



Letter to Editor *Neurophysiology*

## Headache through mental health lens

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### INTRODUCTION

Headache and psychiatry have a known association since the century, but it is one of the most poorly understood relationships in neuroscience. The discussions have been far more clinical than systematic.<sup>[1]</sup> It was not until the 1930s that Harold Wolff's careful and systematic observations about recurrent headache led to the then influential concept of "the migraine personality".<sup>[1]</sup> Although "migraine personality" was subsequently defeated, it did help to root the biopsychosocial conceptualization of headache. If present, psychiatric comorbid illnesses would surely complicate headache management and would herald a poorer prognosis.<sup>[2]</sup>

### EPIDEMIOLOGY

Together migraine and psychiatric disorders are highly prevalent. Depression is twice as frequent in migraine when compared to the general population. The prevalence of odds of depression in migraine varies from 0.8 to 5.8 across various studies.<sup>[3]</sup> Moreso, as part of the bidirectional relationship, a proportion of migraine is present in 10–55% of depressive probands. Whereas, in bipolar disorders (BD), the prevalence of migraine can go up to 55%. Interestingly, migraine would precede the onset of BD.<sup>[3]</sup> Notably, the prevalence of anxiety has been shown to increase with migraine frequency ("dose-response" effect) and may escalate with the additional presence of medication overuse (MO) of opiates and nonsteroidal anti-inflammatory drugs. This MO along with chronic daily headaches has a prevalence of psychiatric disorders of up to 90%.<sup>[4]</sup>

### PSYCHIATRIC ISSUES AND ITS PLACE IN HEADACHE NOSOLOGY

The space attributed to psychiatric disorders in headache classification is rather inept. The addressal started with the first International Classification of Headache Disorders 1 (ICHD-1) where psychopathological factors (such as psychosocial stress, depression, anxiety, and headache as a delusion) were given an additional coding solely under the rubric of tension-type headache (TTH)<sup>[5]</sup> (Headache Classification Committee of the International Headache Society, 1988). Subsequently, 16 years after the first publication, the second ICHD (ICHD-2) made a provision for patients for whom headache was supposedly and causally related to psychiatric illness.

The classification of headache attributed to psychiatric disorder was reserved for these patients where "headache occurs in the context of a psychiatric condition where the headache is known to be a symptom of the psychiatric illness, and not a primary disorder in its own right" (Headache Classification Subcommittee of the International Headache Society, 2004).<sup>[6]</sup> Explicit criteria were provided for two varieties, that is, headache attributed to somatization disorder (ICHD-

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2 12.1), and headache attributed to psychotic disorder (ICHD-2 12.1). Explanations were drafted taking into consideration the temporality of symptoms but disorders such as depression and anxiety [more commonly associated with primary headache (PH)] were coded in the appendix citing a lack of empirical evidence.<sup>[4]</sup> Additional category somewhat addressing substance use disorders under secondary headaches was headache attributed to a substance or its withdrawal (ICHD-2 8), for example, immediate or delayed alcohol-induced headache, cannabis (and cocaine)-induced headache, and opioid/caffeine withdrawal headaches (Headache Classification Subcommittee of the International Headache Society, 2004).<sup>[6]</sup>

The third installment of ICHD (ICHD-3) largely repeats itself with the similar categories “Headache attributed to psychiatric disorders” (ICHD-3 12) and those in the appendix. Descriptive and phenomenological modifications have been done in the third edition, for example, headache attributed to psychotic disorder (Headache Classification Committee of the International Headache Society, 2018).<sup>[7]</sup> As per the criteria, when a new headache occurs for the 1<sup>st</sup> time in close temporal relation to a psychiatric disorder, and causation is confirmed, the headache is coded under ICDH-3 12 akin to the ICHD-2. However, unlike ICHD-2, when pre-existing with characteristics of PH disorder are made meaningfully worse in adjacent temporal relation to a psychiatric disorder (with confirmed causation), both the initial headache diagnosis and a diagnosis of “headache attributed to psychiatric disorders” (ICHD-3 12) are made. In ICDH-2, the use of clinical judgment was suggested when the pre-existing headache was worsened with a subsequent psychiatric disorder to code either the PH or both PH and ICDH-2 12. Interestingly, cannabis-induced headache has been removed in ICDH-3 unlike in ICDH-2.

## NEURAL UNDERPINNINGS IN PSYCHIATRIC SYNDROMES AND HEADACHE

Primary headache such as migraine and TTH has comorbid presence along with psychiatric disorders in greater proportions than just by chance. The most commonly accepted explanation of the comorbidity between the common PH (i.e., migraine) and depression is the existence of a bidirectional relationship. Possible reasons for the common association are the heritability (around 50%) and genes (e.g., 5-HT transporter gene, D2 receptor gene, and MTHFR C677T gene variant), dysfunction in neurotransmitter systems (serotonin, dopamine, and gamma-aminobutyric acid [GABA]), shared involvement of HPA axis, and allostatic “neuro-limbic” pain network.<sup>[3]</sup> Interestingly, default mode network suppression has been shown to be related to both increased rumination in depression and increased functional connectivity with brain areas related to pain during migraine attacks, for example,

thalamus, insula, and left postcentral gyrus.<sup>[8]</sup> Another important neural signature of pain and depression is lateral habenula and its altered activity.<sup>[9]</sup>

## ASSESSMENT OF PSYCHOLOGICAL ISSUES IN HEADACHES: HOW?

Psychiatric comorbidities do affect outcomes and quality of life (QoL) when treating PH. Thus, screening and proper assessment of common comorbid psychological disturbances could play a pivotal role in treatment. As discussed above, triggers can be rated using the Headache Triggers Sensitivity and Avoidance Questionnaire (HTSAQ) which is based on the Trigger Avoidance Model of Headaches. HTSAQ has four scales: (1) Triggers of headaches; (2) sensitivity to triggers compared to others; (3) sensitivity to triggers compared to the time of least sensitivity; and (4) avoidance of triggers.<sup>[10]</sup> For physicians treating PH, the screening of depression and anxiety is better conducted by three scales validated in headache studies: Hospital Anxiety and Depression Scale, Beck Depression Inventory, and the 9-item Patient Health Questionnaire.<sup>[11]</sup> The use of the migraine disability assessment questionnaire (MIDAS) to assess the disability and its use in stratified care is well known. Similar to MIDAS, the 6-item headache impact test (HIT-6) is a validated instrument to assess the impairment of headaches. The six items include the frequency of severe headaches, limitations of daily activities, desire to lie down, irritability, fatigue, and difficulty concentrating.<sup>[12]</sup> HIT-6 has been used as a decent surrogate marker of the response to treatment.<sup>[11]</sup> Barring disability reduction, improvement in health-related QoL too can serve as an important goal during migraine treatment. One of the most important tools is the Migraine-Specific Quality of Life Questionnaire version 2.1 (MSQ v2.1). There are three domains in MSQ v2.1, that is, role function-restrictive, role function-preventive, and emotional function. Higher scores suggest better QoL.<sup>[13]</sup> Futher, Hamer *et al.* developed headache acceptance questionnaire (HAQ) which is based on the principles of acceptance and commitment therapy.<sup>[14]</sup> HAQ would assess psychological responses to headache symptoms, identify adequate treatment targets (those that focus on reducing avoidance), and study mechanisms of change.

## NEED FOR MODIFIED HEADACHE CLASSIFICATION

Triggers (called precipitating factors) are factors that induce headache attacks in vulnerable individuals and usually precede the attack by <48 hours.<sup>[15]</sup> Triggers do explain the variance in headaches – why they occur when they do. Martin and Behbehani (2001)<sup>[16]</sup> have grouped migraine triggers into six categories: (1) Behavioral (included stress, sleep disturbances, and fasting exercise); (2) dietary; (3) environmental (included odors, bright light/visual stimuli, smoke, and weather); (4) infectious; (5) chemical; and (6) hormonal (menstruation).

Interestingly, the most common supposed triggers for PH are stress and sleep. Coping with triggers has been suggested as one of the “seven elements of good headache management” by the World Health Organization.<sup>[15]</sup> Hence, it is imperative that triggers ought to be included in ICHD as an axis or through the use of codes as we are moving headlong from ICHD-3 to ICHD-4 alpha.

Moreover, other simplified diagnostic classifications with probable therapeutic targets could be adapted in the future. For example, short (cluster headache) versus long-lasting (TTH), triptan responsive (e.g., migraine and cluster headache) versus indomethacin responsive (e.g., paroxysmal hemicrania and hemicrania continua) headache, predominantly calcitonin gene-related peptide (CGRP) related (good response to CGRP antagonist like recently approved ubrogepant) or not, and predominantly psychological (good response to antidepressants or psychotherapy) or not.<sup>[17,18]</sup>

#### Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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#### Conflicts of interest

There are no conflicts of interest.

#### Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The author(s) confirms that there was no use of Artificial Intelligence (AI)-Assisted Technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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