prevalent in these individuals but also relevant to predict outcomes of nocicplastic pain such as opioid nonresponsiveness or non-responsiveness to surgery intended to relieve pain [as reviewed in Refs. 2,3]. However, it should be pointed out that the comorbidities are not absolutely necessary for the classification of nocicplastic pain per se. They are only required for the grading of diagnostic certainty for nocicplastic pain.

Dr. Cohen’s argument that a descriptor of pain is a hypothesis of a mechanism, which in the cases of nociceptive and neuropathic pain, has been replaced by concrete confirmation,1 is surprising. As stated in the article on nocicplastic pain, where Dr. Cohen is shared first author,2 it is well recognized that while underlying pathology can usually be documented for nociceptive and neuropathic pain, the relationship between that pathology and pain mechanisms remains elusive. On the contrary, objective evidence of altered nociceptive processing has not only been documented in conditions characterized by nocicplastic pain but has also been related to pain severity [see references in 3], thus supporting the clinical relevance of the term.

We agree with Dr. Cohen that “new concepts in the science underpinning nociception and the practice of pain medicine require careful explication and step-wise logical development,” which is why we took care to clarify the relationships between different clinical terms. Contrary to the statement of Dr. Cohen, we never suggested that the ICD-11 concept of chronic primary pain would be synonymous to nocicplastic pain because “nocicplastic” is a mechanistic term while “primary pain” is a diagnostic concept. However, nocicplastic pain harmonizes with the current view that certain forms of chronic pain are best understood as conditions or diseases of their own, rather than symptoms of other underlying pathology or disease, reflected in ICD-11 classification of primary pain (disease) and secondary pain (symptom).5

Finally, as nocicplastic pain is a term intended for clinical use, we consider it appropriate to provide the readers with examples of conditions where this type of pain may typically feature, eg, fibromyalgia, complex regional pain syndrome type 1, other instances of “musculoskeletal” pain such as “nonspecific” chronic low back pain, and visceral pain disorders such as irritable bowel syndrome and bladder pain syndrome, all classified as chronic primary pain conditions in the ICD-11.5 This is no more “conflicting” nor “unacceptable logically” than stating that nociceptive pain is typically present in severe osteoarthritis or neuropathic pain in patients with painful polyneuropathy, conditions classified as secondary pain in the ICD-11.5

Conflict of interest statement

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Implications of hedonic effects of opioids in clinical practice

I enjoyed the recent article on hedonic and calming effects of opioids, opioid craving, and misuse.6 This study carefully evaluated a large number of factors which might relate to patients’ daily choices as to how they use prescribed medications. Since the authors describe a lack of prior research on the impact of hedonic effects on opioid misuse in the clinical setting, I respectfully present several pertinent publications which were difficult to find in my own literature search. They have both consistent and somewhat differing results from the current study. In addition, I would like to provide a rationale to expand on clinical implications proposed by the authors.

Bieber et al. evaluated the subjective effects of opioids experienced by study participants at the time of their very first
exposure to prescription opioids. This study compared a group on long-term opioid therapy at a pain center with a group whose initial exposure to opioids was for chronic pain but who were currently receiving treatment of opioid addiction. The Addiction Center Research Inventory was completed by both groups. The Addiction Center Research Inventory scores were much higher, indicating more euphoric effects from opioids, in those who later became addicted to opioids. Yet the group that was not addicted also reported frequently experiencing hedonic effects of opioids. 30% recalled “I was full of energy,” 25% noted “things around me seemed more pleasing than usual,” 35% “felt more clear headed than dreamy,” and 25% recalled “feeling more excited than dreamy.”

The Kaiser Family Foundation performed a phone survey of recipients of chronic opioid prescriptions. This was self-published on the website of the Kaiser Family Foundation in December of 2016.20% of survey respondents reported that a major reason for using prescribed opioids was “for fun or to get high,” 14% “to deal with day to day stress,” and 10% “to relax or relieve tension.” An additional 14%, 8%, and 3%, respectively, reported that it was a minor reason to use prescribed opioids for these purposes.

In a phone survey of retired National Football League players,4 participants were asked if they used opioid medications for any of the following purposes: to function; to change mood, be happy, or get high; to relax, calm down or relieve stress; to sleep; or for pain. Roughly 25% exposed to prescribed pain medications during their playing career were currently prescribed opioids. Of those, 45% disclosed current misuse of opioids. 35% of those currently misusing opioids reported that during their playing careers they used opioids to relax or relieve stress, whereas 22% reported opioid use to improve mood.

These articles seem to have substantial agreement with Frimerman et al., in that all show a very high rate of hedonic effects of prescribed opioids. However, patients in the 2 phone surveys reported a wider variety of hedonic effects than were evaluated in this study and a higher rate of opioid misuse.

The authors suggest 2 important clinical implications of these data: to routinely discuss the possibility of hedonic effects with patients and cognitive behavioral or mindfulness interventions for those patients who seek the pleasurable or calming effects of opioids. These seem to be very reasonable responses to their findings and the impact of misuse on clinical outcomes.

I propose another clinical implication: The information that is discussed here, and in the extensive body of research cited in their references, is not already widely shared in the locations where it would seem most likely to be seen by the medical community: in opioid management guidelines, standardized informed consent documents, and medication management agreements. By contrast, the risk of addiction is already covered in these documents. Similarly, ordinary risks common to opioids and many other medications, such as nausea, sedation, constipation, and lack of sufficient therapeutic effects, are also already discussed. Thus, there would seem to be an opportunity for substantially more complete discussions with our patients. For any other medication, to treat any other condition, it would be expected to include such frequent and important side effects in a reasonably thorough informed consent process. Thus, these effects of opioids should be included in each of informed consent documents, medication management agreements, and pain management guidelines.

Conflict of interest statement
The author has no conflicts of interest to declare.

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Reply to Blatt
Letter to Editor:
We thank Dr. Blatt for his thoughtful letter and for sharing his appreciation of our study. Importantly, we thank Dr. Blatt for providing additional perspective on our work and for pointing to other studies on the subjective effects of opioids.

First, we agree with Dr. Blatt that little work has been conducted on the subjective effects of opioids among patients with chronic pain who are prescribed long-term opioid therapy. The bulk of work on opioid subjective effects (eg, hedonic effects) has been conducted in other populations, such as recreational (ie, illicit) opioid users or pain-free healthy volunteers tested under laboratory conditions. In his letter, Dr. Blatt described a study in which patients with chronic pain were