

# Aspects of pain, its assessment and evaluation from an acupuncture perspective

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## Abstract

Pain is a major clinical problem that causes great suffering for the individual and incurs costs for society. Accurate assessment and evaluation of perceived pain is necessary for diagnosis, for choice of treatment, and for the evaluation of treatment efficacy. The assessment of an individual's pain is a challenge since pain is a subjective, multidimensional experience, and assessment is based on the person's own self-report. The results are often varied, possibly due to inter-individual variation, but also in relation to gender and aetiology.

A gold standard for pain assessment is still lacking, but rating scales, questionnaires, and methods derived from psychophysical concepts, such as threshold assessments and perceptual matching, are used. In the evaluation of pain and associated variables, both systematic and individual variation should be taken into account, as should pain-associated symptoms.

Recommendations for pain treatment should be based on the patient's specific needs. Therefore, it is important to assess the level of perceived pain taking individual variation into account. The methods used should preferably have proved to be useful in randomised controlled trials, and analysis of pain assessment should consider its non-metric properties. In the future, the use of studies with a naturalistic protocol together with individual assessment of individual pain responses could increase the internal and external validity.

## Keywords

*Nociception, pain measurement.*

## Introduction

The subjective experience of pain is not to be regarded as a single entity but rather a complex multivariate problem that has to be defined by its different components in diagnostic assessment, and in choice and evaluation of treatment. Given the variability and complexity of subjective pain, it is important to evaluate the individual as well as the group responses in order to understand the patient's pain and to optimise decisions about treatment.

As pain is a uniquely personal experience that is not necessarily proportional to the physiological process of nociception, reliance on patients' self report – pain intensity, unpleasantness, or interaction with thoughts and life – is essential. Methods of assessment, even though they are sophisticated and defined as objective, are most probably influenced by patients' motivation and psychological state; however, they are a valuable complement to the verbal report.<sup>1,4</sup>

Furthermore, pain levels as rated by patients may not agree with ratings made by a physician, another member of the medical team, or a parent, so using these ratings can be problematic.<sup>6,7</sup> Since there is no gold standard in pain assessment, communication about the perceived pain may be optimised by using a measure that the patient prefers.

In clinical work, the phenomenon of pain is both considered and treated differently. Irrespective of the origin of the pain, it is important to attempt to capture the perceived pain, ie to assess and evaluate the perceived pain. In statistical analysis of pain data, there is some discussion whether the intervals of different pain scales like the visual analogue scale (VAS), are equidistant or not, since assumptions about the distribution of the data have major implications for the choice of method of analysis. The chosen method for analysis of pain may influence the quality and validity of the results, having possible implications on evidence based decisions and choice of recommendations of pain treatment.

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The aim of this article is to describe some of the commonly used pain assessment methods and to introduce a newly developed statistical method in order to evaluate experimental and clinical pain from an acupuncture perspective. Also, we discuss the possible use of corticotropin releasing factor (CRF) in urine as a possible marker of symptoms associated with pain.

#### *Pain in society*

Pain is a major clinical problem.<sup>7</sup> The prevalence of chronic pain was recently reported to be approximately 54% and associated with female gender, older age, being on sick leave and early retirement.<sup>8</sup> Also, pain is associated with low self-rated health,<sup>9</sup> and is one of the most frequent causes of seeking healthcare.<sup>10</sup> Consequently pain, including its change and associated symptoms, is probably the most evaluated variable in clinical work.

#### *Definition of pain*

From a biological perspective, the feeling of pain is a somatic sensation, termed nociception. The meaning of nociception is a warning signal essential for survival but also intimately related to homeostasis.<sup>11</sup>

Pain is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.<sup>12</sup> The pain sensation is described as multi-dimensional including sensory-discriminative (eg intensity), affective-motivational (eg unpleasantness), and cognitive-evaluative (eg thoughts, beliefs) dimensions.<sup>13</sup> All three dimensions are like to be activated more or less simultaneously,<sup>14-16</sup> and are all important to include in the assessment of the patient's pain. The sensory-discriminative dimension, ie pain intensity or pain severity, is probably the most commonly evaluated.<sup>17</sup>

The duration of a pain condition is often described in terms of acute or chronic, the latter often exceeding three months, without clear definitions and borders between the two phases. The chronic phase is associated with changes in plasticity in peripheral and central neural structures.<sup>18,19</sup> Therefore, chronic pain is a clinical entity by itself and should not be treated as being an acute condition.<sup>20,21</sup> A long term pain condition is also reported as associated with affective components like depression and anxiety.<sup>22-24</sup>

#### *Pain mechanism*

Depending on the aetiology, pain has been classified into different categories,<sup>25,26</sup> each with its own characteristics. Woolf recently proposed a categorisation of pain based on its mechanisms, into: nociceptive – transient pain in response to a noxious stimulus; inflammatory – spontaneous pain and hypersensitivity to pain in response to tissue damage and inflammation; neuropathic – spontaneous pain and hypersensitivity to pain in association with damage to or a lesion of the nervous system; functional – hypersensitivity to pain resulting from abnormal central processing of normal input.<sup>27</sup>

#### *Biochemical markers of pain associated symptoms*

In long term pain conditions, associated symptoms of physiological and psychological distress are reported,<sup>22</sup> as well as anxiety and depression.<sup>23,24</sup> From a physiological perspective, an aberrant function of the sympathetic nervous system,<sup>28</sup> the hypothalamic-pituitary-adrenal (HPA) axis,<sup>29</sup> or its negative feedback loop,<sup>30,31</sup> have been discussed as plausible causes of the stress related symptoms in pain conditions like fibromyalgia. Corticotropin releasing factor, CRF, synthesised in the hypothalamic paraventricular nuclei, is reported as one physiological mediator of different endocrine, autonomic, and behavioural responses to stress.<sup>32-34</sup> Elevated plasma and cerebrospinal fluid (CSF) concentrations of CRF have been found in patients with fibromyalgia,<sup>22</sup> and in patients with post-traumatic stress disorder.<sup>35</sup> Hyperactive CRF neurons have, therefore, been suggested to play a role in the nociceptive and psychological mechanisms in fibromyalgia.<sup>22,29,31,36</sup> The central autonomic control of stress is complex and not easily assessed by a single test, for which reason a variety of techniques have been tried.<sup>28</sup> CRF concentration is usually measured in CSF, which is a procedure that may be stressful by itself. To reduce the stress that is related to sampling procedures, but also to diminish the influence of diurnal variation, analysis of CRF concentration in 24-hour urinary samples could be an alternative.<sup>37</sup>

#### *Endogenous pain modulation*

Endogenous pain modulation systems, operating in the central nervous system (CNS), both inhibitory and facilitatory, have been described,<sup>38-41</sup> and a

number of different neurotransmitters like opioids, and monoamines have been suggested to play a key role.<sup>42;43</sup>

In order to activate the endogenous pain inhibitory mechanisms, different modes of sensory stimulation like acupuncture are used. The pain inhibitory control is attributed to activity induced by needle stimulation starting in the peripheral receptors and primary afferent nerves leading to an inhibition of propagation of pain impulses in the dorsal horn at the spinal cord level, first described by Melzack and Wall (1965) as the gate control theory.<sup>44</sup> The activity in afferent nerves also leads to inhibitory effects elicited from higher centres in the CNS.<sup>41;45;46</sup> The induced effects of sensory stimulation techniques such as acupuncture are often reported as an increase in pain thresholds and a decrease of rated pain.<sup>47-49</sup>

Acupuncture is increasingly used for alleviation of clinical pain. However, questions of evidence for acupuncture treatment efficacy are discussed in the medical community. In a recent report, the Swedish Council on Technology Assessment in Health Care concluded that there is evidence for the usefulness of acupuncture in different chronic pain states.<sup>21</sup>

### **Assessment of pain**

#### *Rating scale assessments*

Pain is a personal and subjective experience, ie a complex perceptual phenomenon which is not necessarily proportional to the physiological process of nociception. Since pain is subjective, it can only be assessed indirectly based on the patient's self-report. The perception of pain is influenced by internal and external factors,<sup>50-52</sup> and is also reported differently.<sup>53;54</sup>

The variability in pain is also reported as being influenced by gender. Women as compared to men are more sensitive to experimental painful stimuli, perceiving clinical pain at higher severity and greater frequency, of longer duration and present in a greater number of body regions.<sup>55-58</sup> Taking all the above factors into account, evaluation of group effects may be difficult to interpret, whereas individual responses are important, ie what may be true for the individual is not valid for the group. Therefore, it is important to assess the level of perceived pain and its change, taking the individual variation into account, in order to optimise treatment regimes.<sup>59</sup>

For self-reported pain assessments, different types of uni-dimensional rating scales like the Visual

Analogue Scale (VAS),<sup>60</sup> the Numeric Rating Scale (NRS),<sup>61</sup> the Verbal Rating Scale (VRS),<sup>62</sup> the Category Ratio (CR-10 scale),<sup>63</sup> or multi-dimensional instruments like the McGill Pain Questionnaire are used.<sup>64</sup> Pain is also a common sub variable in multi-dimensional instruments such as the Nottingham Health Profile.<sup>65</sup> The VAS and NRS are probably the most commonly used pain assessment instruments but there is so far no evidence for recommending one against the other.<sup>66</sup> In chronic pain clinical trials the NRS has, however, previously been recommended.<sup>67</sup> Due to the lack of gold standard, there is a need to study if the individual score captured on one pain scale is interchangeable with that of another pain scale. In our study, pain intensity assessments using VAS and VRS were found not to be interchangeable due to inconsistency of pain scores between the two scales, and the results showed systematic disagreement when comparing the two scales. This may also indicate that scales can have different interpretations.<sup>68</sup>

#### *Threshold assessments*

An alternative method for pain evaluation, derived from the psychophysical concept, is the use of threshold assessments.<sup>69</sup> The sensory threshold is defined as the least level of stimulation that can be detected by the subjects and the pain threshold as the least level of stimulation required producing the first perception of pain. Different modes of stimulation are applied for the threshold assessments,<sup>70-72</sup> commonly with ascending intensities of stimulation, the Method of Limits.<sup>63;73;74</sup> The assessed threshold levels are generally dependent on the status of the nervous system, and sociocultural and psychological factors.<sup>16;50</sup> In pain patients, the assessed electrical sensory threshold was found to be unaffected,<sup>75</sup> or decreased,<sup>76</sup> and the electrical pain thresholds were found to be lower in comparison with healthy individuals.<sup>77</sup> Further, the electrical pain thresholds were found to increase following successful treatment in patients with painful osteoarthritis,<sup>76</sup> indicating that a shift in pain thresholds could serve as a measure of a change in perceived pain (see Figure 1).

Lowered pain thresholds have been reported in patients with pain within, as well as outside, the painful area.<sup>76;78-81</sup> This may reflect greater pain sensitivity.<sup>82</sup> Threshold assessment is generally not

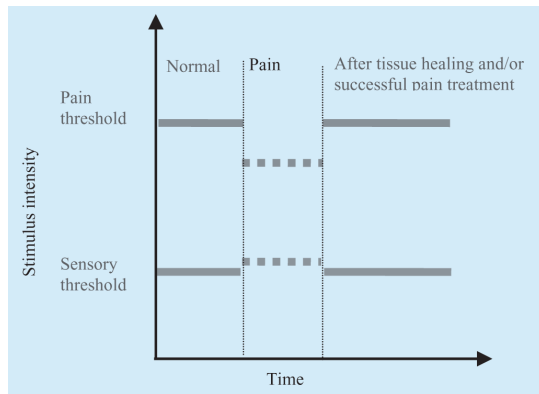


Figure 1 Possible threshold levels, sensory detection and pain, in health and pain. Figure reproduced from dissertation (Lund) with permission.

part of a clinical evaluation of pain and has mostly been restricted to neurodiagnostic and experimental procedures.<sup>83;72</sup> We have reported that threshold assessments are stable and reliable in repeated assessments.<sup>84</sup> We also found that the sensory thresholds had increased and the pain thresholds had decreased in pain patients as compared to healthy subjects. In another study, womens' pain thresholds were found to be lower than mens', and responses to TENS were indicated to be gender related – assessed as increased pain thresholds in women but not in men.<sup>85</sup>

Interestingly, the assessment of supra-threshold stimulation has been suggested as a prognostic tool for patients at risk of developing chronic pain.<sup>86</sup>

#### Matching strategies

Matching the perceived pain, ie a comparison of the intensity of clinical pain with pain derived from a different modality of stimulation, is an additional method for the assessment of pain from the psychophysical perspective,<sup>63;72;87;88</sup> and could serve as another strategy for pain assessment.

#### Properties of assessed pain

It has been suggested that pain data have linear or exponential distributions, or distributions without known size and distance, or just dichotomy into pain or no pain.<sup>4;70;72</sup> See Figure 2a-d for some examples of possible models of pain data.

In the evaluation of pain data the importance of psychometric characteristics has been acknowledged.<sup>90</sup> Support for metric properties of

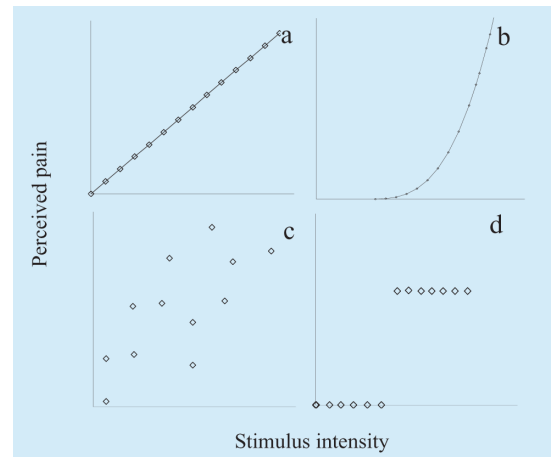


Figure 2a-d Possible models of perceived pain in response to increase of stimulus intensity presented as linear (a) or exponential (b) distributions producing data with known size and distance. Data of perceived pain presented as ordinal (c) or dichotomised into no pain/pain (d) without known size and distance. Figure reproduced with permission.

pain data using VAS comes from work based on direct magnitude scaling methods by means of thermal stimulation in healthy subjects,<sup>70;90</sup> supporting the ideas of psychophysical laws. In the area of psychophysics, general sensations like pain are studied with the goal of describing how a continuum of a sensation is represented in the mind.<sup>91</sup> The properties of these relations have been suggested to follow a logarithmic model (the Weber-Fechner Law) while Stevens, in 1970, suggested that the direct reports of subjective intensity are related to the physical intensity of stimuli by a linear relationship between the logarithm of the stimulus amplitude and the logarithm of the sensory experience.<sup>92</sup>

The general applicability of the psychophysical functions, however, has been questioned by Lockhead, who suggested that the scales are dynamic and that the judgement of a stimulus is dependent not only on its intensity but also on its duration, change of intensity, and relation to its environment.<sup>93</sup>

#### Implications for statistical evaluation

In psychophysics, the linear and ratio models have been suggested as preferred, since they allow for a simpler calculation of sums and differences, but also for the possibility of evaluating magnitude of pain, thereby allowing comparisons between subjects.<sup>53;70</sup>

The possibility of making statistical calculations and predictions is also given as the rationale for using ratio scales or scales with at least semi-ratio properties.<sup>70:94</sup> However, the assumptions of these models can never be perfectly met when analysing pain data of a group of individuals.<sup>94</sup>

Since rated pain is a subjective variable, pain data may be regarded as qualitative with an ordered structure but without metric properties of distance and magnitude, ie ordinal.<sup>95:96</sup> These rank invariant properties imply that arithmetical operations are not appropriate since a numeric ordinal record has no arithmetical meaning but only indicates the ordered structure.<sup>95:97</sup> Therefore, a change of the perceived pain can be assessed by transitional scales with the labels such as much better, somewhat better, unchanged, somewhat worse and much worse.<sup>98</sup> The concepts of interval and ratio levels of data proposed by Stevens (1946)<sup>99</sup> belong to quantitative data with complete metric properties,<sup>100</sup> and are therefore not regarded as appropriate to use in ordered categorical data.

Appropriate statistical approaches for analysis of pain data have been discussed.<sup>97:101-104</sup> Non-parametric methods are recommended since no assumption about the data is required for order, or that the data could be dichotomised into no pain or pain.<sup>104-106</sup> The non-metric properties of ordinal data imply that the median, quartiles, and range are the measures for description and that change in pain assessments can be categorised as increased, (+), unchanged, (0), or decreased, (-), see Figure 3.

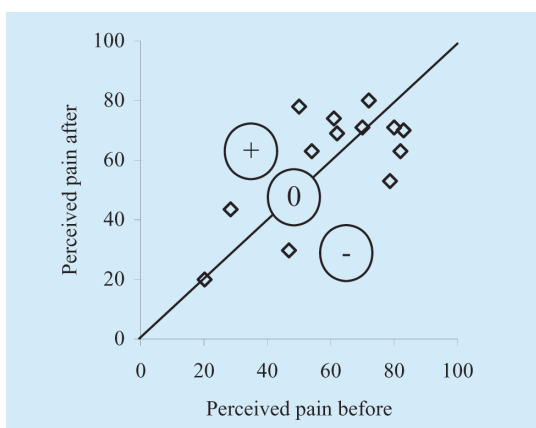


Figure 3 Paired data of rated pain before and after intervention shown as increased (+), unchanged (0) or decrease (-) in a scatter plot. Figure reproduced with permission.

According to the psychometric paradigm, some have recommended parametric methods with or without compensating for normality.<sup>70:101:107</sup> But we recommend caution in using such tests, especially when many patients (>16%) rank their pain at one of the extremes of the rating scale.<sup>107</sup> Furthermore, the use of parametric methods is restricted by the requirements of quantitative and normally distributed data or being transformed to better fit a normal distribution if these assumptions are not met.

As a result of statistical research, new methods taking into account the non-metric, ordered, categorical properties of data from scale assessments has been developed.<sup>97</sup> The methods for paired categorical data enable analyses of systematic and individual changes, but also for inter- and intra-observer agreement as well as comparisons between scales. The advantages of using statistical methods that do not require metric or other distributional properties of data are that the results are reliable and valid without restrictions and can also be used for small samples.

### Implications

The personal experience of pain can only be judged by the person in pain. Therefore the evaluation of pain assessment and treatment effect should take the individual response into account.<sup>108:109</sup> However, present recommendations for treatment are based on studies evaluating the effects preferably on a group level. Using evaluating procedures from recent statistical research<sup>97:110</sup> it is possible to calculate individual as well as group effects.

Randomised controlled clinical trials (RCTs) have become the gold standard for evidence based medicine. Recommendations based solely on RCTs and evaluations of group effects may, therefore, circumvent the possibility of an effect on an individual level. RCTs commonly employ a placebo control group for the control of non-specific effects produced by therapy. The design of RCTs does not allow for evaluation of different types of non-specific effects.<sup>111:112</sup> Also, it is generally not possible to determine placebo response rates in RCTs, since a natural history group is often lacking. However, placebo control in studies using sensory stimulation is, by definition, impossible to conduct. Furthermore, in a recent study aimed at elucidating the placebo response rates in RCTs it was demonstrated that non-

specific treatment effects are more important than specific effects.<sup>113</sup> This highlights the importance of evaluating the non-specific treatment effects.

In a future study, a combination of RCT and naturalistic designs could be adopted.<sup>114,115</sup> Naturalistic studies, where the choice of, for instance, mode of stimulation and number of treatments is offered to patients, are less likely to misrepresent the relationship and influence of these factors upon the assessed outcome when incorporated into standard (randomised) biomedical designs. In this way, a further optimisation of the therapeutic effects would be likely. Furthermore, a naturalistic approach may mimic the practical use of an intervention in a clinical context more closely.

### Conclusion

In conclusion, we have described and discussed the importance of evaluating both the systematic and the individual responses in different pain assessment methods and thereby emphasised not only the need to consider individual responses in the evaluation of pain and variables associated with pain, but also the need for individually designed treatment regimens. However, evaluation of assessed pain should take both systematic and individual variation into consideration. Our findings suggest that the assessment of pain intensity on the Visual Analogue Scale is not interchangeable with assessment on the Verbal Rating Scale and that threshold assessment may be an additional, valuable tool for clinical evaluation given gender separated analyses. Biochemical markers, such as urinary CRF-LI concentrations may be used for measurement of stress related symptoms in pain conditions.

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