

# Towards an Ontology of Pain and of Pain-Related Phenomena

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## Abstract

*We present an ontology of pain and of other pain-related phenomena, building on the IASP definition of pain. Our strategy is to distinguish an evolutionarily basic pain phenomenon, involving unpleasant sensory and emotional experience along with causality by and awareness of localized tissue damage that is concordant with the pain experience. We then show how different variant cases of this canonical case of pain can be distinguished, including pain that is elevated relative to peripheral trauma, pain that is caused neuropathically (thus with no peripheral stimulus), and pain reports arising for example through deception. We describe how our approach can answer some of the objections raised against the IASP definition, and sketch how it might be used to support more sophisticated data analysis in advancing pain research, especially as concerns pain with no identifiable tissue damage.*

## Background: The Physical Basis of Disease

Increasingly, ontologies are being used to support the retrieval, integration and analysis of a variety of different kinds of biomedical data. Ontology-based technology has been successful especially in support of data-driven research in the basic biological sciences and in model organism studies, and efforts are now being made to extend these successes to the domain of human disease and diagnosis. The most successful ontologies, above all the Gene Ontology [1], rest on objective classifications of biological phenomena primarily at the molecular and cellular levels, and we face difficulties in applying the same approach where we are dealing with clinical data pertaining to pain and to other symptoms of human disease marked by the feature of subjectivity. The goal of this communication is to provide the beginnings of an ontological account of pain and of those phenomena closely related to pain that are commonly described as pain in patient reports. Because pain has subtly complex characteristics, its examination may have heuristic value for ontological accounts of symptoms more generally.

Our strategy is to pursue a view of pain as resting in every case on some physical basis perhaps as yet

unknown. This is part of a more general strategy, defended in [2], which views all clinically relevant phenomena on the side of the patient as having some physical basis within the organism. When, for example, there is a persistent pain in a patient's left temporomandibular joint (TMJ), then this is because some physical structure or substance in the organism is disordered (for example, the TMJ is deformed because of arthritis, or that part of the somatosensory cortex that serves as the projection of the left TMJ is disordered). As a result of this disorder, the organism acts in a certain abnormal way.

By 'physical basis' we understand any configuration of one or more physical components within the organism at any level of granularity, from a single nucleotide to an arthritically deformed joint. Where they are non-disordered – which means: such as to reflect the coordinated expression of the corresponding structural genes for an organism of the given type [3] – such configurations support those dispositions in the organism which are realized (manifested) in normal (= ordered) functioning. Where disordered, such configurations support dispositions to abnormal functioning, one family of which is manifested in experiences of pain.

'Symptom', as we here use this term, covers a restricted family of phenomena (including pain, nausea, anger, drowsiness), which are of their nature experienced in the first person. Symptoms can be reported to, and associated behaviors and bodily qualities can be observed by, the clinician; but the symptoms themselves cannot be observed or objectively measured.

## The IASP Definition of Pain

Pain is defined by the International Association for the Study of Pain (IASP) as follows:

**pain (IASP)** =def. an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage [4].

This definition has proved to be of considerable value, having led to 50 years of highly productive fundamental research on pain. On the other hand it has certain problems, as recently reflected by

significant discussion by an IASP task force [5]. The definition ascribes a common phenomenology ('unpleasant sensory and emotional experience') to all instances of pain, together with the recognition of three distinct subtypes of pain involving, respectively: 1. actual tissue damage, 2. what is called 'potential tissue damage', 3. a description involving reference to tissue damage.

Clause 3. may be interpreted to mean that a mere description of a certain sort provides sufficient evidence that pain is present. The intent, as we understand it, is to assign those patient reports of pain that are not sufficiently grounded in observable manifestations of tissue damage to some other (for example psychological) realm. Problems arise, then, in the classification of cases of malingering. (Example: a patient presenting with pain and associated tissue damage was prescribed pain relief medication. While moderate tissue damage remains, the medication is effective, so that *there is no longer pain*. But because the patient has become addicted, he claims that there is still pain in order to obtain more medication.) Such cases *are not pain*; yet as we shall see they will often be so classified by the clinician.

### Strategy for Defining Pain

In providing a modified version of the IASP definition in what follows we define, first, what we shall call 'pain with concordant tissue damage', which we hold to be the canonical (normal, prototypical) and evolutionarily most basic case of pain, followed by a number of variant phenomena which are defined in terms of, and involve specific kinds of departures from, this canonical case.

We distinguish the following five different sorts of cases of pain and of pain-related phenomena (see Table 1):

**PCT: pain with concordant tissue damage:** the patient experiences pain of the evolutionarily most basic sort, which is to say: pain in response to and in concordance with tissue damage;

**PNT: pain with peripheral trauma but discordant (elevated) relative to tissue damage:** there is peripheral trauma, but the patient is experiencing pain of an intensity that is discordant therewith;

**NN: neuropathic nociception:** there is no peripheral trauma, but the patient is experiencing pain in result of a *neuropathic* disorder to the *nociceptive* system. An example is phantom limb pain, where pain-system components in the brain which had been laid down through the **PCT** pain experiences activated

earlier by tissue damage in the once present limb are re-activated.

In addition, we distinguish two related cases of non-pain-phenomena:

**PBWP: pain behavior without pain:** there is, for example, a mere *report*, and no pain is being experienced (a fact which may or may not be detectable by an external observer).

**TWP: Tissue-damage without pain:** tissue damage normally of the sort to cause pain does not activate the pain system.

In a full account, we would need to distinguish also various combination cases, for example where the patient experiences canonical (**PCT**) pain in conjunction with neuropathic nociception; as well as multiple subtypes. In particular, we would need to take account of the fact that pain is divided into two broad subtypes along the temporal dimension: subtype 1. consists of pains of short duration: a cut, a local burn, an abrasion; each involves a brief duration stimulus and evokes a brief, intense experience of pain with accompanying reflex withdrawal that moves the body away from the stimulus. Following the injury there is a prolonged experience of usually less intense pain associated with inflammation that gradually recedes as healing occurs. Subtype 2. is chronic pain, a long-lasting sequence of experiences of pain, which may extend over many years without relief, and which may involve the patient visiting many specialists (ENT, headache, neurologist, TMD, psychologist) with no positive results.

Our strategy is comparable to the way in which the results of genetic mutations or injuries affecting, for example, the human hand, are most effectively described in terms of specific kinds of departures from the anatomical structure of the normal human hand (with its 5 fingers, 10 metacarpal bones, etc.). This strategy has been pioneered by the Foundational Model of Anatomy (FMA) Ontology, a scientifically well-established reference ontology of human (and more generally of mammalian) anatomy [3].

### Pain as an Evolutionarily Basic Mechanism

The canonical pain phenomenon reflects the fact that mammals have components of their brains that are associated with signals to the organism indicating that some part of their structure is damaged or is in danger of being damaged. Such signals result in various consistent outcomes on the side of the organism. This is the *sensory signalling system for pain*.

It is canonical to have pain in a joint when the joint is inflamed. Coordination between pain and tissue

damage is then part of the core orienting function of pain, which is to protect the organism from harm. A patient can thus usually direct the clinician to a particular site on or in the body where the pain is experienced.

The resultant definition of this evolutionary most basic, 'canonical' type of pain reads:

**pain with concordant tissue damage (PCT)** =def. an unpleasant sensory and emotional experience on the part of a human subject S that is caused by damage to tissue located in a certain region of the body of S, and that is of a type that can be experienced as being caused by damage to tissue in this region, and that is of an intensity that is concordant with the tissue damage.

This definition is formulated in such a way that small children and even some animals can experience canonical pain, even though they do not have the cognitive resources to represent their experience as one that is caused in the appropriate way. This addresses one recognized shortcoming of the IASP definition [6].

We can now advance the following definition of pain, which comprehends both canonical pain and the distinguished variant phenomena:

**pain** =def. an unpleasant experience on the part of a human subject that is both sensory and emotional and that is of a type that is either canonical pain (**PCT**) or phenomenologically indistinguishable from canonical pain.

The canonical pain process will involve activity in many components of the central nervous system. Part of the physical basis for this process is localized in the sensory cortex and emotional centers. In addition, **PCT** pain has a physical basis in simultaneously existing peripheral tissue damage. The tissue damage is localized in some part of the body, and the sensation is a sensation *of* processes in that part of the body. The definition of **PCT** pain is 'canonical' also in the sense that it reflects the default understanding brought to each new case by the clinician, who first assumes that the experience of pain reported by the patient is the result of tissue damage.

### Problems of Diagnosis

Pain results in outcomes in animals similar to those observed in humans, but, trivially, only humans experience pain in a way that is linked to the ability to speak of it – the latter reflecting the contribution that cognition has in affecting our basic percepts. The IASP definition, accordingly, gives a prominent role to descriptions containing reference to tissue damage. Such descriptions are central to the clinician's understanding of pain phenomena of both the **PNT** and **NN** types, neither of which has apparent tissue damage at the putative locus of pain, because the

corresponding experiences are heavily influenced by processes occurring within the sensory system itself.

Clinicians have significant problems with evaluating (quantifying) pain intensity, or the presence of pain itself, in those cases where no observable tissue damage or malfunctions in any component of the patient's body can be observed. Indeed, even if tissue damage or malfunctions can be observed, pain intensity cannot be quantified for the same reason that other feelings cannot be quantified.

An example is provided by **PNT** pains commonly referred to under the heading 'allodynia'. The physician applies non-noxious pressure to the gingiva surrounding a tooth; the patient senses the increase in pressure, and reports pain. This case, perhaps best exemplified by the well-known disorder referred to as 'regional myofascial pain', arises where tissue damage is substituted by a mild trauma of the sort that is said to putatively give rise to a myofibril disorder within muscle [7], yet where biochemical exploration has failed to find signs of overt inflammation suggestive of tissue damage, and where microstructure examination suggests alteration in the myofibrils yet such alteration is reported to be instantly reversible given the right therapy. Many theories are associated with both the phenomenon and why it is painful, but controversy is considerable. (We believe that this comes close to what IASP means by 'potential tissue damage'.)

Certainly there are behavior-based measures of pain. Given the **PBWP** phenomenon, however, these are in fact measuring two different things, since in the case of **PBWP** there is *no pain to measure*. Science based on comparing the two sets of data appears empirically ungrounded.

Such cases make diagnosis in matters of pain intrinsically difficult, and although the types of pain-related phenomena described here can be clearly distinguished in general ontological terms, identifying which type is exemplified in any given instance is by no means trivial.

### Ontology of Pain and Ethics of Pain Diagnosis

That the IASP definition is standardly interpreted in such a way as to include the malingerer as a case of pain is for good, diagnostic (ethical) reasons. The experience is *described* by the patient in terms of peripheral tissue damage, and the clinician will standardly not be in a position to assert that the reported experience is *not* correctly so described. It is precisely due to this feature of the IASP definition that pain research has progressed so significantly in the past 50 years. Data could be collected at the margins of pain without the clinician (investigator)

	Symptom	Signs (= Objectively Observable Features)	Physical Basis	Examples
<b>CP: Canonical Pain</b>				
<b>PCT: Pain with Concordant Tissue Damage</b>	Pain	Manifestation of tissue damage Report of pain concordant with stimulus sufficient to cause this tissue damage Protective response	Activation of nociceptive system through peripheral tissue damage	Primary sunburn Pain from strained muscle Pain from fracture Pulpitis
<b>VP: Variant Pain</b>				
<b>PNT: pain with peripheral trauma but no concordant tissue damage</b>	Pain	Report of pain associated with stimulus intensity insufficient to cause tissue damage	Activation of pain system through cognitive mechanisms regarding threat of tissue damage, the latter often based on peripheral non-nociceptive input to the CNS	Secondary sunburn without tissue damage Myofascial pain disorder Tension-type headache Chronic back pain
<b>NN: neuropathic nociception (pain with no peripheral trauma)</b>	Pain	Report of pain No identifiable pathological peripheral stimulus History of probable causes	Disordered nociceptive system Neuropathic (for example in result of demyelination of nerve fibers)	Trigeminal neuralgia Post-herpetic neuralgia Diabetic neuropathy
<b>PRP: Pain-Related Phenomena Without Pain</b>				
<b>PBWP: pain behavior without pain</b>		Sick role behaviors accompanied by normal clinical examination Report of pain discordant with physical signs Grossly exaggerated pain behaviors Identified external incentives	Description of pain relates to mental states such as anxiety, rather than peripheral tissue locus Misinterpretation of sensory signals by the emotional or cognitive systems Deception by patient	Factitious pain Malingering Anxiety-induced pain report
<b>TWP: tissue-damage without pain</b>		Manifestation of tissue damage normally of the sort to cause pain No reported pain	suppression of pain system by one or other mechanism	Stress associated with sudden emergencies Physiological damping of the pain process caused by adrenalin Placebo induced opioid analgesia Genetic insensitivity to pain

**Table 1:** Types of Pain and of Pain-Related Phenomena

having to be judge and jury regarding the patient's reports of his experience. But factitious pain and malingering are significant problems, and if research into the gigantic problem of pain that is experienced as being localized but is without localized tissue damage is to be successful, then some supplement to the IASP definition is needed, of the sort which, we believe, ontology can provide.

Our goal here is to initiate the development of an approach which allows the clinician or researcher better to understand the physical basis underlying a report of pain and not just to stay at the level of reports and of the assumption that, if the patient says that it is pain (within the limits of language relating to tissue damage of one sort or another), then

therefore it *is* pain (or as pain-clinicians will often say for the benefit of patients, ‘all pain is real’).

If the clinician expects concordance between stated intensity (the symptom) and the clinical findings (the signs), then significant problems will ensue, either in the form of dismissing the disorder, or in labeling the patient as ‘psychiatric’. If, in contrast, the clinician understands the neuropathic and other non-peripherally localized contributions to pain experience, then this may serve a more adequate diagnosis.

Increasingly, progress in pain research and in diagnosis of pain patients will require analysis of new types of data, including:

- (1) PET or fMRI data, which will contribute to distinguishing the factitious or malingering disorders on the one hand, and ruling in on-going nociception on the other;
- (2) linking genotype risk to present pain in the interest of making prognostic statements, including predicting likelihood of future relapse on the basis of identified pain genes;
- (3) developing classification structures that will incorporate multiple axes (including data already available concerning pain history, hard and soft tissue imaging, psychological data) so as to generate a multi-dimensional classification.

We believe that ontology-based research has already shown its value in supporting the integration that is required for full exploitation of such bodies of multi-dimensional data, and ontologies in a range of biomedical domains are now being developed in ways designed to serve such integration. [8]

The ontological approach in addition enables us to differentiate the categories involved where we do not know to which categories given patients belong. Knowing what these categories are then allows us to analyze the different types of data in ways which are unavailable on a more diffuse approach.

## Conclusion

Our short-term goal is to construct a single integrated taxonomic structure for a variety of pain disorders currently classified separately as temporomandibular disorders, orofacial pain, mucosal pain, odontogenic pain, regional neuropathic pain, and headache. These disorders span the types of pain described in the above. The long-term goal is a better understanding of medically unexplained symptoms, and thereby also a better classification of patients according to susceptibility to different kinds of therapy. Barriers to improved classification and subsequent research have thus far been due, in part, to the difficulty associated with going beyond traditional clinical perspectives

and assumptions. At issue is the emerging recognition that many body regions have associated chronic pain disorders that are more alike than they are different, whereby one of the primary characteristics is: presence of persistent dysfunctional pain disproportionate to the observed pathology here labeled **PNT**. Repeated observation has indicated that many of these disorders appear to co-occur at a higher rate than chance would suggest; yet research into this complex domain has, we believe, had trouble moving forward in part due to the inadequacy of the classification of pain and related phenomena that is implied by the IASP definition.

We believe that providing an ontological account of pain, and of those phenomena closely related to pain commonly described as pain in patient pain reports, will provide the bases for establishing a model that will permit the organization of the complex mix of basic science and clinical data and so significantly contribute to advancing our ability to more successfully diagnose and treat pain and related phenomena.

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