonged aura, migrainous infarction or migraine aura status, suggesting the need for greater specialist neurology input in the assessment of patients presenting with depersonalization/derealization. Further research on the nature of the association between migraine and depersonalization/derealization is required and may add to our understanding of the underlying pathophysiology of both these disorders. Reports on the response of depersonalization symptoms to treatment for migraine aura would also be welcome.

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