Pain-Track: a time-series approach for the description and analysis of the burden of pain

Wladimir J Alonso (wladimir.j.alonso@welfaremetrics.org)
Federal University of Santa Catarina https://orcid.org/0000-0001-7038-0801
Cynthia Schuck-Paim
Independent Researcher

Research note

Keywords: pain, time-series, pain scales, pain profile, quantitative measurement, burden assessment

Posted Date: March 4th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-286122/v1

Abstract

Objective

to present the Pain-Track, a novel framework for the description and analysis of the pain experience based on its temporal evolution, around which intensity and other attributes of pain (texture, anatomy), interventions and clinical symptoms can be registered. This time-series approach can provide valuable insight on the expected evolution of the pain typically associated with different medical conditions and on time-varying (risk) factors associated with the temporal dynamics of pain.

Results

We illustrate the use of the framework to explore hypotheses on the temporal profile of the pain associated with an acute injury (bone fracture), and the magnitude of the pain burden it represents. We also show that, by focusing on the critical dimensions of the pain experience (intensity and time), the approach can help map different conditions to a common scale directly relating to the experiences of those who endure them (time in pain), providing the basis for the quantification of the burden of pain inflicted upon individuals or populations. An electronic version for data entry and interpretation is also presented.

Introduction

Given the many challenges in the direct assessment of the pain experience [1–3], several scales were developed to evaluate its intensity as perceived by patients, often by means of self-reporting questionnaires [4, 5]. These instruments find widespread use in clinical and research settings [4]. However, while greatly useful to represent the perceived intensity of pain, these scales are not designed to capture two important elements of the pain experience: its duration and pattern of evolution. Like many other biological phenomena, pain is a dynamic process that unfolds along a temporal dimension: it may develop and resolve gradually or suddenly, may be brief or long standing, may be constant or episodic. Yet such a critical component has been often assigned an accessory role in the assessment of pain. Temporal profiles of the pain typically associated with different injuries and diseases have been seldom studied [6]. Consequently, the possibility to examine temporal relationships between pain and other time-varying variables (e.g., risk factors), patterns in the development of pain and the effectiveness of therapeutic protocols over time has also been constrained. Without considering the temporal dynamics of pain, the assessment of the burden of pain (a function of both intensity and duration) associated with different conditions, hence quantitative comparisons, is similarly prevented.

We present an operational framework for the description and assessment of pain as a time series, which we refer to as Pain-Track. As the name implies, it tracks the evolution of pain intensity over time, based on its temporal unfolding along a continuous axis, around which intensity and other attributes of pain (texture, anatomy, clinical symptoms, interventions) can be chronologically placed. Like with other dynamic phenomena, the use of a time series approach can provide valuable insight and modelling potential. In the case of a sensorial experience like pain, it can also foster the explicit representation of hypotheses for the evolution of the pain typically associated with specific medical conditions. Such an approach also opens up the possibility of quantifying the burden of pain experienced by individuals, and populations, using a universal metric with real-world meaning: time spent at different levels of pain intensity. We illustrate the framework to explore hypotheses on the temporal profile of the pain associated with a bone fracture, and the magnitude of the burden it represents. An electronic version for data entry is also made available. Before introducing the framework, we describe the rationale behind the use of four reference levels of pain intensity.

Reference Levels Of Pain Intensity

We use the disruptive character of the pain experience and its effectiveness to promote adaptive behaviors to guide the definition of the intensity categories. Pain is an adaptive warning message of actual or potential danger that must be loud enough to change behavior and reduce the likelihood that survival and reproduction are compromised [3, 7]. The greater the threat, the louder should be this signal to ensure it will take precedence over other bids for behavioral execution, a precedence proportionate to the importance of maintaining bodily integrity [8]. Accordingly, more unpleasant sensations should be in general more disruptive [9]. For example, the degree of unpleasantness associated with severe lack of food, impaired oxygen intake, and imminent dangers should be high enough to ensure that less critical ongoing behaviors and processes are put on-hold until the threat is reduced or removed. The same applies to endogenous threats, as changes in behavior (e.g.resting time) are an important part of a strategy to enable healing [10]. A positive association between pain intensity and the degree of disruption (the extent to which attention to other tasks and ongoing behaviors are affected) is thus expected. This association is also expected from a mechanistic perspective, as higher pain intensities are likely to interfere with the attentional processing of other tasks [11, 12] and impair the ability to attend to other cues [13].

The four reference categories are described in Table 1. We intentionally avoid the terminology mild, moderate and severe, as it has been used in a wide variety of contexts with different meanings. Instead, we use terms that evoke an empathic appreciation of intensity. Since the four levels are divisions imposed on a continuum, there is no theoretical limit to further increases in resolution. These categories focus only on the pain experience, and are neither necessarily correlated with the extent of physical damage or intensity of noxious stimulation [14], nor with conditions that might interfere with life quality (e.g., limitations of functioning) [15].

Table 1
Reference categories of pain intensity.

Category	Definition
Annoying	Pain experiences are not intense enough to disrupt the routine or daily activities of individuals, their possibility to enjoy pleasant (positive) experiences, or their ability to conduct mentally demanding tasks that require attention. Sufferers do not think about this sensation most of the time, and when they do they can adapt to it.
Hurtful	pain experiences that most would consider disruptive of daily routine. Although not entirely preventing individuals from functioning, their ability to do so is impaired as the direct result of pain, and often accompanied by the desire to take painkillers or seek treatment. Frequent complaints are often present. The possibility to enjoy pleasant experiences is impaired, as is performance on mentally demanding tasks [26], alertness and attention to ongoing stimuli.
Disabling	Most forms of functioning or enjoyment are prevented as the direct result of pain. Symptoms are continuously distressing. Individuals affected often substantially reduce activity levels and refrain from moving. Pain at this level can disrupt or prevent sleeping. Only strong analgesia can relieve it.
Excruciating	Threshold of pain under which many people would choose to take their life rather than standing the pain. This is the case, for example, of severe burning events, which may make victims jump from buildings, or other conditions associated with suicidal attempts by sufferers (e.g., cluster headaches). Many forms of torture have been designed to inflict pain at this level. Behavioral patterns can include loud screaming, involuntary shaking and extreme restlessness.

Pain As A Time Series

The binding hub for data capture, visualization and analysis is a standardized visual framework where pain is represented as a time series. In Fig. 1 we use it for the description of the expected temporal evolution of the pain associated with a leg fracture. Since pain experiences can unfold over a wide range of periods (from milliseconds to years), time segments represent different durations to ensure the flexibility needed.

Two are the possible ways to register the evolution of pain intensity: the path (Fig. 1a) and chance (Fig. 1b) modes. In the path mode, pain intensity levels are considered as a continuous (though not necessarily linear) gradient from no pain to excruciating pain. Estimates of variability (eg, confidence intervals) can also be added. This mode is a convenient way of recording pain in the clinical setting. The chance mode (Fig. 1b) is designed to capture (i) the temporal profile of pain at the population level, considering the expected variability in pain perception in a population or (ii) situations where uncertainty in the classification of pain intensity is present, a possibility useful for assessing pain in non-verbal subjects. Accordingly, for each time segment, intensity categories can be filled either (i) with the estimated proportion of the population that experiences pain at each level or (ii) with the probability that the pain belongs to that category of intensity. If stacked cells do not add up to 100%, the remainder percentage is attributed to a state of “no pain”. To incorporate the uncertainty in the duration of segments, each can be represented by a confidence interval.

The detailed justification of the estimates in Fig. 1 is provided in the Additional File 1. Briefly, the initial period represents the sharp, piercing pain that is often described by patients at the time of fracture [16], when mechanosensitive nerve receptors are activated. At this time, pain is most likely of a disabling nature (Fig. 1a), capturing nearly all the individual's attention: sufferers are unable to perform other activities and strong analgesia is commonly required. The chance mode (Fig. 1b) captures the possibility that a small percentage of patients (10%), with a low pain threshold, experience excruciating pain, based on reports that some patients beg to be sedated or have their limbs amputated [17]. Once the fracture is aligned or stabilized, the sharpest, most intense pain is commonly replaced by a dull, sustained pain that would last some days in the absence of analgesic treatment, coinciding with the peak of the inflammatory process [18]. Pain typically subsides during soft callus formation. This period usually lasts 2–4 weeks, from stabilization of the inflammatory process until formation of the hard callus and initiation of bone remodeling. At this stage, the expression of osteoinduction mediators at the injury site, particularly members of the bone morphogenetic protein (BMP) family, underlie the persistent pain that some patients report (BMP2 has been linked to some pain pathways [19], inflammation [20] and the release of neuroinflammatory proteins [21]).

The structure of the Pain-Track offers a means to explore putative associations between pain patterns and temporal variation in brain activity (eg, [6]) or other continuous parameters that may become available [3]. It accommodates data collection processes conducted with traditional instruments and time-indexed information, over which pain experiences can be anchored. The proposed notation has been designed to be of easy use by clinicians, patients and researchers, and amenable to digital capture and processing. The simplicity of this method also allows for patients to self-record pain episodes and the evolution of their chronic conditions, which can improve the accuracy of the description compared with later recall [22]. To facilitate the use of the framework, an electronic version was also developed, freely available at http://pain-track.org.

The use of the Pain-track framework seems similarly promising for the description of conditions leading to physiological discomfort (e.g. hunger, thirst) or psychological pain (e.g., anxiety, depression). The degree to which behavior and attention to other ongoing experiences are disrupted by these experiences can be used as a yardstick to infer the intensity of the sensation.

Quantifying The Burden Of Pain

By focusing on both critical dimensions of the pain experience (intensity and time), the Pain-Track can help map different conditions to a common scale directly relating to the experiences of those who endure them: time in pain.

The assessment of the time in pain requires determining the cumulative load of the painful events experienced [23, 24], namely the sum of the time spent in pain due to the conditions examined. From the parameters in Fig. 1b, it is possible to estimate the time in pain at each intensity level that individuals sustaining a leg fracture are expected to endure. For example, if the first phase lasted precisely 60 minutes, then 6, 42 and 12 minutes of pain at the excruciating, disabling, and hurtful levels would be expected, respectively, during this period (e.g. 60min x 10% of the population experiencing pain at the excruciating level = 6min). The same procedure can be conducted with all segments, and results added up to determine the total time in pain at each level (Table 2).

Table 2

Expected average time (hours) in pain (95% confidence interval) at each level of pain intensity due to a leg fracture. The parameter values used for the calculation (pain intensity and duration) are depicted in Fig. 1B. The uncertainties associated with the duration of each segment were propagated with a Monte Carlo simulation [34], assuming a gaussian distribution for the duration interval.

	i. Immediately after fracture	**Ii. Inflammatory Period**	**iii. Soft callus formation**	**iv. Hard callus & bone remodeling**	**Total Time in Pain (hour)**
Excruciating	**0.12 (0.05–0.2)**				**0.12 (0.05–0.2)**
Disabling	**0.87 (0.35–1.4)**	**45 (26–64)**	**100 (65–130)**		**150 (110–180)**
Hurtful	**0.25 (0.1–0.4)**	**11 (6.5–16)**	**170 (110–220)**	**170 (130–200)**	**180 (130–230)**
Annoying			**67 (43–88)**	**390 (310–470)**	**460 (370–540)**
Duration	30–120 min (0.5-2h)	2–5 days (32-80h)	2–4 weeks (224-448h)	4–6 weeks (448-672h)	

At the population level, the expected times in pain endured by the average member of a population can be determined as the product between the resulting times and the estimated prevalence of leg fractures in that population. Although pain is a concept that inherently concerns individuals, analyses at the population level enable comparing the burden of pain imposed by different injuries and diseases, and how it differs across demographics, geographies and time.

It is easy to appreciate that reducing the time individuals spend in pain of any intensity will improve well-being. However, to what extent can comparisons involving different levels of pain intensity be made? One way to determine the overall burden of pain would be by aggregating pain intensities of different levels into a single metric. Metrics rooted in this concept have been indeed used to determine the burden of diseases, combining the time spent in the disease state with its aversiveness (disability) [25]. However, to represent the burden of pain as a product of pain intensity and duration one must depart from the assumption that we understand the numerical relationship among the intensity categories in terms of the aversiveness they cause. How much worse is the hurtful experience compared to an annoying or disabling pain? How long should an individual endure a mild pain to make it equivalent to a few minutes of excruciating pain? Given the current lack of objective means upon which to attribute numerical equivalences among categories, the analysis of the total time spent in each category of pain intensity represents a more accurate and transparent approach, grounded on explicit parameters with clinical meaning. Importantly, by keeping intensity categories disaggregated, no information is lost. This approach might prove to be more informative, as it enables the assessment of the impact of different interventions along a scale of negative experiences.

Limitations

As with other scales of pain, there is no way around the problems associated with the quality of data and biases related to the accuracy of verbal self-reports of pain. Therefore, any Pain-Track registry must be inspected with the awareness that noise, biases and confounding factors will blur access to a realistic depiction of the pain experience. Additionally, future research is needed to test the psychometric properties (validity and reliability) of the Pain-Track in the clinical setting.

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and materials

Not applicable

Competing interests

The authors declare that they have no competing interests.

Funding

WJA and CSP broader research is supported by Open Philanthropy (https://www.openphilanthropy.org), though it did not specifically request this project or have any say over methods or results.

Authors' contributions

WJA and CSP designed the methodology. WJA coordinated the development of the electronic version of the framework. WJA and CSP wrote the manuscript. All authors read and approved the final manuscript.

Acknowledgements

We are very grateful to Dr. Pedro Eliezer Salinas Salazar for input on earlier versions of the manuscript and on the parameter values used for Figure 1. The Pain-Track app was developed by Blockbuilders LLC. Herickle Mesquita was also very helpful with the implementation of updates and new developments.

References

1. Farrar JT. Chapter 56 The measurement and analysis of pain symptoms. In: Cervero F, Jensen TS, editors. Handbook of Clinical Neurology. Elsevier; 2006. p. 833–42.
2. Moller A. Pain, Its Anatomy, Physiology and Treatment: Second Edition. Second edition. Aage R. Møller Publishing; 2014.
3. Cervero F. Understanding Pain: Exploring the Perception of Pain. MIT Press; 2012.
4. McDowell I. Measuring Health: A Guide to Rating Scales and Questionnaires. 3 edition. Oxford University Press; 2006.
5. Kroenke K. Pain measurement in research and practice. Journal of general internal medicine. 2018;33 Suppl 1:7–8.
6. Cecchi GA, Huang L, Hashmi JA, Baliki M, Centeno MV, Rish I, et al. Predictive dynamics of human pain perception. PLoS Comput Biol. 2012;8:e1002719.
7. Romanes GJ. Mental evolution in animals: With a posthumous essay on instinct by Charles Darwin. Kegan Paul, Trench; 1883.
8. Merker B. Drawing the line on pain. Animal Sentience: An Interdisciplinary Journal on Animal Feeling. 2016;1:23.
9. Eccleston C, Crombez G. Pain demands attention: a cognitive-affective model of the interruptive function of pain. Psychol Bull. 1999;125:356–66.
10. Weary DM, Huzzey JM, von Keyserlingk MAG. Board-invited review: Using behavior to predict and identify ill health in animals. J Anim Sci. 2009;87:770–7.
11. Kahneman D. Attention and Effort. Englewood Cliffs, NJ: Prentice-Hall; 1973.
12. Gentle MJ. Attentional Shifts Alter Pain Perception in the Chicken. Anim Welf. 2001;10:187–94.
13. Weary DM. Suffering, Agency, and the Bayesian Mind. In: McMillan FD, editor. Mental Health and Well-being in Animals. CAB International; 2020. p. 156–66.
14. Beecher HK. Relationship of significance of wound to pain experienced. J Am Med Assoc. 1956;161:1609–13.
15. Mokkink LB, Prinsen CAC, Bouter LM, Vet HCW de, Terwee CB. The COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) and how to select an outcome measurement instrument. Braz J Phys Ther. 2016;20:105–13.
16. Mitchell SAT, Majuta LA, Mantyh PW. New Insights in Understanding and Treating Bone Fracture Pain. Curr Osteoporos Rep. 2018;16:325–32.
17. del Rosario MA, Martín AS, Ortega JJ, Feria M. Temporary sedation with midazolam for control of severe incident pain. J Pain Symptom Manage. 2001;21:439–42.
18. Woolf CJ, Ma Q. Nociceptors—Noxious Stimulus Detectors. Neuron. 2007;55:353–64.
19. Wang W, Jiang Q, Wu J, Tang W, Xu M. Upregulation of bone morphogenetic protein 2 (Bmp2) in dorsal root ganglion in a rat model of bone cancer pain. Mol Pain. 2019;15:1744806918824250.

20. Mitchell K, Shah JP, Dalgard CL, Tsytsikova LV, Tipton AC, Dmitriev AE, et al. Bone morphogenetic protein-2-mediated pain and inflammation in a rat model of posterolateral arthrodesis. BMC Neurosci. 2016;17:80.
21. Nguyen V, Meyers CA, Yan N, Agarwal S, Levi B, James AW. BMP-2-induced bone formation and neural inflammation. J Orthop. 2017;14:252–6.
22. Stone AA, Schwartz JE, Broderick JE, Shiffman SS. Variability of momentary pain predicts recall of weekly pain: a consequence of the peak (or salience) memory heuristic. Pers Soc Psychol Bull. 2005;31:1340–6.
23. European Parliament. European Directive 2010/63/EU on the protection of animals used for scientific purposes. 2010. https://eur-lex.europa.eu/eli/dir/2010/63/2019-06-26. Accessed 20 Oct 2020.
24. Pickard J, Buchanan-Smith HM, Dennis M, Flecknell P, Joannides A, Lemon R, et al. Review of the assessment of cumulative severity and lifetime experience in non-human primates used in neuroscience research. London, UK: Animal Procedures Committee. 2013.
25. Murray CJ. Quantifying the burden of disease: the technical basis for disability-adjusted life years. Bull World Health Organ. 1994;72:429–45.
26. Weiner DK, Rudy TE, Morrow L, Slaboda J, Lieber S. The relationship between pain, neuropsychological performance, and physical function in community-dwelling older adults with chronic low back pain. Pain Med. 2006;7:60–70.

Figures

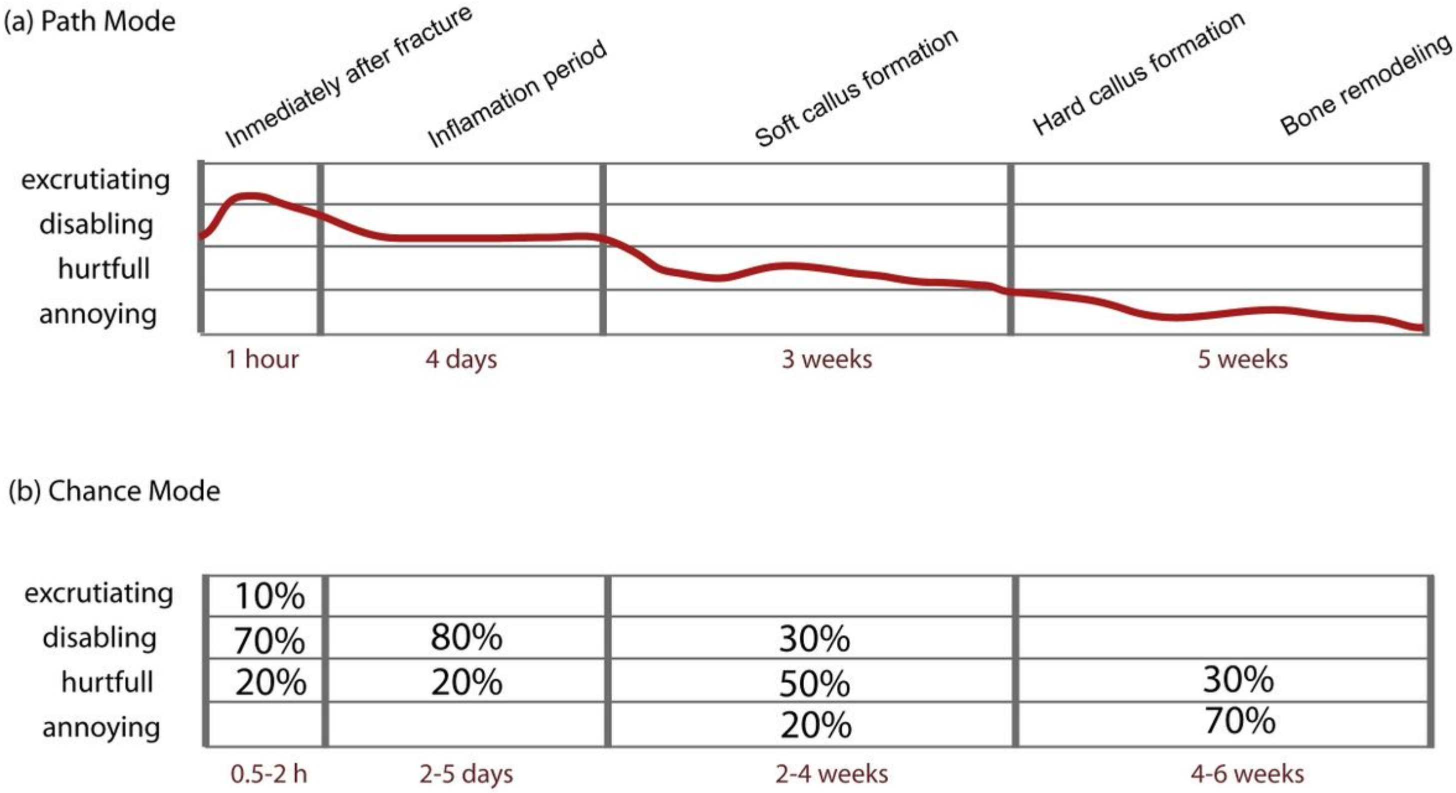

Figure 1

Clinical application of the Pain-Track framework to describe the temporal evolution of the pain associated with a leg fracture. No therapeutic intervention is assumed. Pain intensity is represented in the vertical axis and the range of probable durations below each time segment. (a) Path mode: hypothesized temporal evolution of pain for a patient; (b) Chance mode: time is partitioned into segments used to delimitate intervals when pain intensity changes. Percentages can represent either (i) the percentage of the population that feels pain at the level or (ii) the probability that the pain belongs to that category of intensity. Here, percentages should be interpreted as in (i) (expected temporal profile of the pain associated with leg fractures at the population level). For simplicity, the possibility that chronic pain develops is not depicted. Justification of the estimates of intensity and duration are provided in the Additional File 1.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- AdditionalFile1.pdf