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Original Article

Clinical indicators of 'nociceptive', 'peripheral neuropathic' and 'central' mechanisms of musculoskeletal pain. A Delphi survey of expert clinicians

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ABSTRACT

The clinical criteria by which clinicians determine mechanisms-based classifications of pain are not known. The aim of this study was to generate expert consensus-derived lists of clinical criteria suggestive of a clinical dominance of 'nociceptive', 'peripheral neuropathic' and 'central' mechanisms of musculoskeletal pain.

A web-based 3 round Delphi survey method was employed as an expert consensus building technique. One hundred and three clinical experts (31 Pain consultants, 72 musculoskeletal physiotherapists) were surveyed. Participants were asked to suggest clinical indicators of three separate categories of pain mechanisms (Round 1), then rate (Round 2) and re-rate their level of agreement/disagreement (Round 3) with those clinical indicators. Consensus was defined by a $\geq$80% level of agreement.

Sixty-two (Response rate, 60%), 60 (58%) and 59 (57%) respondents replied to Rounds 1, 2 and 3 respectively. Twelve 'nociceptive', 14 'peripheral neuropathic' and 17 'central' clinical indicators reached consensus.

These expert consensus-derived lists of clinical indicators of 'nociceptive', 'peripheral neuropathic' and 'central' mechanisms of musculoskeletal pain provide some indication of the criteria upon which clinicians may base such mechanistic classifications. Further empirical testing is required in order to evaluate the discriminative validity of these clinical criteria in particular and of mechanisms-based approaches in general.

1. Introduction

Mechanisms-based classifications of pain refer to the classification of pain according to the underlying neurophysiological mechanisms responsible for its generation and/or maintenance (Gifford, 1998, Dallel and Voisin, 2001). Clinically this approach has been advocated based on its perceived ability to provide clinical diagnoses of the operant mechanisms underlying patients' pain which can in turn be useful in helping to explain and account for variations in clinical presentations of pain not otherwise explicable by the conventional medical model, and in guiding treatment and prognostic based clinical decision-making (Butler 2000, Baron, 2006). Their use is predicated on an assumption that mechanisms-based classifications of pain can improve clinical outcomes by directing treatment towards the dominant neurophysiological mechanisms underlying patients' pain. However these assertions have yet to be substantiated empirically (Finnerup and Jensen, 2006).

In the absence of any diagnostic gold standards for mechanisms-based pain diagnoses, it has been suggested that different categories of pain mechanisms (i.e. categorical labels describing an assumed clinical dominance of the neurophysiological mechanisms underlying clinical presentations of pain), such as 'nociceptive', 'peripheral neuropathic' and 'centrally sensitised' pain states, may be identifiable and distinguishable from one another clinically based on the pattern recognition of clusters of symptoms and signs characteristic to each category (Butler, 2000) by means of a standard clinical interview and examination process (Hansson, 2002).

Nociceptive pain mechanisms refer specifically to those pathophysiological processes associated with activation of the peripheral receptive terminals of primary afferent neurones in response to noxious chemical (inflammatory), mechanical or thermal stimuli (Ekman and Koman, 2004; Julius and McCleskey, 2006). Chemically mediated nociception from the inflammatory response associated with tissue injury (McMahon et al., 2006) or from tissue ischemia in response to tissue loading or compression (Butler, 2000) are likely

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mechanisms underlying many clinical presentations of musculoskeletal pain. Peripheral neuropathic pain has been defined as *'Pain initiated or caused by a primary lesion or dysfunction in the peripheral nervous system'* (Merskey and Bogduk, 1994) and describes a mechanistic category of pain involving a number of pathophysiological mechanisms associated with altered nerve functioning and responsiveness, such as changes in electrical hyper-excitability and abnormal impulse generation, and mechanical, thermal and chemical sensitivity (Devor, 2006). And central pain has been defined as '*Pain initiated or caused by a primary lesion or dysfunction in the central nervous system (CNS)'* (Merskey and Bogduk, 1994). The term 'central' pain was used in this study to refer to musculoskeletal pain states characterised primarily by 'dysfunction' within the CNS i.e. central sensitisation/hyper-excitability (Butler, 2000; Lidbeck, 2002) rather than by any distinct lesion within the CNS as might occur with CNS disorders such as multiple sclerosis (Boivie, 2006).

Whilst a number of multi-category pain mechanisms-based classification methods have been described (Jones, 1995; Gifford and Butler, 1997; Arner, 1998; Woolf et al., 1998; Lidbeck, 2002; Woolf, 2004a) what each of these lacks is the description of reliable and empirically validated discriminatory clinical criteria with which to distinguish one category of pain mechanisms from another (Smart et al., 2008).

Whilst some preliminary construct validity evidence exists for clinical criteria associated with the identification of (peripheral) neuropathic pain (Bennett et al., 2007) specific clinical indicators of 'nociceptive' and 'central' pain have not been empirically developed or validated and the clinical criteria upon which clinicians base such classifications has not been empirically studied; although some clinical patterns thought to be suggestive of a dominance of 'nociceptive', 'peripheral neuropathic' and 'central' pain mechanisms have been proposed (Gifford and Butler, 1997; Butler, 2000; Smart et al., 2008) and some evidence for the use of such mechanisms-based classifications has been demonstrated amongst experienced physiotherapists as part of a multidimensional pain-oriented clinical reasoning process (Smart and Doody, 2006, 2007).

The issue of validity as a property of classification systems is particularly significant (Ford et al., 2007). Before its use in clinical practice can be justified any mechanisms-based classification system for pain should be developed and validated using appropriate methodologies (Ford et al., 2007) in order to i) provide evidence that meaningful sub-categories exist, ii) provide clinical criteria that define category membership, and iii) demonstrate that the classification of patients into such categories facilitates optimal clinical decision-making associated with treatment selection, and thus clinical outcomes and predictions.

The aim of this study was to identify those potential clinical criteria upon which clinicians may base such mechanisms-based classifications by generating an expert consensus-derived list of clinical criteria associated with a dominance of 'nociceptive', 'peripheral neuropathic' and 'central' mechanisms of pain.

2. Method

2.1. Study design

An internet-based 3 round Delphi survey method was employed as an expert consensus building technique in this investigation. Ethical approval for this study was granted by the Ethics and Medical Research Committee of St Vincent's University Hospital, Dublin, in November 2006.

Use of the Delphi method has been recommended when collective subjective judgements are needed to solve a particular problem (Nekolaichuk et al., 2005). More specifically, it has been suggested that consensus-derived criteria from the Delphi method can be particularly useful for informing clinical decision-making (e.g. mechanisms-based classifications of pain) in situations of clinical uncertainty (Powell, 2003), where clearly defined, empirically-derived, evidence-based practice procedures with which to guide such decision-making have yet to be established (Cook et al., 2006). As part of a' judgemental approach' towards classification system development (Ford et al., 2007) and in the absence of any alternative diagnostic/classification gold standard (Katz et al., 2000)., the Delphi method provides a means of generating those potentially discriminative clinical criteria that may, on further validity testing, define category membership within the classification system.

2.2. Participants

A purposeful sampling strategy was employed in order to recruit appropriate clinical 'experts'. Participants were recruited based on an assumption of a high level of relevant clinical knowledge and expertise related to the domain (i.e. pain) and constructs (i.e. categories of pain) under investigation, and for their likelihood of generating clinical criteria with a high degree of face/content validity (McCarthy et al., 2006); and included Consultant physicians in Pain Medicine/Anaesthesia recruited from both the British and Irish Pain Societies (BPS, IPS) and specialist musculoskeletal physiotherapists from the Manipulation Association of Chartered Physiotherapists (MACP), a recognised musculoskeletal Clinical Interest Group of the Chartered Society of Physiotherapy.

In order to recruit participants, a period of 'pre-notification' was undertaken during which time the membership lists of relevant organisations with contactable members (BPS $n = 88$, IPS $n = 23$, MACP $n = 553$) were accessed and members informed as to the purpose of the study and invited to participate. After the 'pre-notification' period a final survey sample of 103 clinical 'experts' (31 consultants in pain medicine, 72 expert musculoskeletal physiotherapists) who had expressed an interest in taking part were invited to participate in the survey.

2.3. Procedure

All 103 clinical 'experts' were emailed an Internet link to the online survey tool (EFM Feedback, 2007) which, once clicked, took participants automatically to Round 1 of the Delphi survey. Consent to participate was inferred from the voluntary participation of respondents. The Delphi survey ran from March to September 2007. Participants were given six weeks to respond to each round. In order to maximise response rates, follow-up reminder emails were sent to non-respondents to each round (Dillman, 2000).

Typically, a 'classic' Delphi survey consists of three pre-planned rounds of questionnaires, beginning with Round 1 where a defined panel of 'experts' are invited to give their opinions on a particular topic (Keeney et al., 2006). In Round 1, after soliciting participant demographic data, six open-ended questions invited participants to suggest i) 'subjective', and ii) 'clinical examination' clinical criteria associated with a clinical dominance of three categories of pain mechanisms; 'nociceptive', 'peripheral neuropathic' and 'central' mechanisms of musculoskeletal pain.

The use of open-ended questions allowed participants freedom to volunteer any criteria considered relevant (Powell, 2003). Response data was analysed qualitatively in order to generate criteria that reflect the diversity of opinions from the participants of Round 1 for inclusion into Round 2.

In Round 2 participants were invited to rate their level of agreement/disagreement with the 'subjective' and 'clinical examination' criteria suggested for each category of pain mechanism as

derived from a qualitative analysis of Round 1 respondent data by means of a five point Likert-type scale (5 = Strongly agree, 4 = Agree, 3 = No opinion, 2 = Disagree, 1 = Strongly disagree). Responses were analysed with descriptive statistics in order to ascertain the level of agreement and consensus for each criterion.

In the third and final round, participants were asked to re-rate their level of agreement with the same clinical criteria listed in Round 2 after viewing and in light of graphical illustrations showing the distribution of group opinion for each criterion from Round 2. Response data was then re-analysed for levels of agreement and consensus (Jones and Hunter, 1995).

A consensus level of ≥80% agreement was decided upon by a team of three researchers and set *a priori* as the cut-off point by which to determine and establish consensus for each criterion, meaning that for a criterion to attain consensus status, 80% or more of participants had to either agree or strongly agree with a criterion as a clinical indicator of its respective category of pain mechanism. In the absence of standardised guidelines consensus levels must be set arbitrarily according to the importance of the study's outcomes (Powell, 2003). The criteria generated by this Delphi survey were to be subject to further empirical evaluation as part of an ongoing process of development and preliminary validation of mechanisms-based classifications of pain, as such as a relatively high consensus level, as compared to other studies (Keeney et al., 2006), was set.

2.4. Data analysis

Respondent data from Round 1 was analysed qualitatively via 'content analysis' (Patton, 2002) in order to generate lists of 'subjective' and 'clinical examination' clinical criteria for inclusion in Round 2. The data reduction process included exporting response data from the online survey tool (EFM Feedback, 2007) into 'Word' documents in order to form a database of transcripts, inductive 'content analysis' in order to identify and code themes, categories and ultimately specific clinical indicators within the response data, followed by confirmatory 'content analysis' in order to test and affirm the authenticity and appropriateness of the emergent clinical indicators (Patton, 2002).

Inter- and intra-coder reliability of the coding scheme used to analyse respondent data and was determined in order to check the representativeness of the clinical indicators derived from the Round 1 content analysis. Inter-coder reliability was checked by two separate coders, the primary researcher (KS) and one research supervisor (CD); coding the same response data from the transcripts of 5 randomly selected participants. Intra-coder reliability was checked by the same coder (KS) coding the same randomly selected transcripts on two separate occasions, 2 days apart.

Inter-coder and intra-coder reliability was calculated by percent agreement (Portney and Watkins, 2008) as 89.5% and 97.4% respectively. In addition, Kappa coefficients for inter- and intra-coder reliability of the coding process ranged from 0.6–1.00 (inter-) and 0.8–1.00 (intra-), suggesting good to excellent agreement respectively (Daly and Bourke, 2000).

Response data related to participants' agreement ratings from Rounds 2 and 3 were analysed with descriptive and non-parametric statistics. Graphical representations of frequencies of respondents' ratings for each criterion were illustrated with bar charts. Each bar chart showed the number and percentage of respondents indicating each level of agreement/disagreement, as illustrated for one 'peripheral neuropathic' criterion, *'History of nerve injury, pathology or mechanical compromise'*, (see Fig. 1). In addition, criteria were ranked by the researchers for their importance as clinical indicators by means of a composite score procedure (Cook et al., 2006) whereby the higher the composite score the stronger the criterion

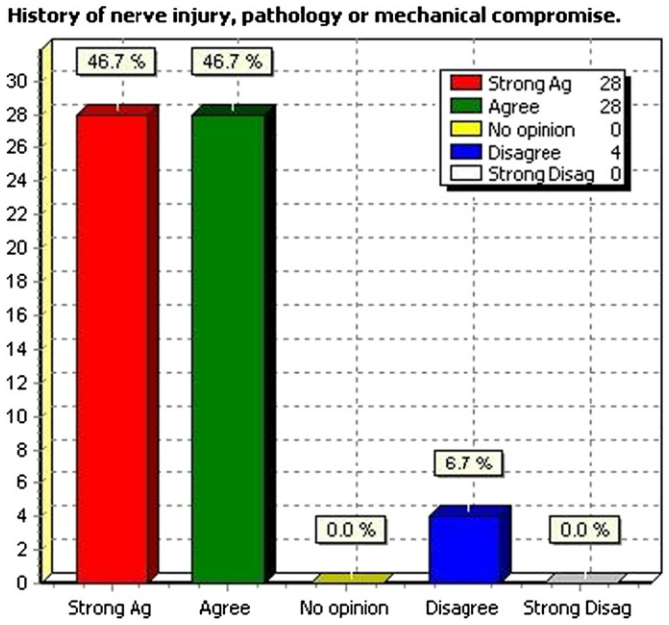

Fig. 1. A graphical example of Round 2 respondent data for one subjective clinical criterion of peripheral neuropathic pain.

was inferred to be as a clinical indicator of its respective category of pain mechanisms, and was calculated as follows:

$$\text{Composite score} = (n\,\text{SA} \times 5) + (n\,\text{A} \times 4) + (n\,\text{NO} \times 3) + (n\,\text{D} \times 2) + (n\,\text{SD} \times 1),$$

where *n* SA, *n* A, *n* NO, *n* D, *n* SD is the number of respondents who rated each criterion as Strongly agree, Agree, No opinion, Disagree, and Strongly disagrees respectively. For example, the Round 2 composite score value for the 'peripheral neuropathic' subjective clinical criterion, *'History of nerve injury, pathology or mechanical compromise'*, as detailed in Fig. 1 was:

$$(28 \times 5) + (28 \times 4) + (0 \times 3) + (4 \times 2) + (0 \times 1) = 260$$

The minimum (maximum disagreement) and maximum (maximum agreement) possible composite score values for Rounds 2 and 3 were 60 and 300, and 59 and 295 respectively.

Kendall's W (Kendall's coefficient of concordance) was calculated in order to evaluate the degree of consensus between respondents' ratings across criteria within each category of pain in Rounds 2 and 3. Kendall's W ranges from 0 (no agreement) to 1 (complete agreement). Data were analysed using 'Statistical Package for the Social Sciences' (SPSS) for Windows version 14.0 (SPSS Inc., Chicago, IL).

Consensus was established when ≥80% of respondents strongly agreed or agreed with a criterion as an indicator of its respective category of pain mechanisms.

3. Results

Sixty-two (response rate 60%), 60 (58%) and 59 (57%) respondents replied to Rounds 1, 2 and 3 respectively. Participant demographics are displayed in Table 1. Three physiotherapists dropped out between rounds giving an attrition rate of 4.8%.

A qualitative 'content analysis' of Round 1 respondent data generated a list of 18 'nociceptive' (11 'subjective' and 7 'clinical examination'), 20 'peripheral neuropathic' (12 'subjective', 8 'clinical examination'), and 25 'central' pain (16 'subjective', 9 'clinical

Table 1
Participant demographics (Round 1) $n = 62$.

Gender	Male = 29 Female = 33
Profession	Medical consultant pain medicine = 11 (BPS[a] = 6, IPS[b] = 5) Physiotherapist (MACP[c]) = 51
Work setting	Clinical hospital = 27 (Med cons[d] = 10, Physio.[e] = 17) Clinical non-hospital = 21 (Physio = 21) Academic/teaching = 10 (Med con = 1, Physio. = 9) Research = 1 (Physio. = 1) Other = 3 (×1 Academic/Clinical non hospital, ×1 Clinical hospital/research, ×1 clinical hospital/non-hospital)
Specialisation	Consultant pain medicine/anaesthesia = 10 Consultant pain medicine/management = 1 Musculoskeletal physiotherapy = 51
Years as specialist	Mean = 10.3 years, range 1–24
Country of residence	U.K. = 47 (Med cons = 6, Physio. = 41) Ireland = 8 (Med cons = 5, Physio. = 3) Other = 7 (Greece, Israel, Sweden = 1; Australia, Channel Islands = 2)

[a] British Pain Society.
[b] Irish Pain Society.
[c] Manipulation Association of Chartered Physiotherapists.
[d] Medical consultants.
[e] Physiotherapists.

examination') clinical criteria for subsequent rating in Rounds 2 and 3. The clinical criteria derived from the Round 1 analysis together with summary data (median, consensus level, composite score and final rank) from Rounds 2 and 3 are displayed in Tables 2–7.

Twelve 'nociceptive' (8 subjective, 4 clinical examination), 14 'peripheral neuropathic' (9 subjective, 5 clinical examination) and 17 'central' pain (13 subjective, 4 clinical examination) clinical criteria acquired consensus status as determined by the *a priori* ≥80% agreement (Strongly agree, agree) cut-off point and are indicated in bold type in Tables 2–7.

Based on the composite score procedure applied to respondents agreement ratings: *'Clear, proportionate mechanical/anatomical nature to aggravating and easing factors'* and *'Clear, consistent and proportionate mechanical/anatomical pattern of pain reproduction on movement/mechanical testing of target tissues'* ranked as the 'subjective' and 'clinical examination' criteria most strongly suggestive of a dominance of 'nociceptive' pain mechanisms.

The top ranked 'subjective' and 'clinical examination' indicators of 'peripheral neuropathic' pain were; *'Pain variously described as burning, shooting, sharp, aching or electric-shock-like'* and *'Pain/symptom provocation with mechanical/movement tests that move/load/compress neural tissue'* and those deemed most suggestive of dominant 'central' pain mechanisms were; *'Disproportionate, non-mechanical, unpredictable pattern of pain provocation in response to multiple/non-specific aggravating/easing factors'* and *'Disproportionate, inconsistent, non-mechanical/non-anatomical pattern of pain provocation in response to movement/mechanical testing'*.

Six criteria (3 subjective, 3 clinical examination) failed to reach consensus status as indicators of 'nociceptive' pain. *'Absence of or non-significantly associated with maladaptive psychosocial factors (*e.g. *negative emotions, poor self-efficacy, maladaptive beliefs and pain behaviours)'* and *'Absence of maladaptive pain behaviour'*, emerged as the subjective and clinical examination criteria least suggestive of a clinical dominance of nociceptive mechanisms of pain.

Six 'peripheral neuropathic' criteria failed to reach consensus status. Of these, *'Pain associated with psychological affect (*e.g. *distress, mood disturbances)'* and *'Signs of autonomic dysfunction (*e.g. *trophic changes)'* were the subjective and clinical examination criteria deemed least suggestive of 'peripheral neuropathic' pain.

Eight criteria (3 subjective, 5 clinical examination) failed to attain consensus status as indicators of predominant central neuropathic mechanisms of pain. Of these *'History of CNS disorder/lesion (*e.g. *Multiple Sclerosis, Spinal cord injury)'* and *'Antalgic postures/movement patterns'* ranked as the subjective and clinical examination criteria least suggestive of 'central' mechanisms of musculoskeletal pain.

Kendall's W (Kendall's coefficient of concordance) for the criteria associated with 'nociceptive' pain in Rounds 2 and 3 was 0.22 and 0.48 respectively. The corresponding values for criteria associated with 'peripheral neuropathic' were 0.18 and 0.31, and for 'central' pain were 0.20 and 0.37. An increase in the values of Kendall's W between Rounds 2 and 3 indicates an increase in consensus between respondents' ratings across criteria within each category of pain.

Table 2
Clinical Indicators: Nociceptive/subjective (Rank order by composite score, post Round 3. Consensus-based criteria indicated in bold type).

Criterion	Median		Consensus level of agreement (%)		Composite score[a]		Rank	
	Round 2	3	2	3	2	3	2	3
Clear, proportionate mechanical/anatomical nature to aggravating and easing factors.	**5**	**5**	**93.3**	**100**	**271**	**283**	**2**	**1**
Pain associated with and in proportion to trauma or a pathological process (Inflammatory nociceptive) or movement/postural dysfunction (Ischaemic nociceptive).	**5**	**5**	**96.7**	**98.4**	**276**	**283**	**1**	**2**
Pain localised to the area of injury/dysfunction (with/without some somatic referral).	**5**	**5**	**95.0**	**100**	**270**	**282**	**3**	**3**
Usually rapidly resolving or resolving in accordance with expected tissue healing/pathology recovery times.	**4**	**4**	**95.0**	**100**	**261**	**253**	**4**	**4**
Responsive to simple analgesia/NSAID's.	**4**	**4**	**88.3**	**96.6**	**247**	**244**	**5**	**5**
Usually intermittent and sharp with movement/mechanical provocation; may be a more constant dull ache or throb at rest.	**4**	**4**	**83.3**	**96.7**	**239**	**241**	**6**	**6**
Pain in association with other symptoms of inflammation (i.e. swelling, redness, heat) (Inflammatory nociceptive).	**4**	**4**	**81.6**	**88.2**	**237**	**233**	**7**	**7**
Absence of neurological symptoms.	4	4	63.4	76.3	223	226	9	8
Pain of recent onset.	**4**	**4**	**71.7**	**84.8**	**225**	**225**	**8**	**9**
Clear diurnal or 24 h pattern to symptoms e.g. morning stiffness.	4	4	63.3	68.5	213	207	10	10
Absence of or non-significantly associated with maladaptive psychosocial factors (e.g. negative emotions, poor self-efficacy).	4	4	61.6	62.7	212	200	11	11

[a] (Please note, Round 2 and 3 composite scores are not directly comparable due to the unequal number of respondents to Rounds 2 and 3).

Table 3
Clinical Indicators: Nociceptive/clinical examination (Rank order by composite score, post Round 3. Consensus-based criteria indicated in bold type).

Criterion	Median		Consensus level of agreement (%)		Composite score		Rank	
	Round 2	3	2	3	2	3	2	3
Clear, consistent and proportionate mechanical/anatomical pattern of pain reproduction on movement/mechanical testing of target tissues.	**5**	**5**	**93.4**	**98.3**	**271**	**282**	**1**	**1**
Localised pain on palpation.	**4**	**4**	**86.7**	**96.6**	**250**	**244**	**2**	**2**
Absence of or expected/proportionate findings of (primary and/or secondary) hyperalgesia and/or allodynia.	**4**	**4**	**80.0**	**91.6**	**235**	**233**	**3**	**3**
Antalgic (i.e. pain relieving) postures/movement patterns.	**4**	**4**	**80.0**	**89.8**	**231**	**230**	**4**	**4**
Presence of other cardinal signs of inflammation (swelling, redness, heat).	4	4	71.6	78.0	223	216	5	5
Absence of neurological signs; negative neurodynamic tests (e.g. Straight leg raise, Brachial plexus tension test, Tinel's).	4	4	60.0	64.4	213	203	6	6
Absence of maladaptive pain behaviour.	4	3	51.7	42.4	206	180	7	7

4. Discussion

This Delphi survey presents an expert consensus-derived list of clinical criteria associated with a clinical dominance of 'nociceptive', 'peripheral neuropathic' and 'central' mechanisms of musculoskeletal pain. These findings provide some indication of the criteria by upon which clinicians base such mechanistic inferences concerning the dominant categories of neurophysiological mechanisms underlying clinical presentations of pain and provide some support for the assertion that clinicians may be able to distinguish between a dominance of 3 different categories of pain mechanisms-based on the pattern recognition of discriminatory clusters of symptoms and signs.

4.1. Nociceptive pain

The 'nociceptive' pain criteria derived from this Delphi survey appear to concur with a number of nociceptive-specific criteria proposed in the limited literature available (Gifford and Butler, 1997; Butler, 2000; Smart et al., 2008) including in particular the preservation of a clear stimulus-response relationship associated with aggravating/easing factors and clinical testing. In addition, two of the consensus criteria in particular appear consistent with some of the likely underlying neurophysiological mechanisms associated with both the generation and treatment nociceptive pain such as the role of inflammatory mediators and modulators of nociceptive pain (McMahon et al., 2006) and the mechanism of action of anti-inflammatory medications (Ekman and Koman, 2004).

In addition to these the international panel of experts sampled in this survey suggested a number of other potential nociceptive-specific clinical criteria, including pain localised to the area of injury/dysfunction, localised pain on palpation, antalgic postures/movement patterns and absent or expected findings of hyperalgesia and/or allodynia.

4.2. Peripheral neuropathic pain

The 'peripheral neuropathic' pain criteria generated form this Delphi survey appear to largely concur with those criteria described in a number of existing screening tools developed specifically to identify pain of (peripheral) neuropathic origin; including the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) (Bennett, 2001; Bennett et al., 2005), pain DETECT

Table 4
Clinical Indicators: Peripheral neuropathic/subjective (Rank order by composite score, post Round 3. Consensus-based criteria indicated in bold type).

Criterion	Median		Consensus level of agreement (%)		Composite score		Rank	
	Round 2	3	2	3	2	3	2	3
Pain variously described as burning, shooting, sharp, aching or electric-shock-like.	**4**	**5**	**86.6**	**93.2**	**259**	**274**	**2**	**1**
History of nerve injury, pathology or mechanical compromise.	**4**	**4**	**91.4**	**100**	**260**	**263**	**1**	**2**
Pain in association with other neurological symptoms (e.g. pins and needles, numbness, weakness).	**4**	**4**	**93.3**	**93.2**	**257**	**248**	**3**	**3**
Pain referred in a dermatomal or cutaneous distribution.	**4**	**4**	**90.0**	**94.9**	**253**	**245**	**4**	**4**
Less responsive to simple analgesia/NSAID's and/or more responsive to anti-epileptic (e.g. Neurontin, Lyrica)/anti-depression (e.g. Amitriptyline) medication.	**4**	**4**	**86.6**	**91.5**	**241**	**244**	**6**	**5**
Pain of high severity and irritability (i.e. easily provoked, taking longer to settle).	**4**	**4**	**76.7**	**88.1**	**231**	**233**	**8**	**6**
Mechanical pattern to aggravating and easing factors involving activities/postures associated with movement, loading or compression of neural tissue.	**4**	**4**	**85.0**	**84.8**	**239**	**229**	**7**	**7**
Pain in association with other dysesthesias (e.g. crawling, electrical, heaviness).	**4**	**4**	**78.4**	**81.4**	**244**	**229**	**5**	**8**
Reports of spontaneous (i.e. stimulus-independent) pain and/or paroxysmal pain (i.e. sudden recurrences and intensification of pain).	**4**	**4**	**70.0**	**79.7**	**225**	**224**	**9**	**9**
Latent pain in response to movement/mechanical stresses.	4	4	63.3	72.9	218	218	10	10
Pain worse at night and associated with sleep disturbance.	4	4	63.4	76.3	217	217	11	11
Pain associated with psychological affect (e.g. distress, mood disturbances).	3.5	3	50	44.1	196	183	12	12

Table 5
Clinical Indicators: Peripheral neuropathic/clinical examination (Rank order by composite score, post Round 3. Consensus-based criteria indicated in bold type).

Criterion	Median		Consensus level of Agreement (%)		Composite score		Rank	
	Round 2	3	2	3	2	3	2	3
Pain/symptom provocation with mechanical/movement tests (e.g. Active/Passive, Neurodynamic, i.e. SLR, Brachial plexus tension test, Tinel's) that move/load/compress neural tissue.	**5**	**5**	**91.7**	**96.6**	**269**	**279**	**1**	**1**
Pain/symptom provocation on palpation of relevant neural tissues.	**4**	**4**	**93.3**	**98.3**	**253**	**255**	**2**	**2**
Positive neurological findings (including altered reflexes, sensation and muscle power in a dermatomal/myotomal or cutaneous nerve distribution).	**4**	**4**	**80.0**	**86.4**	**239**	**240**	**3**	**3**
Antalgic posturing of the affected limb/body part.	**4**	**4**	**75.0**	**83.0**	**236**	**232**	**5**	**4**
Positive findings of hyperalgesia (primary or secondary) and/or allodynia and/or hyperpathia within the distribution of pain.	**4**	**4**	**78.3**	**84.8**	**239**	**230**	**4**	**5**
Latent pain in response to movement/mechanical testing.	4	4	66.6	74.6	221	222	6	6
Clinical investigations supportive of a peripheral neuropathic source (e.g. MRI, CT, nerve conduction tests).	4	4	61.6	66.1	207	205	8	7
Signs of autonomic dysfunction (e.g. trophic changes).	4	4	56.6	50.9	208	192	7	8

(Freynhagen et al., 2006), ID-Pain (Portenoy, 2006), Douleur Neuropathique 4 (DN4) (Bouhassira et al., 2005) and Neuropathic Pain Questionnaire (NPQ) (Krause and Backonja, 2003), such as those related to the quality and spontaneous behaviour of pain, dysesthesias, as well as symptoms and signs associated with allodynia, hyperalgesia and hyperpathia. A number of additional criteria were also suggested such as pain referred in a dermatomal/cutaneous distribution, pain/symptom provocation associated with subjective aggravating/easing factors and clinical tests associated with disturbance of neural tissue and pain/symptom provocation on palpation of relevant neural tissues.

These additional criteria may have the potential to improve the diagnostic accuracy/efficiency (sensitivity, specificity, positive and negative predictive values) of any mechanisms-based classification or screening instrument. Many of these additional criteria whilst not included in any of the existing screening tools have been described as part of a clinical reasoning strategy for determining the relative dominance of peripheral neuropathic mechanisms of pain (Butler, 2000; Nee and Butler, 2007).

Also, the results of this study appear to suggest that supportive clinical investigations (e.g. magnetic resonance imaging) may not be necessary in order for clinicians to classify pain as predominantly 'peripheral neuropathic'.

4.3. Central pain

Standardised methods or validated screening tools for the identification of central mechanisms of pain do not currently exist although a number of theoretically conceived clinical decision-making strategies for pain have suggested that a dominance of central mechanisms (i.e. central sensitisation/hyper-excitability) may be distinguishable clinically based on pattern recognition of characteristic symptoms and signs (Gifford, 1998; Butler, 2000; Lidbeck, 2002). The 'central' pain criteria proposed in this Delphi survey appear to correspond to a number of those described in the limited literature available, including patient reports suggesting diffuse geographies of pain, distortions in the stimulus-response relationship associated with aggravating/easing factors and clinical

Table 6
Clinical Indicators: Central pain/subjective (Rank order by composite score, post Round 3. Consensus-based criteria indicated in bold type).

Criterion	Median		Consensus level of agreement (%)		Composite score		Rank	
	Round 2	3	2	3	2	3	2	3
Disproportionate, non-mechanical, unpredictable pattern of pain provocation in response to multiple/non-specific aggravating/easing factors.	**5**	**5**	**93.3**	**98.3**	**267**	**277**	**1**	**1**
Pain persisting beyond expected tissue healing/pathology recovery times.	**4**	**5**	**91.6**	**96.6**	**262**	**274**	**3=**	**2**
Pain disproportionate to the nature and extent of injury or pathology.	**4.5**	**5**	**93.3**	**94.9**	**265**	**272**	**2**	**3**
Widespread, non-anatomical distribution of pain.	**4**	**5**	**91.6**	**96.6**	**262**	**266**	**3=**	**4**
History of failed interventions (medical/surgical/therapeutic).	**4**	**5**	**83.3**	**89.8**	**257**	**264**	**6**	**5**
Strong association with maladaptive psychosocial factors (e.g. negative emotions, poor self-efficacy, maladaptive beliefs and pain behaviours, altered family/work/social life, medical conflict).	**4**	**4**	**80.0**	**86.5**	**246**	**253**	**8**	**6**
Unresponsive to NSAID's and/or more responsive to anti-epileptic (e.g. Neurontin, Lyrica)/anti-depressant (e.g. Amitriptyline) medication.	**4**	**4**	**95.0**	**93.2**	**261**	**252**	**5**	**7**
Reports of spontaneous (i.e. stimulus-independent) pain and/or paroxysmal pain (i.e. sudden recurrences and intensification of pain).	**4**	**4**	**86.7**	**96.6**	**251**	**250**	**7**	**8**
Pain in association with high levels of functional disability.	**4**	**4**	**75.0**	**88.2**	**240**	**249**	**9**	**9**
More constant/unremitting pain.	**4**	**4**	**80.0**	**91.5**	**235**	**242**	**11**	**10**
Night pain/disturbed sleep.	**4**	**4**	**73.4**	**79.7**	**236**	**231**	**10**	**11**
Pain in association with other dysesthesias (e.g. burning, coldness, crawling).	**4**	**4**	**76.6**	**84.8**	**228**	**230**	**12**	**12**
Pain of high severity and irritability (i.e. easily provoked, taking a long time to settle).	**4**	**4**	**68.3**	**81.3**	**223**	**230**	**14**	**13**
Latent pain in response to movement/mechanical stresses, activities of daily living.	4	4	71.7	76.3	225	227	13	14
Pain in association with symptoms of autonomic nervous system dysfunction (skin discolouration, excessive sweating, trophic changes).	4	3	55.0	49.2	207	198	15	15
History of Central Nervous System disorder/lesion (e.g. Multiple Sclerosis, Spinal cord injury).	4	4	56.6	50.9	197	184	16	16

Table 7
Clinical Indicators: Central pain/clinical examination (Rank order by composite score, post Round 3. Consensus-based criteria indicated in bold type).

Criterion	Median		Consensus level of agreement (%)		Composite score		Rank	
	Round 2	3	2	3	2	3	3	3
Disproportionate, inconsistent, non-mechanical/non-anatomical pattern of pain provocation in response to movement/mechanical testing.	**4.5**	**5**	**90.0**	**96.6**	**262**	**274**	**2**	**1**
Positive findings of hyperalgesia (primary, secondary) and/or allodynia and/or hyperpathia within the distribution of pain.	**4.5**	**5**	**95.0**	**100**	**266**	**271**	**1**	**2**
Diffuse/non-anatomic areas of pain/tenderness on palpation.	**4.5**	**5**	**86.7**	**91.5**	**258**	**265**	**3**	**3**
Positive identification of various psychosocial factors (e.g. catastrophisation, fear-avoidance behaviour, distress).	**4**	**5**	**75.0**	**81.3**	**243**	**253**	**4**	**4**
Absence of signs of tissue injury/pathology.	4	4	73.4	78.0	224	221	5	5
Latent pain in response to movement/mechanical testing.	4	4	63.3	74.6	222	221	6	6
Disuse atrophy of muscles.	4	4	61.7	61.0	216	205	7	7
Signs of autonomic nervous system dysfunction (E.g. skin discolouration, sweating).	4	4	58.4	54.2	208	197	8	8
Antalgic (i.e. pain relieving) postures/movement patterns.	4	4	53.3	50.9	205	191	9	9

tests, spontaneous and paroxysmal pain and pain states with seemingly strong associations to emotional disturbances and maladaptive cognitions. A number of additional criteria were suggested including a history of failed interventions and diffuse/non-anatomic areas of pain and tenderness on palpation.

Whilst 'latency' (i.e. delayed onset of pain in response to mechanical stimuli) has been suggested as a characteristic of central hyper-excitability (Gifford and Butler, 1997; Lidbeck, 2002) this criterion narrowly failed to reach consensus status as both a subjective (Consensus level: 76.3%) and clinical examination (74.6%) criterion as determined by the consensus cut-off point in this study.

4.4. Validity

In the absence of evidence-based classification/diagnostic criteria (Finnerup and Jensen, 2006) and where there is uncertainty concerning the extent to which mechanisms-based categorisations of pain, such as 'nociceptive', 'peripheral neuropathic' and 'central' pain represent valid and distinct clinical constructs (Butler, 2000) and if (Jensen and Baron, 2003) and how they might they be determined and distinguished clinically (Woolf, 2004b; Finnerup and Jensen, 2006) it is acknowledged that the findings from this study reflect academic learning and/or the clinical experience of the participants of this study only and as such should cannot be taken to represent evidence-based classification criteria. However, the Delphi approach provides a suitable methodology from which to commence the process of classification system development and validation by providing clinically meaningful classification criteria with a high degree of face and content validity (McCarthy et al., 2006). Further empirical studies employing methodologies appropriate for classification system development and validation are required in order to provide and accumulate further construct (discriminative) and predictive validity evidence (Buchbinder et al., 1996; Ford et al., 2007; Portney and Watkins, 2008) to support and justify their use in clinical practice (Turk and Okifuji, 2001; Smart et al., 2008).

4.5. Limitations

The findings from this study should be interpreted in light of a number of methodological limitations. The purposeful sampling strategy employed in this survey may limit the generalisability of its findings and the participation of nearly five times as many physiotherapists than pain physicians may have produced results that reflect a dominance of physiotherapy opinion. Also, in the absence of any standardised guidelines for defining and selecting experts, the credibility and expertise of study participants must be inferred and assumed from its composition and professional attributes. An alternatively defined and comprised expert panel may have yielded different results; as such it is possible that other clinical disciplines may base such mechanistic classifications on alternative clinical criteria.

The potential influence of non-response bias is unclear since the characteristics of the non-responders to this Delphi survey are not known. The similarities between a number of the clinical criteria generated from this study with those proposed in the literature suggest that non-response bias may not have acted as a confounder to any significant degree.

Out of concern for participant burden, the criteria in this study were ranked for their relative importance as clinical indicators by means of a composite score procedure, the weightings of which, although arbitrary, were based on those employed in similar studies (Cook et al., 2005, 2006). Alternative rankings may have been produced if the participants themselves had been invited to rank them.

Another cited weakness associated with the use of Delphi studies aimed at discerning clinical indicators is the 'stand-alone principle' (Cook et al., 2005) whereby participants are required to rate their level of agreement with one variable at a time whereas in reality it is likely that some clinical diagnoses may only be made on the basis of the co-existence (and/or relative absence) of clusters of specific symptoms and signs.

Finally, according to our design participants were not afforded the opportunity to suggest additional criteria after Round 1, this may have affected the content validity of findings.

5. Conclusion

This study has generated expert consensus-derived lists of clinical criteria associated with a clinical dominance of 'nociceptive', 'peripheral neuropathic' and 'central' pain mechanisms and as such provides some indication of the criteria by which clinicians infer such mechanistic classifications of musculoskeletal pain. These criteria were found to correlate with some existing criteria described in the literature, however a number of additional clinical criteria were proposed by the participants in this Delphi survey which may, when subjected to further clinical validation testing, improve the classification efficiency and accuracy of mechanisms-based classifications of musculoskeletal pain.

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Conflicts of interest

None declared.

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