What is nociplastic pain?

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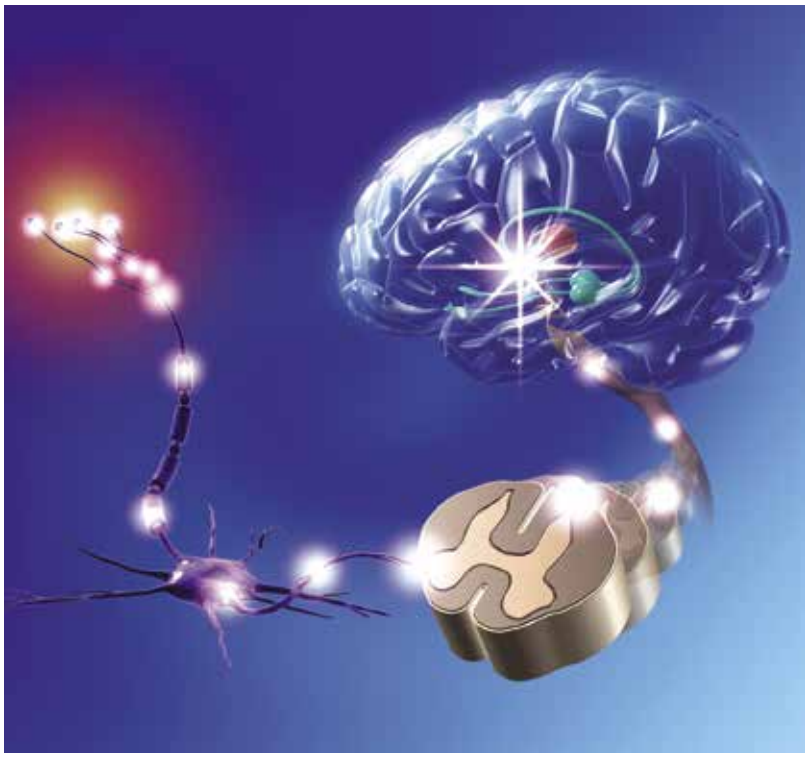
'Nociplastic' is a new, additional descriptor for the somatic component of the experience of pain. It identifies that altered nociceptive function in the central nervous system may be relevant to the pathogenesis of chronic pain in particular.



'Nociplastic' is a new descriptor for the somatic or biomedical component of pain, in addition to the two more established descriptors 'nociceptive' and 'neuropathic'. The term was adopted by the International Association for the Study of Pain (IASP) in 2017. Nociplastic pain is formally 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'.[1] This somewhat clumsy definition can be simplified to: pain that is attributed to altered nociception but is neither nociceptive nor neuropathic. To understand the significance of the introduction of this term, we need to retrace some steps to the definition of pain itself and what is meant by its somatic or biomedical component.

Key points

- **'Nociplastic' is a new, additional descriptor for the somatic component of the experience of pain.**
- **The term differs from 'nociceptive' and 'neuropathic' by indicating that altered central nociceptive function may be the relevant mechanism of pain.**
- **Nociplastic pain may well underlie chronic conditions such as fibromyalgia, complex regional pain syndrome, so-called nonspecific chronic low back pain and irritable bowel syndrome, to name just a few.**
- **Nociplastic pain affords validity to patients whose pain is neither nociceptive nor neuropathic, but who have clinical features suggesting altered central nociceptive function; explanatory confidence to their clinicians; and a pathway to improved assessment now and tailored therapies in the future.**
- **It is important to distinguish between 'nociplastic pain' as a clinical descriptor, 'chronic primary pain' as a taxonomic entity and 'central sensitisation of nociception' as a pathophysiological process. Not only are these terms not synonymous but also none of them is a 'diagnosis'.**

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Definition of pain

Pain has recently been redefined as 'an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage'.[2] Many readers may be familiar with the original IASP definition that stood from 1979: 'an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage'.[3] The change is minimal and intended to cater for those situations in which the person is unable to describe their experience. The arguments for and against this change will not be canvassed here (see 'Further Reading' for a comprehensive overview).

Both definitions emphasise that the experience of pain, firstly, has both somatic (sensory) and psychological (emotional) components and, secondly, is linked to tissue damage, actual or potential. Neither definition stems from or leads to the biopsychosocial framework in which pain is now appreciated, which adds a social dimension (what is happening in the person's world) to the psychological (what is happening to the person herself or himself) and the somatic or biomedical (what is happening to the person's body) dimensions.[4] The Faculty of Pain Medicine of The Australian and New Zealand College of Anaesthetists teaches pain in a sociopsychobiomedical framework to emphasise the importance of the nonsomatic dimensions.

Before these conceptual developments, pain was appreciated clinically only in a biomedical model, linearly related to tissue damage (nociception), whether due to disease or injury. This of course is the commonsense appreciation, especially in acute situations, although the application of this to the chronic condition was and remains problematic. However, pain and nociception – the 'signalling' by the nervous system of tissue damage – are different phenomena. The notes to the revised definition emphasise that the experience of pain cannot be inferred solely from activity in sensory neurons.[2]

In any event, despite the advent of the biopsychosocial framework, clinical thinking and therefore language and indeed taxonomy have remained very biomedical, until recently. This led to the concept of different types of somatic pain, which readers will recognise as nociceptive and neuropathic. The evolution of these terms is instructive in seeking to understand 'nociplastic'.

Evolution of pain descriptors

The modern definition of pain was formulated in 1979;[3] however, the most common type – nociceptive – was not the first to be specifically identified. It was not until 1994 that the first descriptor, neuropathic, appeared, defined as 'pain initiated or caused by a primary lesion or dysfunction in the nervous system'. Only in 2005 was nociceptive pain defined, as 'pain due to stimulation of primary nociceptive nerve endings'. By this time, nociception had been defined as 'the neural process of encoding noxious stimuli', a 'noxious stimulus' and as 'a stimulus that is damaging or threatens damage to normal tissues', and nociceptor as 'a high-threshold sensory receptor of the peripheral somatosensory nervous system that is capable of transducing and encoding noxious stimuli'. The primacy in the definition of pain of the linkage with tissue damage ('nociception') was reflected in these definitions.[5]

The other definitional change that occurred in 2005 was a minor revision of neuropathic pain to 'pain due to lesion or dysfunction of the nervous system'. 'Dysfunction' of the nervous system was not elaborated on. This established a dichotomy of mechanism: if 'stimulation of primary nociceptive nerve endings' by injury or disease could not be established, then 'dysfunction' of the nervous system could be presumed. In other words, anything that was not nociceptive could be termed neuropathic.

However, in 2011 neuropathic pain was redefined as, 'Pain caused by a lesion or disease of the somatosensory nervous system'.[6] This strict definition not only requires demonstration on clinical or imaging grounds of 'a lesion or disease of the somatosensory nervous system' – that is, determination of true neural tissue pathology – but also it excludes the concept of dysfunction.

Although this 2011 redefinition of neuropathic pain continues to make biological and etymological sense, it left a large group of patients without a valid mechanistic descriptor for their experience of pain. Such conditions include those currently labelled as fibromyalgia, complex regional pain syndrome, nonspecific chronic low back pain, irritable bowel syndrome and other functional visceral pain disorders. In these conditions there is neither obvious activation of nociceptors nor evidence of neuropathy (as defined). Yet they have clinical features to suggest that altered nociceptive function has occurred. Typically, these conditions are characterised by

- pain in a regional or more widespread distribution; and
- hypersensitivity, including allodynia, elicited in apparently normal tissues.

The phenomena in hypersensitivity lead to a reasonable inference that a change in nociceptive function has occurred, presumably in the central nervous system.

Introduction of 'nociplastic' as the third mechanistic descriptor for the somatic component of pain

These considerations demanded that a third descriptor be developed, to cater for these cases that now fell in limbo in terms of mechanism of nociception, and, as above, in November 2017, the IASP adopted the term 'nociplastic pain'.[1] The formal definition ('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') can more simply be understood as pain that is attributed to altered nociception but is neither nociceptive nor neuropathic. The key concept is that there is evidence of altered nociception – essentially allodynia to certain stimuli – related to ostensibly normal tissue in a region of pain.

The intention in adopting this term and definition was threefold:

- to confer validity on the experience of pain in those patient groups and thus avoid potentially stigmatising labels such as 'pathological', 'dysfunctional' and 'unexplained'

- to facilitate communication between patients, clinicians and other stakeholder groups
- to stimulate clinical and basic discussion and research into the phenomena of altered nociceptive function, with the ultimate goal of developing new treatment strategies.

In the IASP taxonomy, a 'descriptor' of pain is in fact a hypothesis of a mechanism of nociception. In the cases of nociceptive and neuropathic, that hypothesis has been replaced by concrete confirmation. Although nociplastic is cognate with those other two descriptors, it remains at this stage a hypothesis of mechanism, the essence of which is 'characterised by altered nociception/nociceptive function but not nociceptive or neuropathic'.

How can nociplastic pain be recognised clinically?

Consensus regarding formal clinical criteria for identifying nociplastic pain, whether in musculoskeletal or visceral contexts, has not yet been achieved and is best regarded as a work in progress.[7] This is partly due to conflation by some between a descriptor, a mechanism, a disease, a diagnosis and a syndrome (see below). However, some guidance can be given.

The essence of clinical recognition of nociplastic pain depends on three sets of phenomena, as follow.

- The pain is:
  - regional in distribution; and
  - criteria for nociceptive pain are not met; and
  - criteria for neuropathic pain are not met.
- Hyperaesthetic phenomena can be elicited clinically in the region of pain.
- There is a history of hypersensitivity in the region of pain.

It follows that the descriptor nociplastic is applicable only when there is evidence of hypersensitivity. In a musculoskeletal context, such hypersensitivity might be reported or demonstrated as hyperaesthetic (increased normal) or allodynic (frankly painful) responses to non-noxious stimuli applied to the skin, such as point pressure with a blunt pin or stroking or brushing, or applied to deeper tissues, such as blunt pressure or passive movement of joints.

These three pain descriptors are not mutually exclusive. One can have a combination of neck pain (nociceptive) and cervical radicular pain (neuropathic), while an example of a combination of nociceptive and nociplastic pain descriptors would be symptomatic osteoarthrosis in which the pain spreads beyond the affected joint(s) and is characterised by hypersensitivity of apparently normal tissues.[8]

Potential for confusion: is nociplastic pain a diagnosis, a mechanism, a disease or a syndrome?

This whole discussion very much concerns the correct use of words and the concepts they are intended to convey, to help patients and clinicians communicate effectively and understand these conditions better. The potential for confusion and frustration is readily appreciated. Pain medicine as a discipline is used to this, as a systematic diagnostic nomenclature has yet to be developed. For example, pain in and of itself is not a diagnosis. The sociopsychobiomedical (or biopsychosocial) framework demands that factors in the somatic, psychological and social dimensions be sought in understanding a person's experience of pain.

Another new concept in the pain literature has been chronic primary pain, which will appear in the *International Classification of Diseases, 11th Revision*.[9] This is defined as 'pain in one or more anatomical regions that:

- persists or recurs for longer than three months; and
- is associated with significant emotional distress or functional disability (interference with activities of daily life and participation in social roles); and
- cannot be better accounted for by another chronic pain condition.'

Chronic primary pain is a taxonomic entity, not a clinical diagnosis. It may well be that so-called nonspecific low back pain is an example of both chronic primary pain and of nociplastic pain, but the latter refers only to the somatic dimension and serves as a placeholder hypothesis of mechanism in the current state of knowledge. Neither term is a clinical diagnosis. (In the case of neuropathic pain, the IASP taxonomy specifically asserts, 'Neuropathic pain is a clinical description (and not a diagnosis) …'. The same applies to nociplastic pain.)

It is important to recognise that nociplastic pain is not synonymous with central sensitisation of nociception.[1] It is probable that central sensitisation of nociception is a relevant underlying mechanism in many cases of nociplastic pain;[10] however, it is equally possible that somatic hypervigilance, for which the underlying mechanism(s) are unknown, is also relevant. That is, both bottom-up and top-down mechanisms that may result in altered central nociceptive function need to be considered.

By the same token, nociplastic pain may be a feature that occurs in a variety of syndromes – or, more correctly, symptom clusters – such as fibromyalgia or irritable bowel syndrome, but caution needs to be exercised in potentially sheltering all difficult-to-diagnose pain conditions under the one umbrella, reminiscent of a proposal for 'overlapping chronic pain conditions'.[11]

Conclusion: what is the utility of nociplastic pain?

The concept of nociplastic pain is based on a synthesis of clinical observation and evolving knowledge of the biological substrate of nociception. This recognition, that altered nociceptive function rather than a necessary requirement for structural disease or damage in tissues or in the somatosensory system may be contributing to the experience of pain, confers validity for patients and explanatory confidence for clinicians. At the same time, it invites research into processes underlying altered central nociceptive function, how that might better be identified clinically, and implications for patient management.

This is an evolving area of knowledge and is not without some controversy. However, in patients with, for example, chronic low back pain, chronic widespread musculoskeletal pain or chronic visceral

pain, primary care practitioners may well recognise clinical features that attract the descriptor nociplastic, from which it can be inferred that a disturbance in central nociceptive function may have occurred.

An example of such a diagnostic formulation might be, 'In this patient presenting with chronic low back pain, I have identified the following contributors:

- nociplastic is an appropriate descriptor for the pain (somatic or biomedical dimension)
- major depression (psychological dimension)
- social withdrawal and unemployment (social dimension).'

As well as providing a cogent explanation, identifying nociplastic pain may lead to more rational use of diagnostic tests and to safer, more targeted and therefore more effective treatment strategies. **PMT**

Further reading

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COMPETING INTERESTS: None.