Further defining and conceptualizing opioid misuse in chronic pain

Letter To Editor:

The recent review by Vowles et al.⁵ on the rates of opioid misuse, abuse, and addiction in chronic pain is a sorely needed step in the right direction toward better defining and understanding the prevalence of opioid misuse, abuse, and addiction among individuals with chronic pain. The authors are to be applauded for both synthesizing and advocating for literature using explicit definitions of opioid misuse (ie, not taken exactly as prescribed), abuse (ie, intentional use for nonmedical purposes such as euphoria), and addiction (ie, continued use despite harm or with impaired control, compulsion, or craving). Unfortunately, these distinct terms have too often been conflated in past research and surveillance, which may result in inaccurate data collection, interpretation, and counterproductive treatment approaches.⁴

Although the authors provide a compelling synthesis of the literature using these terms, still a more precise definition of opioid "misuse" is needed. In their review of 38 studies, the authors found misuse to be the most common form of problematic opioid use (at a weighted average rate of 21%-29%). However, as noted in the discussion, the actions constituting misuse in the studies were extremely broad, many of which may not be appropriately classified as problematic opioid misuse. For instance, "underuse," "overuse," and "erratic or disorganized use" of opioids all fell under the definition of problematic misuse, whereas we would argue that these classifications should remain distinct from one another. Furthermore, "use of opioids in conjunction with alcohol or illegal substances (eg, marijuana)" was classified as opioid misuse, presumably even if an individual continued to take their opioid medication exactly as prescribed. Such a classification is problematic in that it: (1) seems to suggest that any opioid-prescribed individual who uses alcohol or other substances is automatically considered to be misusing opioids, when in reality the misuse may be more related to the other substance being used rather than the opioid; (2) does not coincide with the growing body of research exploring adjunct analgesic treatments to opioid therapy for chronic pain, such as the potentially beneficial effect of cannabinoids alongside opioid therapy¹⁻³; and (3) perpetuates the dangerous notion that remains prevalent in the literature and in clinical care, which assumes that substance use and pain are mutually exclusive conditions and that individuals who use illicit substances in addition to opioid therapy may be immediately suspected to be "drug seekers" or "misusers" of opioid treatment.

Another important area of consideration is the adequacy of pain treatment among individuals in these studies. Many studies of opioid misuse in pain patients tend to focus on the behaviour of the patient as a primary concern, while neglecting to assess the adequacy of pain treatment provided by prescribers or clinicians. For instance, if an individual's pain is severely undertreated, and they consequently decide to take an additional dose of their opioid medication, should this behaviour still be given the

stigmatized label of problematic misuse? Thus, we propose that measures of treatment efficacy also be reported in future studies and reviews of problematic opioid use in chronic pain.

The potential for misclassified opioid misuse in this review may be heightened by the authors' use of definitions meant for rigorous patient assessment in clinical trials rather than opioid misuse in real-world clinical or observational settings, which constituted the setting for the majority of the studies on which the review was based. Nevertheless, the authors are to be commended for highlighting low-intensity interventions through which clinicians can attempt to ameliorate potential opioid misuse and for suggesting that alternative treatment options be explored for high-risk patients rather than completely denying care for these vulnerable individuals.

Overall, the authors have provided intriguing insights into the rates of opioid misuse, abuse, and addiction in chronic pain according to more tightly defined classifications and have provided important insights and recommendations for future research in this area.

Conflict of interest statement

The author has no conflicts of interest to declare.

References

- [1] Elikkottil J, Gupta P, Gupta K. The analgesic potential of cannabinoids. *J Opioid Manag* 2009;5:341-57.
- [2] Lucas P. Cannabis as an adjunct to or substitute for opiates in the treatment of chronic pain. *J Psychoactive Drugs* 2012;44:125-33.
- [3] Narang S, Gibson D, Wasan AD, Ross EL, Michna E, Nedeljkovic SS, Jamison RN. Efficacy of dronabinol as an adjuvant treatment for chronic pain patients on opioid therapy. *J Pain* 2008;9:254-64.
- [4] Voon P, Kerr T. "Nonmedical" prescription opioid use in North America: a call for priority action. *Subst Abuse Treat Prev Policy* 2013;8:39.
- [5] Vowles KE, McEntee ML, Julnes PS, Frohe T, Ney JP, van der Goes DN. Rates of opioid misuse, abuse, and addiction in chronic pain: a systematic review and data synthesis. *PAIN* 2015;156:569-76.

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Reply

Letter To Editor:

We wish to thank Voon for her comments regarding our review of opioid misuse and addiction in chronic pain.² We note agreement with the major points that she raises in her letter,¹ particularly with regard to the need for improved precision in the definition of opioid misuse.

Conflict of interest statement

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References

- [1] Voon P. Further defining and conceptualizing opioid misuse in chronic pain. *PAIN*; In press (this issue).
- [2] Vowles KE, McEntee ML, Siyahhan P, Frohe T, Ney JP, van der Goes DN. Rates of opioid misuse, abuse, and addiction in chronic pain: a systematic review and data synthesis. *PAIN* 2015;156:569–76.

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Respondent learning in chronic pain: how precise is imprecision?

Letter To Editor:

We read the topical review by Moseley and Vlaeyen¹¹ with great interest. The authors propose “a new hypothesis of chronic pain,” termed the “imprecision hypothesis” that “explains the most common painful disorders.”

This hypothesis builds on classical conditioning and consists of 2 primary assumptions: (1) pain can be a conditioned response (CR) to initially neutral conditioned stimuli (CS) that are associated with initial painful events (unconditioned stimuli [US]); (2) the degree of generalization of such a CR to other stimuli depends on how precisely a “multisensory and meaningful event” during initial pain was encoded. In chronic pain, this encoding is assumed to be imprecise, leading to dysfunctional, exaggerated generalization.

Although we agree that both concepts contribute to chronic pain, we cannot concur with the authors that these are novel concepts. The role of classical conditioning in chronic pain is textbook knowledge. More than 35 years ago, Gentry and Bernal⁴ proposed a stimulus–response model of the maintenance of chronic pain: acute pain leads to muscular tension, which in turn increases the pain experience. This sets a pain-tension cycle in motion that is complemented by avoidance, immobility, fatigue, and anxiety. Lethem et al.³ specifically proposed that fear of pain may lead to avoidance and exaggerated pain perception.

Linton et al.⁹ further elaborated the role of neutral stimuli in pain: a nociceptive stimulus (US) leads to pain that is accompanied by sympathetic activation, tension, and fear (unconditioned responses), which become associated with neutral stimuli present during the incident (CS). These CS then elicit arousal, muscular tension, and anxiety as CRs. The CRs facilitate the perception of a secondary pain, which may be of a different type than the original US.

Flor et al.³ expanded this model to all levels of the pain response, including central processes.

Moseley and Vlaeyen write that their “idea is fundamentally different to the large body of work on aversive conditioning”. Indeed, there is a difference: while classical accounts assume that pain-related responses, not pain, are the CRs, they propose “to extend this associative learning framework of pain-related fear

to an approach that has pain itself as the response”. However, all previous models considered pain as the end product of the conditioning process. That the pain itself is an immediate CR, however, is arguable. Linton et al.⁹ concluded that “the conditioned response (CR) is not “pain,” but it can be pain provoking.” However, classical conditioning influences pain perception and can bring innocuous stimuli into a painful range (cf. Refs. 1,12).

Moseley and Vlaeyen hypothesize that more stimulus generalization occurs if the “encoding” of acute pain is “imprecise”. The authors assume that this is the case in chronic pain. However, they do not clarify the mechanisms of such “encoding” and the meaning of “imprecise”. The given examples for “imprecision” in chronic pain range from widespread pain to impaired tactile acuity and proprioception, cortical reorganization, and distorted mental body representations. Yet, these examples relate to very different levels of pain-related perception and it is likely that they stem from altered percepts due to learning-related modulatory processes that have been well described in perception and learning.

A relationship between perception and generalization has been shown in learning theory. For example, the “inverse hypothesis” by Guttman and Kalish^{6,7} states an inverse relationship between stimulus discrimination and generalization: the less an organism is able to discriminate stimuli, the stronger is the generalization. However, this hypothesis refers to the CS, not to the CR. At present, we do not know whether discrimination ability is reduced with respect to the CR and how this relates to generalization and chronic pain. Moreover, emotional, motivational, and cognitive processes likely also play a major role in generalization.⁵

In summary, the mechanisms of conditioning and generalization described in the “imprecision hypothesis” are important, but not novel, concepts in the understanding of chronic pain. That pain can result from conditioning has been discussed before. The term “imprecision” lacks precision. It might be more fruitful to investigate perceptual, emotional, cognitive, and motivational processes related to learning and pain within existing conceptual frameworks. Finally, it is unlikely that the primary disturbance is in the acquisition of pain-related responses, which is crucial for survival. Rather, extinction might be most important for chronicity processes.² We commend the authors for putting a new focus on respondent learning processes in pain, complementing operant learning accounts¹⁰ and hope for a new focus of research on learning processes involved in chronic pain.

Conflict of interest statement

The authors have no conflicts of interest to declare.

References

- [1] Diesch E, Flor H. Alteration in the response properties of primary somatosensory cortex related to differential aversive Pavlovian conditioning. *PAIN* 2007;131:171–80.
- [2] Flor H. Extinction of pain memories: importance for the treatment of chronic pain. In: Castro-Lopes J, editor. *Current topics in pain: 12th World Congress on Pain*. Seattle: IASP Press, 2009. p. 221–44.
- [3] Flor H, Birbaumer N, Turk DC. The psychobiology of chronic pain. *Adv Behav Res Ther* 1990;12:47–84.
- [4] Gentry WD, Bernal GAA. Chronic pain. *Behavioral approaches to medical treatment*. Vol. 16. Oxford: Ballinger, 1977.
- [5] Geschwind N, Meulders M, Peters ML, Vlaeyen JWS, Meulders A. Can experimentally induced positive affect attenuate generalization of fear of movement-related pain? *J Pain* 2015;16:258–69.
- [6] Guttman N, Kalish HL. Discriminability and stimulus generalization. *J Exp Psychol* 1956;51:79–88.