Chronic nociplastic pain affecting the musculoskeletal system: clinical criteria and grading system

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1. Introduction

The term “nociplastic pain” was introduced by the International Association for the Study of Pain (IASP) in 2017 as a third mechanistic pain descriptor in addition to nociceptive and neuropathic pain [15, IASP website https://www.iasp-pain.org/Education/Content.aspx?itemNumber=1698]. Nociplastic pain is defined as “pain that arises from altered nociception despite no clear evidence of actual or threatened tissue damage causing the activation of peripheral nociceptors or evidence for disease or lesion of the somatosensory system causing the pain.” The term is intended for both clinical and research usage to identify individuals in whom there is pain and hypersensitivity in regions with apparently normal tissues and without any signs of neuropathy. Although central sensitization is most likely a dominating mechanism in nociplastic pain conditions, the term nociplastic pain should not be regarded as synonymous with the neurophysiological term “central sensitization”. In addition, a contribution of peripheral sensitization cannot be excluded. The concept of nociplastic pain harmonizes with the current view that certain forms of chronic pain are better understood as conditions or diseases of their own, rather than symptoms of other underlying pathology or diseases. The latter is reflected in the ICD-11 classification of chronic pain into primary—pain as a disease—and secondary—pain as a symptom—where most, if not all, of the primary pain subgroups consist of conditions with nociplastic pain. However, it must be recognized that the terms reflect different dimensions as “nociplastic” is a mechanistic term, whereas “primary pain” is a diagnostic concept.

Chronic pain conditions such as fibromyalgia, complex regional pain syndrome type 1, and irritable bowel syndrome are examples of pain conditions, where nociplastic pain is typically present. These conditions have documented changes of nociceptive processing in the nervous system, thus precluding the classification of their pain as “pain of unknown origin” (idiopathic pain). The classifier “pain of unknown origin” should be reserved for patients with pain that cannot be designated as nociceptive, neuropathic, or, now, nociplastic and is a label awarded by exclusion.

It is becoming increasingly understood that many individuals have pain states, wherein there is more than one pain mechanism present. For example, patients with lumbar disk herniations often suffer from a nociceptive pain in the back and neuropathic pain (radiculopathy) in the leg. Nociplastic pain can also co-occur with neuropathic and particularly with nociceptive pain mechanisms. The latter is highlighted by the note in the nociplastic pain definition stating that “patients can have a combination of nociceptive and nociplastic pain.” In fact, it seems as though having ongoing nociceptive pain is a risk factor for developing nociplastic pain because hypersensitivity is associated with longer duration of nociceptive pain, and high rates of nociplastic pain states, such as fibromyalgia, are seen in individuals with osteoarthritis, rheumatoid arthritis, and other nociceptive pain disorders. Given that hypersensitivity is often seen also in nociceptive pain, the clinician is faced with an unresolved problem, namely, when should a patient with nociceptive pain be classified as also having nociplastic pain?

In nociplastic pain states has used sophisticated techniques to specifically identify the dysfunctions involved. Quantitative sensory testing may be useful for assessing temporal summation and conditioned pain modulation, whereas offset analgesia and functional neuroimaging can identify changes in cerebral pain processing. However, these techniques are not always available for use in clinical practice or even in all research settings.
settings. Thus, the need for clinical criteria for nocicepastic pain was recognized by the IASP, and an IASP Terminology Task Force (TTF) was formed to develop clinically useful criteria for nocicepastic pain. It was recognized that different sets of clinical criteria would most likely be required for nocicepastic pain manifested in the musculoskeletal system and viscera. Therefore, the criteria presented in this article are designed for nocicepastic pain manifested within the musculoskeletal system. The intention is that criteria for nocicepastic pain perceived in the viscera will be defined by another IASP task force consisting of experts in visceral pain and presented in a future article.

2. Procedures and processes

The objective was to use a consensus procedure within an expert group consisting of the IASP TTF, to define a set of clinically and research applicable criteria for nocicepastic pain presented in the musculoskeletal system. From a preliminary draft of classification criteria proposed by the chair to initiate further discussions, each member of the IASP TTF, ie, the authors, was asked to present his or her own set of criteria. Eight anonymized propositions were reviewed and voted on by the task force with 3 votes per member. Four propositions with the lowest amounts of votes (1, 2, 2, and 3, respectively) were excluded. Two very similar propositions received 4 votes each and were pooled into alternative A after a slight modification. In addition, the 2 alternatives that received the highest number of votes from the TTF members (alternative B: 6 votes and alternative C: 8 votes) were kept for further consideration.

In collaboration with the IASP office an “external” stakeholder group was identified, consisting of experts suggested by the TTF members and IASP “leaders” (IASP Councilors, Chapter Presidents, the SIG Leadership, and a few other IASP representatives) identified by the office. Feedback was received from 21 “experts” and 34 “leaders”. The group voted on the criteria, answered 3 questions (Table 1), and could freely provide comments or suggestions. The questions were based on issues that raised particular debate within the TTF. Among the stakeholders, 35% voted for alternative A, 25% for alternative B, and 40% for alternative C. The main differences between alternatives A and C was that alternative A included examination with quantitative sensory testing (QST), but not nonpain symptoms, whereas alternative C included nonpain symptoms, but not QST. In a separate vote, 57% of the stakeholders voted for including nonpain symptoms and 6 provided personal comments advising against QST because the method is not widely available. Furthermore, several stakeholders stated that the criteria should be kept simple. The proposed grading was based on the classification of neuropathic pain as possible, probable, or definite (Table 1). Most felt that grading possible or probable nocicepastic pain was the most appropriate choice (43%), rather than no grading (19%) or grading possible, probable, or definite (38%). For 2/3 of the criteria, most agreed that the proposed clinical criteria developed for musculoskeletal pain would not be suitable to use also for visceral pain. After the voting, the TTF continued working on the set of clinical criteria preferred by the “external” group as well as the TTF (C), discarding the 2 other alternatives. To accommodate suggestions for improvement from the “external” group as well as the TTF, the criteria were clarified to reduce the need of long notes, referred pain on palpation was omitted as a sign of nocicepastic pain, the word comorbidities was used instead of nonpain symptoms, and the order of the criteria was changed to a better fit clinical practice (ie, history first and examination last).

3. Clinical criteria for nocicepastic pain affecting the musculoskeletal system

Following the procedures outlined above, the IASP TTF proposes the set of criteria with a grading system encompassing possible and probable nocicepastic pain, as outlined in Table 2. A flow chart depicting the algorithm for assessing nocicepastic pain is presented in Figure 1.

4. Discussion

The main purpose of the clinical criteria is to define aspects that must be considered before assigning the descriptor nocicepastic pain. In summary, to classify nocicepastic pain, the subject has to meet the requirements of the first and fourth section of the criteria, ie, 4 conditions have to be fulfilled: (I) pain duration > 3 months (1), (II) a regional rather than discrete distribution (1), (III) the pain cannot entirely be explained by nociceptive or neuropathic mechanisms (1), and (IV) clinical signs of pain hypersensitivity are present in the region of pain (4). The presence of a history of pain hypersensitivity in the region of pain (2) and defined comorbidities (3) strengthen the probability of nocicepastic pain, and both have to be present to designate probable nocicepastic pain. All the elements of the proposed criteria are discussed below.

4.1. Obligatory criteria

The working group carefully considered all the elements of the proposed criteria and found that the clinical relevance of defining acute pain as nocicepastic is doubtful, given that altered nociception increases with longer pain duration. Therefore, the proposed criteria are meant to be used to identify individuals with chronic nocicepastic pain, using the classic demarcation of 3 months of pain. The emphasis in the criteria on regional rather than discrete pain is meant to stress the fact that when central sensitization is present as the underlying neurophysiological mechanism, the receptive fields of the sensitized neurons expand. The resulting perception ranges from an expanded single region of pain to multifocal pain or widespread pain, and the distribution of hypersensitivity also increases. It is extremely common for nocicepastic pain to be superimposed on nociceptive pain, and patients can also have coincidental nocicepastic and neuropathic pains. In the first case, the spatial involvement of the pain (ie, how widespread the pain is) will be greater than one would

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Table 1

Questions sent out to the stakeholders.

<table>
<thead>
<tr>
<th>Question</th>
<th>1. Should nonpain symptoms (eg, disturbed sleep, fatigue, cognitive symptoms, and/or increased sensitivity to light, sound, or odors) be included in the criteria for nocicepastic pain?</th>
</tr>
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<tr>
<td>(2) Should there be a grading of “possible,” “probable,” and “definite” nocicepastic pain (similar to the neuropathic pain classification)?</td>
<td></td>
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<td>(3) The intention of the IASP Terminology Task Force is to develop clinical criteria for nocicepastic visceral pain at a later stage, intended for conditions such as irritable bowel syndrome, bladder pain syndrome, and the like. Would any of the presented alternatives be suitable also for visceral nocicepastic pain conditions?</td>
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IASP, International Association for the Study of Pain.
Clinical criteria and grading for nociplastic pain affecting the musculoskeletal system.

1. The pain is
   1a. Chronic (>3 mo);
   1b. Regional (rather than discrete) in distribution‡;
   1c. There is no evidence that nociceptive pain (a) is present or (b) if present, is entirely responsible for the pain; and
   1d. There is no evidence that neuropathic pain (a) is present or (b) if present, is entirely responsible for the pain.†

2. There is a history of pain hypersensitivity in the region of pain.
   Any one of the following:
   - Sensitivity to touch
   - Sensitivity to pressure
   - Sensitivity to movement
   - Sensitivity to heat or cold

3. Presence of comorbidities:
   Any one of the following:
   - Increased sensitivity to sound and/or light and/or odors
   - Sleep disturbance with frequent nocturnal awakenings
   - Fatigue
   - Cognitive problems such as difficulty to focus attention, memory disturbances, etc.

4. Evoked pain hypersensitivity phenomena can be elicited clinically in the region of pain.
   Any one of the following:
   - Static mechanical allodynia
   - Dynamic mechanical allodynia
   - Heat or cold allodynia
   - Painful after-sensations reported following the assessment of any of the above alternatives.

Possible nociplastic pain: 1 and 4.

Probable nociplastic pain: all the above (1, 2, 3, and 4)‡

‡ The purpose of the grading system is to indicate the level of certainty that a patient has nociplastic pain and, as mentioned above, was inspired by the current grading system for neuropathic pain. However, because of the lack of clinically useful, reliable diagnostic tests to confirm the presence of altered nociception, currently nociplastic pain is graded as possible or probable but not definite. If future diagnostic tests are developed and validated, the introduction of the term “definite nociplastic pain” should be considered.

4.2. How should the history of pain hypersensitivity be assessed in the clinic?

To fulfill the second criterion, a history of pain hypersensitivity to touch, pressure, movement, or heat cold must be present. It is therefore recommended to question patients regarding their current hypersensitivity to these modalities. Patients may perceive the touch of clothing against the skin and/or the pressure from belts, handbags, and bras as unpleasant or painful. They may report hugging to be painful and/or note that it is painful to sit in a chair for any prolonged periods. Hypersensitivity to movement can be assessed by asking if the patient perceives being touched by a brush or cotton pad to be painful. Dynamic mechanical allodynia can also be tested by gently rubbing over the skin with an object kept at room temperature (approx. 20°C) against the skin, and the same descriptor of pain itself. Others argued that data show that these nonpain symptoms are nearly always present and, in many settings, have been shown to be discriminative in identifying individuals with nociplastic pain mechanisms. In addition to a history of hypersensitivity to somatosensory stimuli as noted above, individuals with nociplastic pain will typically report increased sensitivity to sound, light, and odors. In addition, although not specific for nociceptive pain, disturbed sleep, fatigue, and cognitive problems are common. Furthermore, in nociplastic pain conditions such as fibromyalgia, the widespreadedness of pain (eg, measured as the Widespread Pain Index in the 2011/2016 fibromyalgia criteria) as well as the presence and severity of these comorbid symptoms (as measured in the accompanying symptom severity score) each contribute nearly equal variance in predicting outcomes of nociplastic pain such as opioid nonresponsiveness or nonresponsive-ness to surgery intended to relieve pain and also the relative responsiveness to other nonopioid pharmacological treatments addressing comorbidities.

4.4. How should the pain hypersensitivity phenomena be assessed in the clinic?

Dynamic mechanical alldynia can be assessed by gently stroking the skin with a brush or a cotton pad and asking whether the resulting sensation is painful or not. Static mechanical alldynia is usually assessed by digital palpation with a weight of approximately 4 kg (nailbed blanching) and reporting pain on this palpation would be considered pressure alldynia. Cold alldynia can easily be tested by holding a metal object kept at room temperature (approx. 20°C) against the skin, and the same
A single object can be heated with water to assess heat alldynia (approx. 40°C). After each examination, the subject is asked whether the sensation lingers after the stimulus has ended to check for the presence of after-sensations. Furthermore, it is helpful to first assess whether there is hypersensitivity only in the region of reported pain or whether, as typically seen in nociplastic pain, the hypersensitivity is more widespread.

In case quantitative sensory testing can be performed, pain hypersensitivity is typically assessed using special brushes, calibrated needles or filaments, pressure pain algometry, and various thermal testing devices, and normative data have been published. In addition, assessments indicative of central aberrations of sensory processing such as increased temporal summation or dysfunctional conditioned pain modulation or exercise-induced hypoalgesia can be performed, but the reliability of these tests in the clinical setting remains to be established.

**4.5. The strengths and weaknesses of the clinical criteria**

The proposed criteria are supported by expert opinion, which is a potential source bias. A research agenda including studies exploring the clinical validity (ie, test–retest reliability, interobserver reliability, concurrent validity, content validity, etc.) of the proposed criteria is needed. Furthermore, future field testing of the criteria would be valuable. A major limitation of the criteria is the dependence on clinical judgement to decide when nociceptive and/or neuropathic mechanisms can be regarded as being entirely responsible for the pain and when not, a difficulty that is inherent every time pain mechanisms are to be attributed to painful conditions in the clinic. However, these judgments can be made. For example, in a patient suffering from polyneuropathy, bilateral pain below the knees would be considered neuropathic, but the patient’s low back pain would not, and could be nociplastic. Another example would be a patient with rheumatoid arthritis initially presenting with pain localized to inflamed, tender, and swollen joints, regarded as nociceptive pain. Yet, when this patient, despite excellent inflammatory control, continues to complain of joint pain with tender, but not swollen joints, as well as muscular pain and tenderness in the extremities and back, the nociplastic pain criteria would most likely be fulfilled.

The classification of nociplastic pain is not a new diagnosis; rather this mechanistic term indicates the likely presence of...
specific pain mechanisms, regardless of the underlying di-
agnosis (eg, osteoarthritis, fibromyalgia, etc). The concept
should be integrated into the clinical reasoning process
because it points towards specific pain mechanisms, which
can affect the treatment approach because patients with
nociceplastic pain are likely to respond better to centrally
than peripherally targeted therapies. The term has the potential
to facilitate communication and validate the patient’s pain expe-
rience. Clinicians should explain the meaning of nociceplastic pain
to their patients providing simple explanations that help patients
make sense of their pain and understand what can be done (and
what they can do) about it, including the implications for
treatment and prognosis as a result of the pain being classified
with this mechanistic descriptor.

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