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Review

The downward spiral of chronic pain, prescription opioid misuse, and addiction: Cognitive, affective, and neuropsychopharmacologic pathways

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ABSTRACT

Prescription opioid misuse and addiction among chronic pain patients are emerging public health concerns of considerable significance. Estimates suggest that more than 10% of chronic pain patients misuse opioid analgesics, and the number of fatalities related to nonmedical or inappropriate use of prescription opioids is climbing. Because the prevalence and adverse consequences of this threat are increasing, there is a pressing need for research that identifies the biobehavioral risk chain linking chronic pain, opioid analgesia, and addictive behaviors. To that end, the current manuscript draws upon current neuropsychopharmacologic research to provide a conceptual framework of the downward spiral leading to prescription opioid misuse and addiction among chronic pain patients receiving opioid analgesic pharmacotherapy. Addictive use of opioids is described as the outcome of a cycle initiated by chronic pain and negative affect and reinforced by opioidergic-dopamingeric interactions, leading to attentional hypervigilance for pain and drug cues, dysfunctional connectivity between self-referential and cognitive control networks in the brain, and allostatic dysregulation of stress and reward circuitry. Implications for clinical practice are discussed; multimodal, mindfulness-oriented treatment is introduced as a potentially effective approach to disrupting the downward spiral and facilitating recovery from chronic pain and opioid addiction.

Contents

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1. Introduction

1.1. The scope of chronic pain and prescription opioid misuse

Misuse of prescription opioid analgesics is an emerging public health concern that confers significant risks for overdose, unsafe drug interactions, and the full panoply of adverse social, legal, and adaptive consequences associated with dependence on any psychoactive drug. Though the prevalence of prescription opioid misuse across the general U.S. population has increased more than threefold over the past two decades (Hall et al., 2008), it is presently unclear to what extent this explosion in prevalence reflects an increase in opioid misuse by persons without a prescription for opioids versus an increase in nonmedical use of opioids by persons prescribed opioids for analgesia. This distinction notwithstanding, nationally representative surveys indicate that prescription opioid misuse is endemic among U.S. adolescents and adults; prescription opioids are now among the most commonly misused drugs in the U.S. (Wilson, 2007). For instance, results of the National Survey on Drug Use and Health (NSDUH) for 18–25 year-olds revealed that 23.8%, 11.1%, and 4.8% reported lifetime, past year, and past month misuse of prescription "pain killers" (Substance Abuse and Mental Health Services Administration, 2011). NSDUH findings further indicated that rates of initiation of nonmedical pain reliever use were second only to those of marijuana, with more than two million persons initiating nonmedical use of opioid analgesics annually. These findings underscore the pervasive availability and misuse of these agents in the U.S. The ready accessibility, prevalent misuse, and euphorigenic effects of prescription opioids would seem to create conditions for widespread dependence on these agents (Mendelson et al., 2008). Recent research does, in fact, suggest that rates of publically funded chemical dependency treatment and emergency department care for prescription opioid use have increased dramatically in recent years and it is estimated that well over a million Americans are currently dependent on prescription opioids (Manubay et al., 2011; Mendelson et al., 2008). As previously underscored, these statistics do not clearly differentiate opioid misusers with and without chronic pain; yet, this is a critically important distinction with serious clinical ramifications.

1.2. Diagnostic classification of opioid use patterns

The issue of prescription opioid misuse is further complicated by the diversity of nosological categories used to classify opioid use patterns and their biopsychosocial consequences. As defined by *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV), *prescription opioid abuse* involves a maladaptive pattern of repeated opioid use that: results in failure to fulfill social, occupational, academic, or familial obligations; continues despite recurrent legal problems related to opioid use; persists in spite of interpersonal problems caused or exacerbated by opioids; and occurs in physically hazardous contexts. In contrast, DSM-IV defines *prescription opioid dependence* as involving physical symptoms of dependence, including tolerance and withdrawal, as well as behavioral symptoms including: taking higher doses than intended; an inability to reduce or stop taking opioids; spending substantial amounts of time using, obtaining, recovering, or thinking about opioids; and continued use in spite of adverse physical or psychological consequences (Zacny et al., 2003). However, some clinicians believe these behavioral criteria for abuse and dependence are inappropriate for opioid-using chronic pain patients, because patients who take opioids as prescribed may be unable to reduce their opioid use or may continue opioid use despite adverse health consequences due to the intractability of their chronic pain. Instead, many pain and addiction specialists use the American Pain Society (2002) criteria to identify *prescription opioid addiction* among chronic pain patients, including symptoms of impaired control over opioid use, compulsive opioid use, continued use despite harm, and craving for opioids (Sullivan et al., 2008; Wilson, 2007). Addictive tendencies among prescription opioid users may be presaged by the presence of *opioid misuse* behaviors such as selling medication or injecting oral formulas (Ives et al., 2006; Sullivan et al., 2008), although less serious forms of opioid misuse like unauthorized dose escalation are relatively common among undertreated chronic pain patients and may not indicate opioid addiction. The presence of more serious misuse behaviors may mark the transition from sanctioned use of opioids to development of opioid use disorders and addiction (Butler et al., 2007).

1.3. Epidemiology of prescription opioid misuse

Parsing apart these conditions, structured psychiatric interviews conducted for the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) study of more than 43,000 U.S. adults identified 4.7% of respondents as lifetime prescription opioid misusers; whereas 1.4% of respondents met criteria for a DSM-IV prescription opioid use disorder (opioid abuse or dependence; Huang et al., 2006). Men, adults with Axis I and Axis II DSM-IV diagnoses, respondents residing in the West, and young or middle aged adults were at greatest risk for prescription drug misuse and a prescription opioid use disorder. Other studies have identified a history of alcohol or illicit drug misuse, anxiety, depression, and chronic pain as significant risk factors for prescription opioid misuse and dependence (Amari et al., 2011; Pohl and Smith, 2012; Turk et al., 2008). Individuals suffering from chronic pain disorders, who are at risk for becoming physically dependent on opioid analgesics when adhering to their prescribed medication regimen, may be particularly vulnerable to prescription opioid misuse (Butler et al., 2007; Ives et al., 2006; Sullivan et al., 2010).

Though the prevalence of prescription opioid misuse and addiction among chronic pain patients has yet to be firmly established by nationally representative, population-level surveys, chronic pain itself is highly prevalent in modern society; a meta-analysis of 13 studies reported a weighted mean prevalence of 35.5% for chronic pain of any kind and a weighted mean prevalence of 11% for severe chronic pain (Ospina and Harstall, 2002). Many patients with chronic pain have serious medical conditions that require long-term opioid pharmacotherapy, and a subset of these individuals are at significant risk for escalating from appropriate opioid use to misuse and finally to opioid addiction. The best available prevalence estimates for opioid misuse and addiction among chronic pain patients may be derived from research by