

The Association Between Negative Affect and Prescription Opioid Misuse in Patients With Chronic Pain: The Mediating Role of Opioid Craving

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Abstract: Over the past decade, considerable research has accumulated showing that chronic pain patients experiencing high levels of negative affect (NA) are at increased risk for prescription opioid misuse. The primary objective of the present study was to examine the factors that underlie the association between NA and prescription opioid misuse among patients with chronic pain. In this study, 82 patients with chronic musculoskeletal pain being prescribed opioid medication completed the Current Opioid Misuse Measure, a well-validated self-report questionnaire designed to assess prescription opioid misuse. Patients were also asked to complete self-report measures of pain intensity, NA, and opioid craving. A bootstrapped multiple mediation analysis was used to examine the mediating role of patients' pain intensity and opioid craving in the association between NA and prescription opioid misuse. Consistent with previous research, we found a significant association between NA and prescription opioid misuse. Interestingly, results revealed that opioid craving, but not pain intensity, mediated the association between NA and opioid misuse. The Discussion addresses the potential psychological and neurobiological factors that might contribute to the interrelationships among NA, opioid craving, and prescription opioid misuse in patients with pain. The clinical implications of our findings are also discussed.

Perspective: Our study provides new insights into the factors that underlie the association between negative affect and prescription opioid misuse in patients with chronic pain. Our findings could have important clinical implications, particularly for patients being prescribed opioid medication, and for reducing rates of opioid misuse in patients with pain.

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Key words: Chronic pain, prescription opioid misuse, negative affect, opioid craving.

Over the past decade, there has been a substantial rise in the use of opioids for the treatment of chronic noncancer pain. Despite the potential

benefits of opioid therapy, the rise in the use of opioids has been accompanied by escalating rates of prescription opioid misuse and abuse.^{7,20,26,46,67,77} Prescription opioid misuse, which broadly refers to the use of opioids in a manner other than how they are prescribed, has become a major concern for clinicians involved in the treatment of pain.^{8,46,61,68,76,82} Because of these concerns, increasing efforts have been devoted to examining the factors that may be associated with prescription opioid misuse among patients with chronic pain.

One of the most consistent findings that have emerged from previous studies among patients with chronic pain is the association between psychiatric symptoms and prescription opioid misuse (for a review, see⁸²). For example, symptoms of negative affect (NA), such as anxiety and depression, have emerged as robust and powerful predictors of opioid misuse. In some

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studies, it has been found that patients with high levels of NA were 2 to 3 times more likely to misuse prescription opioids than patients with low levels of NA.^{11,27,36,52,85,90} To date, research has yet to determine the factors that are responsible for the association between NA and prescription opioid misuse in patients with pain. It is possible, for example, that NA leads to higher levels of pain, which in turn leads to an increased risk for opioid misuse. In previous research, increased NA has been found to be prospectively associated with increased pain intensity.^{3,12,34,35,79,95} High pain intensity, in turn, has been found to be associated with an increased risk for opioid misuse.^{2,36,43}

Findings from recent studies suggest that opioid craving might also be responsible, in part, for the association between NA and prescription opioid misuse. The concept of craving is commonly used in the substance use literature and refers to the need or desire to consume certain drugs or illicit substances.^{24,65,74,80} Among individuals with drug use problems, it has been shown that increases in NA may trigger drug craving.^{6,19,28,39,72,73} Drug craving, in turn, has been found to increase the likelihood of drug use and abuse (for reviews, see^{71,74,81}). Interestingly, similar findings have been reported among patients with chronic pain being prescribed opioid medication, with higher levels of NA being associated with higher levels of opioid craving.⁸⁹ In patients with pain, self-reports of opioid craving have been found to be prospectively associated with various indices of prescription opioid misuse, including physician ratings of opioid misuse and abnormal urine toxicology screens.^{16,86,89} Given that self-reports of opioid craving have been found to be associated with both NA and prescription opioid misuse, there are reasons to believe that opioid craving may be responsible, at least in part, for the increased rates of prescription opioid misuse observed among patients with high levels of NA.

The primary purpose of the present study was to examine the potential role of pain intensity and opioid craving as mediators of the association between NA and prescription opioid misuse among patients with chronic pain. In this study, a sample of 82 patients with chronic musculoskeletal pain being prescribed opioid medication completed the Current Opioid Misuse Measure (COMM¹⁵), a well-validated self-report questionnaire designed to assess prescription opioid misuse. Patients also completed self-report measures of pain intensity, NA, and opioid craving. A bootstrapped multiple mediation analysis was used to examine the mediating role of pain intensity and opioid craving in the association between NA and opioid misuse.

Methods

Participants

The Human Subjects Committee of Brigham and Women's Hospital approved the study procedures, and

written informed consent was obtained from every participant. This was a cross-sectional, between-subjects study performed in a single, large urban university-based pain management center. Patients included in the present study were part of a larger study in which patients were enrolled in a randomized clinical trial of a behavioral intervention designed to improve prescription opioid compliance (for methods of the trial, see⁴⁵). Data included in the present study were collected at the beginning of the randomized clinical trial (ie, baseline), following patient recruitment and double-blinded randomization.

The study sample consisted of 82 patients (50 men, 32 women) with a diagnosis of chronic back or neck pain, with or without radicular symptoms. All patients were prescribed opioids by Board-certified, fellowship-trained, pain medicine physicians with at least 5 years of consultant-level experience. All patients were evaluated by a physician and underwent a physical examination. Patients met the following inclusion criteria: 1) chronic back or neck pain for more than 6 months; 2) an average pain score of 4 or greater on a pain intensity scale of 0 to 10, with medication; 3) able to speak and understand English; 4) prescribed opioid medication for more than 6 months; and 5) at risk for prescription opioid misuse based on their responses on the Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R scores ≥ 18 ¹⁴), or based on past records of abnormal urine screens and/or physician ratings of opioid misuse (Addictions Behavior Checklist⁹⁴).

Patients were excluded from participation if they met any of the following criteria: 1) current diagnosis of cancer, 2) acute osteomyelitis or acute bone disease, 3) present or past *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*⁵ (DSM-IV) diagnosis of any psychotic disorder, 4) active substance abuse or dependence of any other kind within the past year (ie, positive on the Mini-International Neuropsychiatric Interview [M.I.N.I.] v.5.0.⁶⁹).

Measures

Demographic Questionnaire

Patients were asked to complete a demographic questionnaire, which included information about patients' age, gender, ethnicity, and education level. Patients were also asked to report any history of medical, psychiatric, and/or substance use problems and to report which opioid medication they were currently taking. Patients' reports of medication were verified by a research assistant using the electronic medical record system, and published tables were used to convert daily opioid dosages into morphine equivalents.

Screening for Substance Use Disorders

The M.I.N.I. was used to screen for active opioid addiction or any other active substance use disorder. The M.I.N.I. was designed as a brief structured interview for the major Axis I problems included in DSM-IV⁵. We used section K to assess the presence of a current nonalcohol psychoactive substance use

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