Pain Overview: Classification, Conceptual Framework, and Assessment

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Abstract. *The ability to evict noxious stimulus increases the likelihood of surviving. It is the result of interactions between specialized cells, the spinal cord, and the brain. Nociceptive pain is related to direct injury of the body. Other forms of pain may not be linked to visible injury. Being multidimensional in nature, classification attempts are unable to embark the plethora of elements that constitute pain. Pain theories can explain the nociceptive quality of it while failing to explain other qualities. Efforts culminated in the development of gate control theory, which spawned many advances in pain management. Assessment tools are useful to determine the intensity of pain and its impact on quality of life. Judicious use of these scales allows healthcare professionals to proper manage patients pain and are validated instruments widely used in research. This short review aims to expand awareness about the phenomenon of pain, its mechanisms, and its measurement.*

Keywords. Nociception, pain classification, gate control, pain scales, brief pain inventory

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1 Introduction

Throughout history, humans had to deal with pain and its consequences. Our understanding of the mechanisms of pain allowed us to improve its management in a variety of contexts. Despite of this, pain is still considered *"…the oldest medical problem and the universal physical affliction of mankind…"*, has Marcia Meldrum highlights in her article *"A capsule history of pain management"* [1].

According to the International Association for the Study of Pain (IASP) the revised definition of pain is "An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage."[2]**.**It is noteworthy that there wasn't always a consensus regarding pain definition. The revised definition, although with limitations, has become globally accepted by non-governmental organizations, including the World Health Organization (WHO), health care professionals, researchers in the pain field and governments [2]. To recognize what pain is, what causes it, how it is perceived and detected by the body, several studies were carried out over more than a century. A brief description of the anatomy and physiology of pain is presented below.

2 Anatomy and physiology description

2.1 Nociceptors

Nociceptors are specialized neurons which are peripherally localized and respond to a noxious stimulus. According to their action potential, conduction velocity and morphology, nociceptors can be classified in A-beta (Aβ), A-delta (Aδ) and C-fibers. Aδ-fibers are myelinated and can conduct pain signals at velocities of 5-30m/s.[3], [4]. Aβ-fibers are quicker (30-70m/s) but not exclusively nociceptors since they enervate skeletal muscle (muscle contraction) and are mechanoreceptors, not always responding to noxious stimulus. C-fibers are unmyelinated, smaller in diameter and slower than the previous ones (0,5-2,0m/s), constituting most of the nociceptors [3]. A-fibers respond to mechanical and thermal (mainly heat but also cold) insults. C-fibers are polymodal in nature and respond to mechanical, thermal (mainly heat) and/or chemical insults, which displays the rich functional heterogeneity of these nociceptors and their role in monitoring tissue conditions. A-fibers respond to mechanical and thermal (mainly heat but also cold) insults. C-fibers are polymodal in nature and respond to mechanical, thermal (mainly heat) and/or chemical insults, which displays the rich functional heterogeneity of these nociceptors and their role in monitoring tissue conditions [4].

Nociceptors project distally to the skin, where they end in the proximity of Keratinocytes, Mast cells and Langerhans cells. Furthermore, they also project centrally to the central nervous system, past the dorsal root ganglia and the trigeminal ganglion to synapse with second order neurons or interneurons of the spinal cord or the trigeminal subnucleus caudalis respectively, one of the three subnuclei of the spinal trigeminal nucleus [4]. After entering the

spinal cord through the dorsal horn, C-fibers mostly, but also some A-fibers, ascend vertically along the Lissauer tract until they synapse in the Rexed laminae. C-fibers (slower, diffuse pain) synapse mostly in lamina II and some in lamina I with interneurons, while A-fibers (fast, well localized pain) synapse preferably in lamina V directly with second order neurons, despite axons of these fibers crossing the lamina II, allowing for crosstalk between the two pain pathways [4]. Second order neurons ascend through the spinal cord in several tracts, after decussating, carrying the pain signal to the thalamus. Modulation is accomplished by nucleus in the spinal cord [3].

3 Classification of pain

When considering a classification scheme for pain the primary guide should always be that it must have clinical relevance. Healthcare professionals should be able to apply the classification(s) effectively so that the experienced pain can be tackled with the best evidence-based approach, thus improving the patient's quality of life [5]. Also, when classifying patient's pain, healthcare professionals must be aware that these classifications may overlap.

The traditional way of classifying pain is using the temporal factor which can be either "acute" or "chronic". Acute pain (sometimes called "good pain") is considered nociceptive since it relates to the activation of nociceptors when tissue injury occurs. It serves the purpose of alerting the body of tissue injury [6]. Some examples of acute pain are the post-operative pain, trauma and acute back pain [7]. Usually, acute pain subsides after a few months when tissue heals, albeit if not properly managed in some situations can lead to persistent (chronic) pain. Chronic pain is considered persistent or intermittent pain for a long period of time, which is most often arbitrarily set at 3 to 6 months. The chronification of pain is not well understood, however it is suggested that central and peripheral sensitization along with genetic predisposition and psychological factors may be responsible for it [5], [6].

Pain is also anatomically classified which is very useful for physicians. When the specific region of the body where pain is perceived is identified it allows for rapid action [5].

Etiological classification of pain is predicated on the underlying condition causing the pain. It is often divided in malignant and non-malignant causes to distinguish between cancerous and non-cancerous pain even though there is no reason to believe that the mechanisms responsible for cancerous pain are different from the non-cancerous pain [5].

The pathophysiological classification is one of the most useful classifications since it compiles the mechanistic and pathological causes as well as anatomical location. Pain can then be categorized in nociceptive and neuropathic pain. Nociceptive pain can be further divided into somatic and visceral pain. Somatic pain refers to injuries of the skin, muscle, and bone, while visceral pain refers to internal organ tissues which is felt indirectly [5], [6]. Similarly, neuropathic pain can be attributed to injury, although in this case it's the peripheral or the central nervous system that is damaged. Because of these injuries to nervous tissue, abnormal neural activity takes place, resulting in tingling, numbness, shooting pain

and other somatosensory perceptions. Examples of neuropathic pain are diabetic neuropathy and phantom limb pain [5].

4 Models of pain

In a groundbreaking paper by *Ronald Melzack* and *Patrick D. Wall* in 1965, the gate control theory was postulated. This theory was a milestone, given that reconciled concepts from the two dominant theories at the time, the specificity theory, and the pattern theory, both corroborated by physiological data although seemingly incompatible. A discussion of the notions brought forth by these theories is essential to better understand our current knowledge related to the processes of pain.

Specificity theory, postulated by *Max Von Frey*, in 1894 put forth the existence of specialized fibers responsible for pain signaling. The theory relied on two major concepts, 1) the body exhibits specialized structures which only respond to a kind of stimuli and 2) these specialized structures have a direct connection to the brain. Thanks to *Von Frey* four somatosensory modalities were defined: cold, heat, pain, and touch [8]. All the other skin senses were derived from these four senses. The theory, albeit very intuitive and relatable, especially considering current knowledge about pain pathways, had a main shortcoming. *Melzack* elegantly explains why the second concept of the theory (the direct line between specialized nerve fibers in the skin and the brain) is not a physiological fact but a psychological assumption which is not in accordance with clinical, and psychological evidence. Indeed, when considering pain from an amputated limb (phantom limb pain), causalgia (burning pain originating from lesion of peripheral nerves) or neuralgias (resulting from partial or full damage of fibers from infections or degenerative diseases) the concept of a direct connection from the periphery to the brain doesn't hold up [9]. Furthermore, non-noxious stimuli can also elicit pain (allodynia), or it may occur without a stimulus in some situations. All of these conditions argue against the existence of a direct connection, from the periphery to the brain [9].

The psychological assumption made by specificity theory was put into question by other pain models. Generally, the so called **"pattern theories"** are based on the concept of a summation effect by *Goldscheider*. An initial proponent of specificity theory, *Goldscheider* later postulated that repeated sub threshold stimulation could cause pain and that these inputs converged and summate centrally in the grey matter of the spinal cord [8]. From this concept emerged *Nafe's* proposal that all fiber endings are similar and consequently the sensation of pain is produced by a specific firing pattern, while its intensity and other qualities are connected to the spatial and temporal profiles of excitation of these nonspecific receptors. This model completely ignored observations of specialized nerve endings and others supporting specificity theory [8].

In 1965 a new model of pain was proposed that unified specificity theory concepts and pattern theory central summation and modulation [8]. The **gate control theory** recognizes the physiological evidence of touch fibers and nociceptors stating that these peripheral

afferents transmit their signal to discrete structures in the spinal cord. The signal is relayed to three hubs, according to the model, 1) the substantia gelatinosa (SG), 2) the dorsal column and 3) a group of cells they called the transmission cells (T cells). Signals reaching these hubs are modulated, primarily in substantia gelatinosa which functions as the main "gate". In the dorsal column system, afferent patterns function as a central control trigger, meaning they activate selective brain processes that influence the modulation of the gate control system. Furthermore, the T cells relay information to the so called "action system" responsible for pain perception and behavior. As shown in Fig. 1, large A-fibers and small C-fibers activate T cells while SG projections, inhibit the signal produced by the afferent fibers. In turn, A fibers increases activity of SG inhibitory effect (negative feedback) and C-fibers decrease activity of SG (positive feedback).

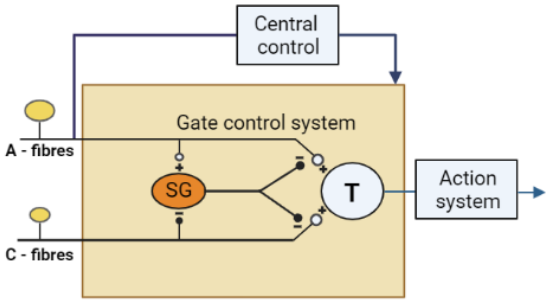

Figure 1. Depiction of the gate (SG) and it's interactions with different fibers and cells. The gate is opened when C-fiber stimulation prevails over the inhibitory effect of A-fibers. The central control (descending pathways) modulates the signal.

When a stimulus is applied to the skin, A-fibers and C-fibers may be activated, and, depending on the intensity and type of stimulus, the produced signal may be relayed by one or the two type of fibers in different patterns. It is implied that C-fibers and others small fibers are "tonically" active and adapt slowly, holding the gate in a relative opened position. A-fibers only fire when a stimulus is applied [9]. A-fibers adapt more quickly than their smaller counterparts, resulting in further opening of the gate, unless there is some event that overcomes the rapid adaptation of these fibers like rubbing or scratching the skin. When this happens, A-fibers signaling prevails, closing the gate and preventing summation of the small fibers signal. If the signals arriving at the SG and T cells reach a threshold the gate opens, and ascending pathways are triggered which result in the experience of pain [9]. Gate control theory spawned remarkable research in the field of pain. Many of the discoveries regarding the anatomy and physiology of somatosensory systems, made since its postulation is remarkably consistent with the theory, however the model is not without its flaws. For example gate control theory is unable to explain in detail how does the inhibition of small C-fibers occurs by the large A-fibers [10].

5 Pain Assessment

The attempt to "quantify" pain is always a challenging task. The different qualities of pain, along with its personal and subjective traits makes it difficult and maybe impossible to develop a common metric from which we can measure and compare the described pain experiences.

Instruments for acute pain are very practical and focus primarily on one quality of pain which is intensity. They are **unidimensional pain scales**. Conversely, when assessing chronic pain which is much more insidious, complex and may cause or be caused by other confounding factors, instruments rely on qualitative aspects of pain and its impact on daily function capability. In this case **multidimensional pain scales** are necessary to give an in-depth comprehensive picture of the patient's pain experience [7], [11].

Unidimensional scales are very sensitive in determining the intensity of pain by patient's and are systematically used in post-operative and trauma scenarios. It should be kept in mind that these instruments depend on patient's willingness and capability of reporting their pain, consequently they cannot be used in patients with cognitive impairment, dementia or with which physicians cannot communicate [7], [11]. There are 3 main scales for pain intensity that are validated and can be used. They are the Numeric Rating Scale (NRS) the Visual Analogue Scale (VAS) and the Verbal Rating Scale (VRS). The NRS is simple and easy to understand, doesn't require dexterity, paper, or pen, unlike VAS, and can be applied in telephone interviews. It consists of an 11-point integer scale where zero is no pain and 10 the worst pain ever felt [11]. VAS consists of a 100-mm horizontal line in which the left-hand end represents no pain (=0) and the right-hand end represents the worst pain imaginable (=100). The patient is asked to mark a point on the line [7]. Finally, the VRS is a categorical scale of intensity where the patient is given four words (none; mild; moderate; severe) to describe the pain. Given that VAS produces a continuous variable it seems logical that the power to detect meaningful variations in pain intensity would be attained with this scale. As discussed in a review paper by *Marianne Jensen Hjermstad et al.* that compared these different scales in pain assessment, it is said about VAS that "This *scale potentially offers the greatest opportunities for discrimination, although in practice this is illusory if most respondents are unable to discriminate PI with precision beyond nine or 10 distinct levels*." being PI the abbreviature for "pain intensity" [12]. In fact, this reflects the preference for the more widespread scale used, the NRS which along with the VAS as shown better discriminatory power of intensity of pain when compared to VRS.

Considering chronic pain, the use of validated multidimensional scales is useful enough to guide and evaluate pharmacological treatment and intervention therapies. This is not to say that these instruments can embrace the full spectrum of sensations and experiences of chronic pain. Indeed, chronic pain includes not only the obvious sensory dimension, but also physiological, psychological, and environmental dimensions, which combined cannot be fully measured by any assessment tool. There are two main multidimensional assessment tools, the Brief Pain Inventory (BPI) and the Mcgill Pain Questionnaire (MPQ), with the following common features: They are qualitative in nature, comprehensive (focusing on description of

the pain) and measure physical functioning [7]. The BPI is validated for many of the chronic pain syndromes and widely use in clinical practice. It consists of a 17-item rating scale. A body outline is presented so that the patient can shade the body part(s) where pain occurs. Several NRS scales are also used to determine intensity of pain in the last 24 hours and another NRS scale is used to determine pain interference is several domains of activities and daily functions (i.e.: mood; general activity; walking ability; sleep) [13]. The MPQ contains 20 subgroups of list words used to describe sensory (sub-group 1-10), affective (sub-group 11-15), evaluative (sub-group 16), and miscellaneous (sub-group 17-20), components of pain [13]. Each word as a different score and the use of this instrument gives two indexes, the pain rating index (PRI) and present pain index (PPI). PRI is the sum of ranked scores and PPI is determined on a 6-point (0-5) NRS scale. Used in different settings and translated to various languages, the MPQ is largely used in research on acute and chronic pain demonstrating high reliability and validity [13]. A brief mention to another scale, the 36 -Item Short Form Survey (SF-36) is noteworthy. This questionnaire, albeit not specific for pain, can be useful in pain contexts. Extensively used in research and a wide range of illnesses, it gives a standardized measure of the quality of life (QOL) of individuals and populations [14].

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