

Editorial Comment

Disentangling the Gordian Knot of Migraine Comorbidity

Two papers in this issue by Gretchen Tjetjen and colleagues address migraine comorbidity in a subject population drawn from subspecialty headache clinics.^{1,2} Both papers from an ongoing research project investigating the psychobiology of migraine highlight the significance of affective disorders.^{3,4}

Comorbidity has been termed the Achilles heel of at least 3 contemporary trends in medicine: specialist-centered care, guideline driven care, and disease management. Despite more than a decade of efforts to standardize and promulgate evidence-based headache treatment, management of the patient burdened not only with headaches, but with other bodily pains and emotional problems depends, more often than not, on the disorder the patient happens to “present,” and the corresponding medical specialty that happens to provide treatment. Research funding, researchers, and scientific journals also tend to have a disorder-specific or medical-specialty focus. This patient could thus end up a research subject in psychiatry, rheumatology, dentistry, pain medicine, or headache medicine, with each specialty focusing on a “different” disorder. More likely, she will be excluded from research *because* she presents with multiple disorders, and thus be invisible in the scientific literature. Is it surprising we lack a systematic scientific understanding of headache comorbidity?

As the number of identified migraine comorbidities with support from population studies has increased into the double digits, the problem of conceptualizing comorbidity has become increasingly complex. This abstract scientific problem comes home to roost in the reality of the headache clinic where the *typical* migraine sufferer presents with multiple problems—

in these 2 studies^{1,2} over half present with at least an affective disorder. Clinicians have long recognized that “comorbid” disorders occur together in recognizable patterns that appear to be systematically linked to psychosocial problems and damaging environmental conditions. Without a replicable, empirically validated method of classifying such patterns, however, clinical observations remain unverified by the scientific method, and any insights they may have offered are lost to the science of headache.

Tietjen and colleagues explore one approach to this classification problem.¹ Cluster analysis of data from 233 female migraine patients identified 2 subgroups of patients defined by distinguishable patterns of disorders (as well as a subgroup of patients defined by the absence of these disorders). One patient subgroup, largely older ($M = 51$ years) and male (74%), was defined by the diagnoses of hypertension, hyperlipidemia, diabetes mellitus, and hypothyroidism. The second subgroup, primarily (91%) female, was defined by the presence of an affective disorder (anxiety, depression) and other bodily pain (possible fibromyalgia). The affective disorder subgroup reported more severe (ie, frequent and disabling) migraine, and more toxic environmental conditions (higher stress levels, rates of abuse) than patients in the other 2 subgroups. Other research suggests that this affective disorder subgroup also may exhibit widespread pain sensitivity or “pain amplification,” report high levels of somatic symptoms and possess different biological vulnerabilities than the other 2 patient subgroups.⁵⁻⁷ In their second study, Tietjen et al found affective disorders similarly prominent.² Looking for deleterious effects of obesity (BMI), they

examined data from 721 patients with a full range of ICHD-2 migraine diagnoses at 8 headache clinics. No clear deleterious associations between obesity and either migraine severity or migraine-related disability were observed if the confounding presence of an affective disorder was taken into account; in fact, the only clear deleterious association again was found to involve the presence of an affective disorder with both migraine severity and disability.

Statistically derived clusters of patients and relationships between variables such as obesity and affective disorder may be sample or population (eg, headache clinic) specific and thus require replication. As the authors note, some disorders of interest could not be assessed or were too infrequent in the study sample to be properly evaluated as defining characteristics for a patient cluster. Self-report symptom measures, patient reports of medical diagnoses, and medical records also have methodological limitations, particularly for the diagnosis of disorders such as fibromyalgia or for the assessment of abuse history.⁸⁻¹⁰ However, an exploratory study is never the final word, but, instead, points to an unexplored and promising new approach to a problem.

The identification of replicable “essential feature” patient subtypes has the potential to improve the management of complex migraine presentations by stimulating the development of broad spectrum treatment strategies matched to patient subtypes. Patient subtypes also may provide clues to shared pathophysiological mechanisms underlying subtype defining disorders.^{5,6}

A piecemeal, fragmented, and specialty-driven approach to the migraine comorbidity problem has not served the severely impaired migraine patient or the science of headache medicine well. Promising alternative treatment and research strategies that are inte-

grative in character deserve our attention. May many flowers bloom!

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