Chronic Pain and Mental Health Disorders: Shared Neural Mechanisms, Epidemiology, and Treatment

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CME Activity

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Abstract

Chronic pain and mental health disorders are common in the general population, and epidemiological studies suggest that a bidirectional relationship exists between these 2 conditions. The observations from functional imaging studies suggest that this bidirectional relationship is due in part to shared neural mechanisms. In addition to depression, anxiety, and substance use disorders, individuals with chronic pain are at risk of other mental health problems including suicide and cigarette smoking and many have sustained sexual violence. Within the broader biopsychosocial model of pain, the fear-avoidance model explains how behavioral factors affect the temporal course of chronic pain and provides the framework for an array of efficacious behavioral interventions including cognitive-behavioral therapy, acceptance-based therapies, and multidisciplinary pain rehabilitation. Concomitant pain and mental health disorders often complicate pharmacological management, but several drug classes, including serotonin-norepinephrine reuptake inhibitors, tricyclic antidepressants, and anticonvulsants, have efficacy for both conditions and should be considered first-line treatment agents.

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Chronic pain and mental health disorders are common in the general population; the prevalence of chronic pain ranges from 2% to 40%,[1] and the prevalence of mental health disorders range from 17% to 29%.[2,3] Concomitant with the high prevalence of both conditions, epidemiological and functional imaging studies suggest that a bidirectional relationship exists between chronic pain and mental health disorders. This is relevant to clinical practice because this bidirectional relationship may be partly mediated by shared neural mechanisms, which, in turn, may necessitate the use of targeted pharmacological and behavioral interventions aimed at treating both conditions. In addition, adults with chronic pain are at risk of other mental health problems including suicide and cigarette smoking and many have sustained sexual violence. Therefore, the objectives of this review were to (1) provide a working definition of the pain matrix, which is a proposed neural network responsible for the experience of chronic pain; (2) summarize the prevalence of commonly occurring mental health disorders in frequently encountered chronic pain conditions; and (3) identify behavioral and pharmacological treatments with efficacy for both chronic pain and mental health disorders.

METHODS

Similar to previously published strategies, databases of MEDLINE using the PubMed and Ovid platforms were searched using the keywords *pain matrix*, *neuromatrix*, *chronic pain*, *depression*, *anxiety*, *substance use*, and *suicide* with no date restrictions.[4] Keywords related to specific topics (eg, low back pain, fibromyalgia, migraine headache, behavioral treatment, and antidepressants) were cross-referenced with the initial search terms using the identified databases. Search terms were cross-referenced with review articles, and additional articles were identified by manually searching the reference lists.

Pain Matrix

The term *pain matrix* refers to a constellation of brain regions activated by nociceptive stimuli. The neurobiological tenets of the pain matrix stem from the conceptual framework of the neuromatrix that was espoused by Melzack[5] to describe a pattern of neural activation initially believed to represent the "neurosignature" of pain. However, numerous neuroimaging studies have since shown that brain regions activated by nociceptive stimuli can also be affected by various emotional and behavioral states.[6] This is relevant because the pain matrix provides the neural mechanistic basis for better understanding of how psychological factors affect pain.

The pain matrix was originally conceptualized as a constellation of interrelated brain regions functioning as a uniplanar circuit. However, a growing body of research suggests that the pain matrix may be more accurately construed as a hierarchical multilevel neural network progressing from the encoding of nociceptive stimuli to the conscious modulation and memory formation of the pain experience. Garcia-Larrea and Peyron[7] have proposed a pain matrix composed of 3 tiers, or levels, of interrelated neural activity (Figure 1). In this 3-tiered model, "first-order" processing refers to nociceptive activation of the spinothalamic tract, which comprises neurons in the dorsal horn of the spinal cord with axonal projections terminating in the posterior thalamus. Nociceptive stimuli are then posited to undergo "second-order" processing in the anterior cingulate cortex (ACC), insula, prefrontal cortex (PFC), and posterior parietal cortex. As a result, nociceptive stimuli are consciously perceived, subjected to attentional and cognitive modulation, and transformed into somatic, or "vegetative," responses. The perception and modulation of pain is further affected, or "reappraised," by the emotional context of the stimuli and further individualized by psychological factors that together coalesce in memory formation. Neural structures implicated in this final "third-order" process include the oribitofrontal, perigenual ACC, and anterolateral PFC regions. Brain regions comprising the second and third tiers interact with various descending tracts in the spinal cord, resulting in either inhibitory or facilitatory modulation of incoming nociceptive stimuli in a process termed *descending control*. In this 3-tiered model of the pain matrix, the experience of pain is the consequence of progressively complex and interrelated "orders" of neural activity aptly designated by Garcia-Larrea and Peyron[7] as the "nociceptive,"

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