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## Definitions of nociception, pain, and chronic pain with implications regarding science and society

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### Abstract

The terminology used in pain research has strong implications regarding conducted science as well as how scientists, clinicians and society interpret our findings. This article goes over the standard definitions and their nuanced modifications recently proposed. Then, evidence and interpretation pitfalls are expounded, concluding with a plea to keep terminology precise, at least in scientific reporting.

### Introduction

Our field is pushing at the seams of knowledge. From novel genes, to molecules, to circuits, to brain networks, we are expanding the biological components that define pain, from the scale of the keratinocyte (furthest edge where organism meets environment) mediating noxious touch [6], to the brain connectome, where disruption of information sharing throughout the brain is proposed to be a signature for chronic pain [5]. Thus, it is imperative that we revisit the nuances of definition of terms we use in our literature.

The pain research literature is replete with statements like, “pain fibers”, “pain neurons”, “pain pathways”, “pain centers”, “pain circuits”. We all agree that such pronouncements are a shortcut for the statements that these are components of the nociceptive system which when strongly activated may give rise to pain perception. Yet such inaccurate terminology can mislead the field and provide opportunities for abuse by political interest groups within society.

### Nuanced definitions

From the International Association for the Study of Pain (IASP) definition of pain: “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage” it is very clear that it requires subjectivity, which in turn requires consciousness and the ability to evaluate a stimulus/situation. The corollary is that nociceptive neurons, pathways, peptides, etc. may or may not give rise to

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pain perception/report/behavior. In fact we have recently argued that nociceptive activity must be present and ongoing throughout life, lived mostly pain-free [1]. From this behavioral perspective, we have advanced the concept that pain is the detection/evaluation/perception of *failure* to protect the body from injury (actual or potential). In contrast, ongoing nociceptive processes, in the absence of pain, control behavioral repertoires that continuously and sub/pre-consciously *protect* the body from the everyday noxious environment which all organisms navigate. Thus, pain perception by humans or other animals requires the ability to evaluate the environment, form a subjective judgement about incoming nociceptive information, based on past experiences and memories. Therefore, pain requires consciousness, the details and exuberance of which varies across organisms. These definitions are a slight, but important, deviations from the standard notion that pain per se is the signal to protect tissue from injury, in which case the affective valence should be positive rather than negative. Instead, subconscious nociceptive processes successfully enabling the navigation of the environment without injuries, itself should give rise to subtle positive affective signals that promote and empower mobility within the environment. In contrast, conscious pain becomes a signal that nociception has failed and urgent decisions need to be made, given that the situation is not tolerable and thus consistently associated with negative affect.

Perhaps the most rigorous and poignant evidence for the concept of pain/nociception and body space being inter-related comes from studies regarding responses to noxious stimuli relative to the peripersonal space. A series of psychophysical studies by Iannetti's group have delineated this relationship [2, 7]. The primary observation is reflexive responses to noxious stimuli being modulated by relative proximity of the body site stimulated, in a pattern that reflects assessment of threat within a gravitationally determined peripersonal space. The basic demonstration is that threshold for a blink reflex to a fixed intensity noxious stimulus, applied to the hand, varies by the location of the hand in relation to the face. Such adjustments are important given that nocifensive responses have a cost: a continuously stronger blink can impede the view of a predator or of a prey, and the nervous system continuously judges the costs and benefits of actions. When such judgment is incorrect or too costly, pain occurs, as an error signal.

The generalization of the idea leads to the conclusion that thresholds to pain perception throughout the body are dynamically modulated as the different body portions change their relative locations during mobility. This concept then is consistent and complementary to the subconscious nociceptive system dynamically determining the body motion limits and thus continuously protecting it from injury during mobility. On the other hand, then the state of being in pain results in adaptively or mal-adaptively adjust the rules governing those choices.

Within this construct the definition of chronic pain becomes more coherent as well. The standard definition of chronic pain remains tautological, basically stating persistence of pain, either after healing or due to other unknown reasons, for long durations (usually > 3–6 months) is chronic pain. From a behavioral viewpoint, when pain becomes disassociated from adaptive options, that is when bodily adjustments, escape from the environment (regarding somatic pains) or immobility (usually during visceral pains) are no more relevant

to the experience of pain, we could then define it as chronic pain. This definition assumes per se that chronic pain is a maladaptive state. Damasio's latest book opening lines refer to pain: "When we are wounded and suffer pain, no matter the cause of the wound or the profile of the pain, we can do something about it" [3]. This is the concept of pain as a consequence of failure to protecting the body, and its corollary is subconscious nociception carving behavioral limits to continuously protect the body from injury. Consequently, when pain is present in the absence of the possibility of "doing something about it" then it is pathological and most likely chronic.

The other extreme of mixing perceptual categories is the conflation of negative emotional states with pain; exemplified by pronouncements like: "pain of separation", "pain of longing", "empathic pain", etc. The science of pain research hinges on the simple concept that pain is a somatically embodied negative affect ("stubbing the toe"). Thus, referring to negative emotions with no direct reference to body parts as pain, mixes moods and emotions with nociceptivedriven pain. Human brain imaging studies have mixed these concepts with both positive and negative pronouncements regarding brain activity overlap between somatic and "non-somatic" pain conditions [4, 8]. This approach further confuses the field rather than sharpen our understanding of underlying mechanisms.

## Conclusions

By mixing out terminology between pain and nociception we create the false impression that we have strong scientific understanding of processes underlying pain. Although we have extensive understanding of nociceptive processes, we lack any concrete theories or scientific data as to how subjective perceptions come about (the qualia of pain), be it for pain or vision or any other conscious subjective state. Imprecise use of such terminology also has a large toll on society. Recently, the US Senate rejected the Pain-Capable Unborn Child Protection Act, a bill proposing to ban most abortions after 20 weeks of pregnancy. What is amazing about this bill is its entanglement with the science of pain. The Pain-Capable Unborn Child Protection Act is based on bogus so-called "science" arguing that the presence of a thalamus in the 20-week old fetus is sufficient for pain perception, meaning that the fetus is pain-capable and would therefore suffer if a pregnancy is terminated. When, if ever, a fetus feels pain will not be covered here. The contention of this article is that we, as a community of pain scientists, are culpable for such interpretations and must acknowledge and take appropriate action by, at the minimum, properly constraining the terminology we use.

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