Features and methods to discriminate between mechanism-based categories of pain experienced in the musculoskeletal system

Research Paper

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Features and methods to discriminate between mechanism-based categories of pain experienced in the musculoskeletal system: a Delphi expert consensus study

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Abstract

Classification of musculoskeletal pain based on underlying pain mechanisms (nociceptive, neuropathic, and nociplastic pain) is challenging. In the absence of a gold standard, verification of features that could aid in discrimination between these mechanisms in clinical practice and research depends on expert consensus. This Delphi expert consensus study aimed to: (1) identify features and assessment findings that are unique to a pain mechanism category or shared between no more than 2 categories and (2) develop a ranked list of candidate features that could potentially discriminate between pain mechanisms. A group of international experts were recruited based on their expertise in the field of pain. The Delphi process involved 2 rounds: round 1 assessed expert opinion on features that are unique to a pain mechanism category or shared between 2 (based on a 40% agreement threshold); and round 2 reviewed features that failed to reach consensus, evaluated additional features, and considered wording changes. Forty-nine international experts representing a wide range of disciplines participated. Consensus was reached for 196 of 292 features presented to the panel (clinical examination—134 features, quantitative sensory testing—34, imaging and diagnostic testing—14, and pain-type questionnaires—14). From the 196 features, consensus was reached for 76 features as unique to nociceptive (17), neuropathic (37), or nociplastic (22) pain mechanisms and 120 features as shared between pairs of pain mechanism categories (78 for neuropathic and nociplastic pain). This consensus study generated a list of potential candidate features that are likely to aid in discrimination between types of musculoskeletal pain.

Keywords: Pain mechanisms, Expert consensus, Clinical examination, Quantitative sensory testing, Imaging, Diagnostic tests, Questionnaires

1. Introduction

Persistent musculoskeletal pain is a global health issue.[34] The complexity and heterogeneity of pain presentations make management of musculoskeletal conditions challenging and have led to unhelpful terms such as nonspecific low back pain and temporomandibular joint dysfunction, which cannot guide treatment. Selection of treatment based on identification of the neurobiological mechanisms that maintain an individual's pain is a plausible approach to improve outcomes.[5,10,29,32] A major challenge is whether pain mechanisms can be accurately identified in clinical practice and research.[19] The International Association for the Study of Pain (IASP) identifies 3 main pain mechanism categories to explain pain (nociceptive, neuropathic, and nociplastic pain—**Table 1**),[13] but there is considerable debate whether or how these mechanisms can be identified and differentiated from each other.[25,26]

Operationalisation of a treatment approach for musculoskeletal conditions that target specific pain mechanisms requires agreement of a feature, or more likely a cluster of features, which can identify the probable underlying mechanisms. This approach could include methods to identify features that are present in 1 or 2 but not all pain mechanism categories. Several methods to discriminate between pain mechanisms have been proposed based on narrative review[4,36] and by clinical experts from a single[7] or unknown discipline(s).[23] There has been a recent rapid expansion of research regarding pain mechanisms, rigorous testing of measurement paradigms, and changes to terminology (eg, endorsement of nociplastic pain by IASP[19]). As a first step towards refinement of a consensus and evidence-based approach to discriminate between pain mechanisms, 2 studies systematically reviewed literature regarding the features that characterize the different mechanisms[25] and the methods proposed to discriminate between them.[26] Although some convergence was apparent, the reviews highlighted divergence in opinion.

Three major issues challenge the development of an accepted method to discriminate between pain mechanism categories. First, because no direct in vivo measures are available to confirm the putative neurobiological mechanisms responsible for pain in many individuals, there is no gold standard method to validate the discrimination between mechanisms.[3,32] Second, many individuals likely present with pain that includes a combination of pain mechanisms, although one might be predominant. Third, interpretation of the literature is hampered by divergence of opinion regarding features that might be unique to a specific pain mechanism category or shared between multiple categories. When evidence is contradictory, divergent, or unavailable, consensus of experts is necessary.[14]

Table 1

IASP pain mechanism definitions.

Pain mechanism	Definition
Nociceptive pain	Pain that arises from actual or threatened damage to non-neural tissue and is due to the activation of nociceptors.
Neuropathic pain	Pain caused by a lesion or disease of the somatosensory nervous system.
Nociplastic pain	Pain that arises from altered nociception despite no clear evidence of actual or threatened tissue damage causing the activation of peripheral nociceptors or evidence for disease or lesion of the somatosensory system causing the pain.

Definitions of pain mechanism categories as proposed by the IASP.[13]

The primary aim of this study was to use a Delphi process to reach consensus amongst experts on features that are unique to 1 pain mechanism category, shared by 2 major categories, or present in all 3 and therefore unhelpful for discrimination. This study was built on the recent systematic review of features advocated to discriminate between pain mechanisms.[26] The secondary aim was to develop a ranked list of features based on agreement between experts. Such a list could form the foundation for future development of a consensus-based approach to identify and discriminate between pain mechanism categories in individuals presenting with pain experienced in the musculoskeletal system.

2. Methods

2.1. Study design and overview

An online Delphi design[33,35] was used to evaluate expert opinion on features/assessment findings that have been proposed to guide discrimination between the pain mechanisms that contribute to an individual's pain experience. This approach involves multiple rounds of questionnaires that include rating of items and/or open-ended responses.[33] This study involved 2 rounds undertaken and reported as recommended by guidelines for Delphi studies.[15,27] Round 1 involved presentation of a list of features and assessment findings derived from systematic reviews[25,26] that have been proposed to aid discrimination between pain mechanism categories. Participants were asked to indicate which (if any) pain mechanism would be attributed to each, to propose additional features, and to provide comments on terminology/wording. Round 2 involved clarification of outcomes of round 1 to refine the final ranked list. This study was approved by the institutional Human Research Ethics Committee (#2020002324) at the University of Queensland, and participants provided informed consent.

2.2. Steering committee

A steering committee was established to oversee the project, including preparation of the list of features and assessment findings to be evaluated in round 1, evaluation of the outcome of round 1, and review of responses to round 2. The committee involved 4 members with backgrounds in pain neurobiology. All were physiotherapists, but each with different research expertise and clinical experience (years of experience: M.A. Shraim—pain, neuroscience—5 years; M. Sterling—pain, clinical research—37 years; K. Sluka—basic neuroscience, translational and clinical pain science—36 years; and P.W. Hodges—pain, neuroscience—30 years). Two members (M.S. and K.S.) had been involved in IASP projects related to definitions of pain and pain mechanisms[19,24] and 2 members (M.A.S. and P.H.) had published extensive literature reviews that provided a foundation for this work.[25,26]

2.3. Expert selection

Selection of an expert panel is an essential part of the Delphi process.[16] Expert panelists should be committed to the project,

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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credible, and sufficiently heterogeneous to represent the range of experts who have an interest in results.[17] No standard method is available to calculate a panel size to undertake a Delphi process.[6] Because this project required diversity of opinion, a minimum sample size of 40 panelists from different countries was defined a priori for each round. Heterogeneity of the sample was critical to ensure a wide spectrum of opinions.[21,35] To meet this goal, it was considered essential to include researchers, academics, clinicians, and individuals with pain with consideration of diversity of discipline, international location, career level, and sex.

The steering committee developed a preliminary list of potential panelists who met at least 2 of the following criteria: (1) contribution to at least 3 published works related to pain in the preceding 3 years; (2) keynote or invited presentations at major meetings related to pain; (3) contribution to major working groups/committees of pain organisations; (4) contribution to organisation of major pain meetings/conferences; (5) contribution to pain textbooks; (6) contribution to clinical practice guidelines/systematic reviews related to pain; (7) membership of any international pain organisation; and (8) postgraduate certification in pain or pain management. The final list was refined based on diversity of expertise, clinical discipline, international distribution, career level, and sex. In addition, the steering committee identified 2 representatives with lived experience of chronic pain who have had additional training in pain mechanisms. Potential experts were contacted through an email invitation letter, and reminders were sent after 2 weeks if no response was received. Experts who agreed to participate were provided with a link to more detailed information and to provide consent. Demographic data collected included the following: age, sex, country, discipline, major topic area in the pain field, years working in the pain field, and number of publications related to pain. Although data were presented to the panelists in a de-identified manner, they were informed that data could be re-identified by the steering committee if clarification of responses was required.

2.4. Development of the initial list of features/assessment findings

A list of features/assessment findings that have been proposed to aid the discrimination between pain mechanism categories was derived from 2 recent systematic reviews[25,26] and categorised under 4 main method groupings: (1) clinical examination, (2) quantitative sensory testing, (3) imaging and diagnostic testing, and (4) pain-type questionnaires. This initial list was refined during 5 meetings of the steering committee. The following refinements were made: (1) subjective descriptors of pain were converged under groupings described by the McGill pain questionnaire where applicable[22] (descriptors that could not be grouped in this manner were retained separately); (2) features/assessment findings that had similar meaning were converged (eg, clinical bedside sensory testing was converged with quantitative sensory testing); and (3) items that did not describe specific assessment findings (eg, diagnosis of a pain mechanism category by exclusion of another) were excluded. The completed list of features/assessment findings is presented in supplemental digital content 1 (available as supplemental digital content at http://links.lww.com/PAIN/B565).

2.5. Delphi process

The Delphi process was undertaken on an online surveying platform (Qualtrics, Seattle). Experts participated in 2 rounds (**Fig. 1**). In the first Delphi round, experts were presented with a description of the purpose of the study, a brief definition of pain mechanism categories (from the IASP[13]), and a list of features/assessment findings. They were asked to nominate the category (nociceptive, neuropathic, and nociplastic pain) in which each feature/assessment finding might be observed. Experts could select none, 1, 2, or 3 pain mechanism categories. If 1 category was selected, the feature/assessment finding was considered to be unique to that category. If 2 categories were selected, it would be considered to aid discrimination between those 2 categories and the third category but not between them. If 3 categories were selected, it was considered that this feature, while present in each condition, would not aid the discrimination between them. Experts could also select unsure. Contributors had the opportunity to suggest changes to the terminology or wording applied to a feature/assessment finding or nominate others that they believe might aid discrimination between pain mechanism categories.

From round 1, a list of features was generated that experts agreed might aid discrimination between pain mechanism categories that contribute to an individual's pain experience. Because of the diversity of opinion in the field and the absence of a gold standard to address disputes in opinion and because the features identified in this study would be subjected to additional evaluation before reduction to the minimum set of measures, it was decided to use a lenient threshold that is lower than that commonly used in Delphi studies.[8] This was set at 40% agreement to ensure that the process eliminated measures that the group very consistently did not consider helpful[2] but retained features that might be controversial yet have some potential to aid discrimination between pain mechanisms and worthy of further testing. To be retained in this list, features would need to reach agreement as: (1) unique to 1 pain mechanism category—if >40% of experts state that the feature/finding is present in only 1 category (must be the same category identified by each expert); or (2) shared by 2 pain mechanism categories—if >40% of experts state that the feature/finding is present in the same 2 categories. If a feature failed to reach either of these thresholds, but the sum of unique to 1 category and shared by 2 categories exceeded 40%, the feature was retained and allocated according to the category or a combination of categories with the highest score or both if the score was equal. A ranked list was generated of features/assessment findings using the percentage agreement.

In round 2, features/assessment findings that did not reach threshold to be retained in the list as being helpful to discriminate between pain mechanism categories (ie, failed to reach threshold for unique or shared by 2) were represented to panelists who were asked whether any of the pain mechanism categories not meeting threshold should be retained. Panelists were also given an opportunity to provide justification and/or evidence to support their opinion. To be retained, at least 15% of respondents should independently identify that the feature/assessment finding should be retained. Panelists were also presented with a list of the additional feature/assessment findings that were nominated in the first round. These were judged with the same consensus criteria applied in round 1. Finally, any suggested changes to terminology/wording from round 1 were presented to panelists to indicate their agreement/disagreement with the suggested changes. Wording changes were accepted if most of the panelists (>50%) and the steering committee were in agreement. The steering committee also considered additional refinements of wording based on panelist input. The complete list of additional features/assessment findings added in round 2 is included in supplemental digital content 1, http://links.lww.com/PAIN/B565.

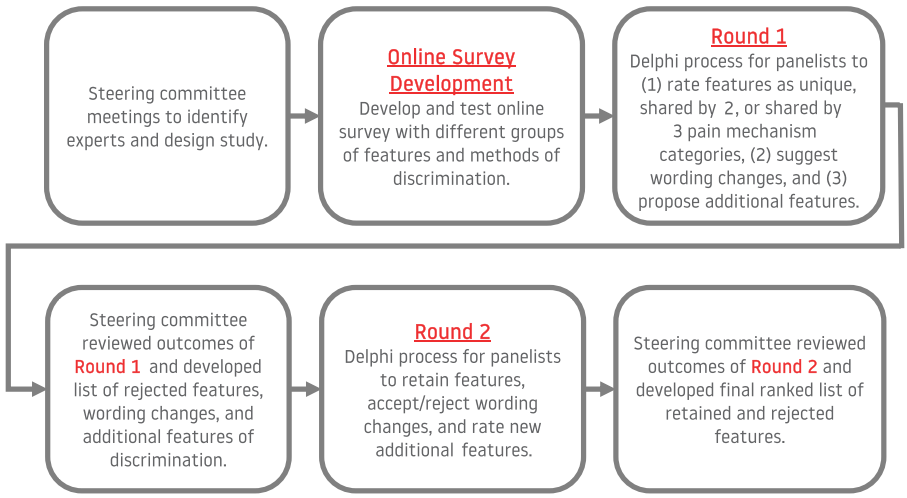

Figure 1. Flow diagram of the process of developing and conducting the Delphi process.

3. Results

Seventy-three potential panelists were identified and invited to participate in this consensus study. Fifty-five panelists accepted the invitation and 49 (89%) and 48 (87%) panelists provided responses to rounds 1 and 2 of this Delphi process, respectively.

3.1. Contributor demographics

The 49 panelists (average [SD] age; 55[10] years) included 29 male (56[11] years) and 20 female individuals (54[9] years) from 15 countries. Together they represented a total of 1291 years working in the pain field(average 26 years) and 8388 publications related to pain (average 171, median 102 [range 0-1000] publications related to pain). The country, role designation, and major discipline/research field related to pain are provided in **Table 2**.

3.2. Delphi round 1—quantitative results for features/assessment findings of pain mechanism categories

A total of 185 from 277 (67%) features that represented each of the main method groupings were identified as having potential to discriminate between pain mechanism categories (unique to 1 pain mechanism category or shared between 2 pain mechanism categories—identified by >40% of contributors). Regarding the method groupings, 124 features were identified from the clinical examination grouping (75% of 165), 33 features from quantitative sensory testing (83% of 40), 14 features from imaging and diagnostic testing (34% of 41), and 14 features from pain-type questionnaires (47% of 30). A total of 70 features were identified as unique for 1 category—17, 33, and 20 for nociceptive, neuropathic, and nociplastic pain, respectively (**Table 3**). A total of 115 features were identified as being shared between 2 categories—26, 19, and 75 for nociceptive + neuropathic, nociceptive + nociplastic, and neuropathic + nociplastic pain, respectively (**Table 4**). The remaining features (n = 92) did not meet any of the consensus criteria for inclusion. (supplemental digital content 1, http://links.lww.com/PAIN/B565).

Three steering committee meetings were held to discuss the panelists' feedback and suggestions. This generated a list of 18 wording changes to original features (changes to 56 features) and 15 additional features (for a complete list, see supplemental digital content 1, http://links.lww.com/PAIN/B565) to be included in round 2.

3.3. Delphi round 2—features/assessment findings to retain, wording changes, and additional features/assessment findings

From a total of 92 features/assessment findings that were not recommended for retention (failed to reach threshold agreement), only 1 feature was nominated to be retained by at least 15% of panelists. This feature was considered to be present in 1 pain mechanism category (neuropathic pain) after a change to wording based on panelist's feedback/comments and after gained consensus amongst the steering committee (**Table 3**). All wording changes were supported by >50% of panelists with some minor modifications suggested by contributors, which were approved by consensus amongst the steering committee. From the 15 additional features that were proposed in round 1, a total of 10 were retained as features with potential to discriminate between pain mechanism categories—5 unique to 1 category and 5 shared between 2 categories (**Tables 3 and 4**), and 5 features did not meet any of the cutoff criteria (supplemental digital content 1, http://links.lww.com/PAIN/B565).

With the refinements and additions from round 1, a final list was generated that included a total of 196 features to be retained. Of these features, 76 were unique to 1pain mechanism category (17, 37, and 22 for nociceptive, neuropathic, and nociplastic pain, respectively), 120 were shared between 2 pain mechanism categories (27, 20, and 78 for nociceptive + neuropathic, nociceptive + nociplastic, and neuropathic + nociplastic pain, respectively, in 5 cases, agreement was similar for 2 pairs of categories). When the retained features were categorized based on methods, clinical examination contained 134 features (74% of 180, unique: 61), quantitative sensory testing contained 34 features (83% of 41, unique: 2), imaging and diagnostic testing contained 14 features (34% of 41, unique: 7), and pain-type questionnaires contained 14 features (47% of 30, unique: 6).

3.3.1. Conflicting views on wording changes

Although most of the panelists (>50%) in round 2 agreed to the wording changes that had been suggested in round 1, conflicting views were expressed for some. Of note, there were differing opinions regarding the terms primary/local and secondary/

Table 2

Country of the panelist, role designation, and expertise.

Region of the Americas (19, 39%)	European region (17, 35%)		Western Pacific region (12, 24%)	African region
Country (n, %)				
The United States (16, 33%)	Denmark (5, 10%)	Germany (2, 4%)	Australia (9, 18%)	South Africa (1, 2%)
Brazil (2, 4%)	United Kingdom (4, 8%)	Netherlands (1, 2%)	Japan (1, 2%)	
Canada (1, 2%)	Belgium (2, 4%)	Ireland (1, 2%)	New Zealand (1, 2%)	
	Sweden (2, 4%)		Malaysia (1, 2%)	
Role designation (n, %)				
Clinical scientist/researcher (32, 65%)	Basic scientist (8, 16%)	Clinician (7, 14%)	Consumer (2, 4%)	
Discipline/major field (n, %)*				
Physiotherapy (14, 29%)	Basic science (9, 18%)	Neurology (4, 8%)	Occupational therapy (3, 6%)	Nursing (1, 2%)
Pain medicine (7, 14%)	*Musculoskeletal* (7, 14%)	Psychology (4, 8%)	Dentistry (2, 4%)	Rheumatology (1, 2%)
Rehabilitation medicine (5, 10%)	*Neuroscience* (5, 10%)	Anaesthesiology (3, 6%)	Chiropractic (1, 2%)	People with lived pain experience (2, 4%)
	Neuropharmacology (3, 6%)	Orthopaedic surgery (3, 6%)		
	Neurophysiology (2, 4%)			
	Neuropathic pain research (2, 4%)			

* The sum of disciplines/major fields exceeds the number of panelists because most nominated more than 1.
n, number.

remote hyperalgesia/allodynia in the quantitative sensory testing category. Some suggested that only the terms local and remote should be used, whereas others recommended that secondary should be described separately from remote because it specifically relates to areas adjacent to the primary area of pain. The steering committee resolved to use the terms local and remote with a note that remote excludes areas adjacent to the primary area of pain.

Regarding the feature proportional and direct relationship with aggravating factors, some suggest the use of the term direct is redundant because only a direct relationship can be proportional. Conflicting comments arose for the feature generalized pain hypersensitivity, which was reworded to generalized hypersensitivity. Some panelists suggested that it is not possible to be sensitive to pain because it is a response and not a stimulus. Other panelists suggested that hypersensitivity is restricted to nociceptive modalities and NOT to other modalities or precepts. Relating to pain location, the feature of a nondermatomal or non-neuroanatomic distribution of pain was challenged because the term non-neuroanatomic was considered by some to be unclear, whereas others suggested using not neuroanatomically plausible to be consistent with the NeuPSIG guideline's definition and criteria of neuropathic pain.[9,11,31] The final wording was finalised by the steering committee based on input from the panelists.

Finally, there was disagreement regarding the description of psychological features. Some suggested such terms are unclear because it is difficult to define whether features differ from a normal psychological response to the pain experience. There were some conflicting comments whether the psychological features have to be related to the pain experience or just have bearing on the pain experience (eg, post-traumatic stress disorder may not be related to the pain experience but might affect the pain experience). Both alternatives were included in the final wording.

4. Discussion

This Delphi study involved international experts from diverse disciplines and 2 people with lived pain experience to reach consensus on a list of features and assessment findings that could aid in discrimination between mechanisms that underlie pain experienced in the musculoskeletal system. From an original list of 277 features identified from systematic reviews and 15 suggested by panelists, 196 reached the a priori defined threshold for agreement. Pain maintained by neuropathic mechanisms comprised the greatest number of unique features (n = 37), followed by nociplastic (n = 22), and nociceptive (n = 17) mechanisms. The greatest number of features shared between 2 (but not 3) categories was identified between neuropathic and nociplastic mechanisms (n = 78), followed by nociceptive and neuropathic (n = 27) mechanisms, whereas nociceptive and nociplastic mechanisms shared the fewest (n = 17). Overall, the findings highlight that overlap of features presents an inherent challenge for discrimination between pain mechanism categories. Although neuropathic pain may be identified by a higher number of unique features, it shares a greater number of features with nociplastic pain. This reinforces that discrimination between pain mechanisms will depend on consideration of a combination of features.

4.1. Features that achieved top consensus for discrimination between pain mechanism categories

This study identified, for each pain mechanism category, the features that are most agreed upon by panelists. Of note, this does not indicate that these features are prevalent amongst individuals with a specific pain mechanism. Instead, it indicates if certain features were present, most panelists would identify a most likely pain mechanism category.

Unique features achieving greatest consensus for nociceptive pain were as follows: responsiveness to NSAIDs, 71%; signs of inflammation, 67%; and predictable pain recovery based on expected time of tissue recovery, 65%. These features are unsurprising as they likely present in an acute injury, with clear relevance of nociceptive mechanisms.[1] Similar features have been endorsed in other consensus studies.[28] Although the rationale that these features indicate a nociceptive mechanism is clear, they might be specific to the acute phase and not beyond

Table 3

Features identified as unique to 1 pain mechanism category.

				Contributor responses (%)								
	Feature/assessment finding	Method category (subcategory)		Nociceptive	Neuropathic	Nociplastic	Nociceptive + neuropathic	Nociceptive + nociplastic	Neuropathic + nociplastic	All nociceptive + neuropathic + nociplastic	None	Unsure
Nociceptive	Generally responsive to anti-inflammatory drugs (NSAIDs).	Response to drugs	W	71%			8%	12%		2%	2%	4%
	Signs of inflammation (redness, heat/warmth, tenderness, swelling).	Associated signs and symptoms		67%	2%		10%	10%		4%		6%
	Pain recovery or healing time predictable based on expected time of tissue recovery.	Recovery/healing period	W	65%			20%	2%		2%	8%	2%
	Proportional and direct relationship with aggravating factors (eg, provocative movements).	Aggravating factors	W	57%		2%	12%	4%		14%	8%	2%
	Consistent pain provocation by testing of specific movements (eg, specific movement tests for the shoulder, tests of temporomandibular joint motion)	Movement, joint, and functional testing	W	53%	2%		22%	4%		6%	2%	10%
	Localised distribution of pain.	Pain location		51%			39%	2%		6%		2%
	NO generalised hypersensitivity.	Pain location	W	51%	2%		27%			6%	6%	8%
	Findings from imaging of body regions of potential relevance to the pain experience.	Imaging/radiography	W	51%			22%			8%	10%	8%
	Mechanical testing shows a clear, consistent, and proportional pattern of pain or symptom provocation.	Movement, joint, and functional testing		49%		2%	22%	4%		4%	8%	10%
	Generally responsive to tissue-based treatments (eg, manual therapy, massage, acupuncture, heat/cold, removal of tissue pathology, occlusal splints).	Response to physical treatments	W	47%			12%	12%	2%	22%		4%
	Consistently provoked by specific postures.	Aggravating factors		45%		4%	27%	6%		8%	2%	8%
	Generally NOT responsive to anticonvulsants.	Response to drugs	W	45%				16%		8%	6%	24%
	Joint testing consistently demonstrates painful response.	Movement, joint, and functional testing		45%		2%	4%	16%		8%	6%	18%
	ABSENCE of autonomic symptoms and/or signs.	Associated signs and symptoms		43%	2%	2%	4%	4%		8%	10%	27%
	Consistently provoked by specific movements.	Aggravating factors		41%			29%	10%		20%		
	Generally NOT responsive to antidepressants.	Response to drugs	W	41%		2%	4%			8%	16%	29%
	Below cutoff (≤12).	Neuropathic questionnaires (Modified PainDETECT)		41%			2%	10%		2%	10%	35%

(*continued on next page*)

Table 3 (*continued*)

	Feature/assessment finding	Method category (subcategory)		Contributor responses (%)								
				Nociceptive	Neuropathic	Nociplastic	Nociceptive + neuropathic	Nociceptive + nociplastic	Neuropathic + nociplastic	All nociceptive + neuropathic + nociplastic	None	Unsure
Neuropathic	Dermatomal or peripheral nerve distribution of pain.	Neurological testing		2%	86%		4%			2%		6%
	Demonstrate evidence of lesion or disease of nervous system.	Imaging/radiography			86%		2%				4%	8%
	Dermatomal or peripheral nerve distribution of pain.	Pain location			84%		8%		4%	2%		2%
	Sensory deficits (eg, numbness) in dermatomal pattern.	Associated signs and symptoms	A		79%		4%		6%	2%	2%	6%
	Evidence of damage/disease to the nervous system.	Neuroimaging/electrophysiological testing (Electroneuromyography)			78%		2%		2%		4%	14%
	Demonstrates evidence of lesion or disease of nervous system.	Neuroimaging/electrophysiological testing (Neuroimaging [eg, CT, MRI])			73%		10%		4%	2%	4%	6%
	Hypoaesthesia.	Associated signs and symptoms			69%				20%	4%		6%
	Abnormal nerve conduction velocity.	Neuroimaging/electrophysiological testing (Electroneuromyography)			69%		4%		8%		4%	14%
	Electric shock-like, lightning.	Subjective descriptors			67%		2%		20%	2%	2%	6%
	Negative symptoms (eg, numbness, hypoalgesia).	Neurological testing			67%		2%		18%	4%	2%	6%
	Sensory deficits (eg, numbness) relevant to territory of innervation of injured peripheral nerve or central somatosensory projection area relevant to lesion or disease of CNS.	Associated signs and symptoms	W		61%		2%		24%	8%		4%
	Altered or absent deep tendon reflexes.	Neurological testing		2%	61%				4%		2%	31%
	Pins and needles.	Associated signs and symptoms			57%				33%	4%		6%
	Prickling.	Associated signs and symptoms			57%	2%			31%	2%	2%	6%
	Itchy.	Associated signs and symptoms		2%	57%	2%	4%		10%	6%	6%	12%
	Provoked by movements that load or compress neural tissue.	Aggravating factors		4%	55%		12%		8%	12%	2%	6%
	Formication (sensation that resembles that of small insects crawling on or under the skin when there is nothing there).	Subjective descriptors			55%	8%			12%	2%	8%	14%
	Hypoalgesia.	Associated signs and symptoms			55%	6%	2%		6%	4%	8%	18%
	Altered deep tendon reflexes.	Associated signs and symptoms			55%		6%	2%	10%		2%	24%
	Tingling.	Associated signs and symptoms			53%				35%	6%	2%	4%
	Increased threshold/hypoalgesia.	Mechanical testing (LOCAL mechanical/pressure pain threshold OR NOXIOUS touch/pressure)			53%	2%			4%	4%	20%	16%
	Increased threshold/hypoaesthesia.	Mechanical testing (LOCAL mechanical detection threshold OR NON-NOXIOUS touch/pressure)			53%		2%		8%	6%	18%	12%
	Decreased deep tendon reflexes.	Neurological testing	A		52%	4%			4%	2%	8%	29%
	Fire-like.	Subjective descriptors			49%	2%	4%		20%	6%	4%	14%
	Cool, cold, freezing.	Subjective descriptors			49%	2%	2%		20%	4%	4%	18%
	Crawling.	Associated signs and symptoms		2%	49%	8%			16%	4%	2%	18%
	Positive findings (eg, pain provocation, Tinel sign—pins and needles).	Nerve provocation testing (palpation/tapping)			49%		4%		18%	10%	2%	16%
	Myotomal muscle atrophy.	Associated signs and symptoms	A	2%	48%		6%			4%	6%	33%
	Shooting, jumping, flashing.	Subjective descriptors		2%	47%		6%		20%	8%	4%	12%
	Phantom pain.	Other pain qualities			47%	16%	2%		14%	4%	2%	14%
	Above cutoff (≥4).	Neuropathic questionnaires (Douleur Neuropathique 4 [DN4])			43%				20%		2%	35%
	Above cutoff (≥0).	Neuropathic questionnaires (neuropathic pain questionnaire (NPQ))			43%				22%		2%	33%
	Tingling, itchy, smarting, stinging.	Subjective descriptors		2%	41%	4%	2%		20%	12%	6%	12%
	Hot, burning, scalding, searing.	Subjective descriptors			41%	2%	4%		27%	14%	4%	8%
	Muscle spasticity.	Associated signs and symptoms		4%	41%		4%	2%	8%	4%	20%	16%
	Skin biopsy demonstrates reduced intraepidermal nerve fiber density.	Other diagnostic tests			41%				18%		8%	33%
	Motor deficits (eg, weakness) in a neuroanatomically plausible distribution.	Neurological testing	R, W 15%	4%	20%		10%		10%	41%	2%	12%

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Table 3 (*continued*)

	Feature/assessment finding	Method category (subcategory)		Contributor responses (%)								
				Nociceptive	Neuropathic	Nociplastic	Nociceptive + neuropathic	Nociceptive + nociplastic	Neuropathic + nociplastic	All nociceptive + neuropathic + nociplastic	None	Unsure
Nociplastic	Diffuse, widespread, or poorly localised distribution of pain.	Pain location				82%		6%	10%			2%
	Generalised hypersensitivity.	Pain location	W		2%	71%			12%	10%		4%
	Multiple somatic symptoms (eg, fatigue, memory difficulties, concentration difficulties, sleep disturbances, mood disturbances).	Associated signs and symptoms				65%			12%	12%	6%	4%
	Varying distribution of pain.	Pain location				59%		4%	18%	8%	2%	8%
	Presence of hypersensitivity to stimuli (eg, pressure, temperature, sound, odor, taste, and light).	Associated signs and symptoms	W		2%	57%		2%	22%	8%	4%	4%
	Generally NOT responsive to local anaesthetics.	Response to drugs	W			55%		2%	14%	2%	12%	14%
	Variability or no consistency in descriptors.	Subjective descriptors		2%		55%			8%	10%	8%	16%
	Generally NOT responsive to surgery.	Response to physical treatments	W			53%	2%		20%	8%	2%	14%
	Inconsistent, confusing, and ambiguous responses and findings to clinical tests that vary over sessions.	Other pain qualities				53%			22%	4%	4%	16%
	NO findings from imaging of body regions of potential relevance to the pain experience.	Imaging/radiography	W			53%		12%	4%	18%	6%	6%
	Positive findings (no cutoff proposed).	Other questionnaires (Fibromyalgia criteria and severity Scales [FCSS])				53%		2%	4%	2%	4%	35%
	Generally NOT responsive to peripheral nerve block (where relevant).	Response to drugs	W	4%		51%		10%	10%	4%	12%	8%
	Positive findings (no cutoff proposed).	Other questionnaires (Revised Fibromyalgia Impact Questionnaire [RFIQ])				51%		2%	2%	2%	4%	39%
	Mechanical testing shows a disproportionate, inconsistent, nonmechanical pattern of pain or symptom provocation.	Movement, joint, and functional testing				49%			24%	14%	2%	10%
	Above cutoff (≥40).	Central sensitisation questionnaires (central sensitization Inventory (CSI))				49%			18%	2%	8%	22%
	Multisite pain (3 or more regions)	Pain location	A			46%		13%	13%	25%		4%
	Nonspecific neurological findings or ABSENCE of clear findings.	Neurological testing				45%		16%	6%	6%	6%	20%
	Pain experienced in a nondermatomal or non-neuroanatomic distribution in a body region.	Pain location	W		2%	43%		18%	14%	16%		6%
	More concern for bodily function.	Associated signs and symptoms		4%		43%		2%	4%	8%	6%	33%
	Spread of pain over time to new body sites/areas.	Pain location	A			42%		4%	23%	25%		6%
	History of failed, variable, or unpredictable response to interventions.	Recovery/healing period				41%			33%	16%	2%	8%
	Disproportionate or abnormal reaction during and after the patient's assessment and/or treatment.	Other pain qualities			2%	41%			31%	14%	2%	10%

Features are ranked by percent of contributors in descending order. A = additional features proposed by contributors. W = wording changes proposed by contributors. R = retained features where >15% of contributes indicated that the feature should be retained with generally consistent rationales/reasoning. The corresponding percent of contributors is included.

Table 4

Features identified as shared between 2 pain mechanism categories.

				Contributor responses (%)								
	Feature/assessment finding	**Method category (subcategory)**		**Nociceptive**	**Neuropathic**	**Nociplastic**	**Nociceptive + neuropathic**	**Nociceptive + nociplastic**	**Neuropathic + nociplastic**	**All nociceptive + neuropathic + nociplastic**	**None**	**Unsure**
Nociceptive + neuropathic pain	Generally responsive to surgery.	Response to physical treatments	W	35%	2%		39% (76%)			4%	8%	12%
	Movements decompressing structure provide pain relief.	Movement, joint, and functional testing		12%	22%		27% (61%)		2%	6%	4%	27%
	Normal threshold/absence of hyperalgesia in areas remote to the area of primary pain.	Mechanical testing (REMOTE mechanical/pressure pain threshold OR NOXIOUS touch/pressure)	W	37%	2%		18% (57%)	2%	2%	2%	20%	16%
	Positive response.	Diagnostic anaesthetic injections/ blocks (sensory/motor spinal blocks)		8%	14%		33% (55%)			12%	6%	27%
	Localised muscle atrophy.	Associated signs and symptoms	A	4%	23%		27% (54%)	2%	4%	21%	4%	15%
	Intermittent or transient pain.	Other pain qualities		20%	8%	2%	24% (53%)	2%	10%	24%	2%	6%
	Generally response to opioid analgesics (eg, fentanyl).	Response to drugs	W	27%	2%	2%	22% (51%)	6%	4%	27%	2%	8%
	Generally responsive to peripheral nerve block (where relevant).	Response to drugs	W	10%	22%		49%			12%		6%
	Sharp, cutting, lacerating.	Subjective descriptors		14%	27%	2%	8% (49%)	6%	6%	22%	4%	10%
	Knife-like.	Subjective descriptors		6%	29%		14% (49%)	4%	10%	20%	4%	12%
	Efficient conditioned pain modulation (increased pain threshold).	Pain modulation testing (conditioned pain modulation [eg, pressure cuff, cold pressor test])		39%	2%	2%	8% (49%)		2%	8%	22%	16%
	Generally responsive to local anaesthetics (eg, lidocaine).	Response to drugs	W	29%	6%		47%		2%	14%		2%
	Unilateral distribution of pain.	Pain location		10%	6%	4%	31% (47%)	2%	2%	27%	4%	14%
	Minimal or absent psychological features, disturbances, or behaviours related to the pain experience or having bearing on the pain experience.	Psychological assessment	W	24%	2%		20% (47%)			14%	27%	12%
	Primary hyperalgesia.	Other pain qualities		16%	18%		12% (47%)	2%	20%	24%	2%	4%
	Normal threshold/absence of heat hyperalgesia in areas remote to the area of primary pain.	Heat testing (REMOTE heat pain threshold OR NOXIOUS heat application)	W	33%		2%	14% (47%)		6%	10%	12%	22%
	Nonenhanced temporal summation.	Pain modulation testing (temporal summation [eg, repetitive mechanical/ heat/cold/electrical stimuli using monofilaments, thermode, or electrodes])		39%	4%	2%	2% (45%)		4%	6%	31%	12%
	Below cutoff (<40).	Central sensitisation questionnaires (central sensitization inventory [CSI])		24%			20% (45%)		2%	4%	18%	31%
	Stimulus-dependent or evoked pain.	Other pain qualities		29%			16% (45%)	2%	6%	39%		8%
	Normal threshold/absence of cold hyperalgesia in areas remote to the area of primary pain.	Cold testing (REMOTE cold pain threshold OR NOXIOUS cold application)	W	29%	4%	2%	12% (45%)	2%	4%	8%	4%	35%
	Referred pain or distal pain radiation.	Pain location		2%	27%	4%	14% (43%)	8%	12% (43%)	29%		4%
	Stretching.	Subjective descriptors		29%	8%		6% (43%)	8%		12%	10%	27%
	Normal TPD threshold (normal tactile acuity).	Higher sensory function testing (2-point discrimination testing)		35%	4%		4% (43%)	8% (43%)		12%	14%	22%
	Throbbing, pulsing/pulsating, pounding, beating, flickering quivering.	Subjective descriptors		18%	16%	4%	6% (41%)	10%	6%	24%	4%	10%
	Jabbing.	Subjective descriptors		12%	20%	2%	8% (41%)	6%	6%	14%	6%	24%
	Muscle atrophy.	Associated signs and symptoms		6%	12%	2%	22% (41%)		10%	22%	6%	18%

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Table 4 (*continued*)

				Contributor responses (%)								
	Feature/assessment finding	**Method category (subcategory)**		**Nociceptive**	**Neuropathic**	**Nociplastic**	**Nociceptive + neuropathic**	**Nociceptive + nociplastic**	**Neuropathic + nociplastic**	**All nociceptive + neuropathic + nociplastic**	**None**	**Unsure**
	Positive findings (eg, pain provocation/ muscle spasm with decreased range of movement).	Neurodynamic testing		10%	24%	2%	6% (41%)		10%	18%	2%	27%
Nociceptive + nociplastic	Arthralgic (joint) and/or myalgic (muscle) pain.	Subjective descriptors	W	35%		6%		31% (71%)	2%	6%		20%
	Normal deep tendon reflexes.	Neurological testing		20%		4%		37% (61%)		10%	4%	24%
	Consistently provoked by localised pressure (eg, palpation).	Aggravating factors		37%		6%	18%	16% (59%)	2%	20%		
	Sensory abnormalities in localized nondermatomal distribution.	Neurological testing		16%	18%	27%	4%	14% (57%)	2%	4%	2%	12%
	ABSENCE of negative symptoms.	Neurological testing		31%		4%		20% (55%)		8%	22%	14%
	Myofascial trigger points.	Mechanical testing (LOCAL mechanical/pressure pain threshold OR NOXIOUS touch/pressure)		16%		16%		22% (55%)	4%	12%	8%	20%
	Below cutoff (<19).	Neuropathic questionnaires (PainDETECT)		39%			2%	16% (55%)		2%	10%	31%
	Negative findings (absence of abnormal findings).	Nerve provocation testing (palpation/ tapping)		35%	2%	2%		16% (53%)		4%	8%	33%
	Dull, sore, hurting, aching, heavy.	Subjective descriptors		16%		4%	4%	33% (53%)	2%	29%	4%	8%
	Reduced joint range of motion due to stiffness.	Associated signs and symptoms		39%			2%	14% (53%)		29%	4%	12%
	ABSENCE of neurological findings.	Neurological testing	A	4%		4%		40% (48%)		13%	4%	35%
	Negative findings (absence of abnormal findings).	Neurodynamic testing		18%		14%		14% (47%)		8%	14%	31%
	Provoked by all activity/movements.	Aggravating factors		8%		29%		10% (47%)	12%	14%	18%	8%
	Aggravated by fatigue or overexertion.	Aggravating factors				31%		14% (45%)	10%	39%	2%	4%
	Predisposed by previous experiences including emotional and/or physical trauma.	Aggravating factors				37%		8% (45%)	8% (45%)	39%	4%	4%
	Tender, taut, rasping, splitting.	Subjective descriptors		22%	4%	4%	6%	16% (43%)	4%	16%	6%	20%
	ABSENCE of positive symptoms.	Neurological testing		29%		2%	4%	12% (43%)		8%	31%	14%
	High Waddell score.	Psychological assessment		4%		35%		2% (41%)	6% (41%)	12%	4%	37%
	Inconsistency between structural changes and pain.	Imaging/radiography		2%		29%	4%	10% (41%)	12% (41%)	29%	8%	6%

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Table 4 (*continued*)

				Contributor responses (%)								
	Feature/assessment finding	**Method category (subcategory)**		**Nociceptive**	**Neuropathic**	**Nociplastic**	**Nociceptive + neuropathic**	**Nociceptive + nociplastic**	**Neuropathic + nociplastic**	**All nociceptive + neuropathic + nociplastic**	**None**	**Unsure**
Neuropathic + nociplastic	NOT consistently provoked by specific movements, activity, or changes in position or posture (pain independent of these factors).	Aggravating factors		2%	14%	39%			27% (80%)	4%	8%	6%
	Signs and/or symptoms of autonomic dysfunction or vasomotor instability (trophic abnormalities eg, shiny atrophic skin, cracking or excess growth of nails, bone atrophy, hair loss; sudomotor abnormalities eg, sweating, swelling, edema; vasomotor abnormalities eg, skin color or temperature changes).	Associated signs and symptoms	**W**		37%	14%	2%		29% (80%)	4%	2%	12%
	Decreased threshold/allodynia in areas remote to the area of primary pain.	Mechanical testing (REMOTE mechanical detection threshold OR NON-NOXIOUS touch/pressure)	**W**		10%	39%			31% (80%)	6%		14%
	Pain and/or symptoms are disproportionate or in excess to the nature and extent of the pathological changes or inciting injury.	Aggravating factors			2%	39%		2%	37% (78%)	16%	2%	2%
	Paroxysmal episodes or sudden pain attacks.	Other pain qualities			31%	8%	2%		35% (73%)	8%	2%	14%
	Above cutoff (≥19).	Neuropathic questionnaires (PainDETECT)			39%				35% (73%)		2%	24%
	Mind of its own, bizarre, indescribable, ineffable.	Subjective descriptors			10%	37%			24% (71%)	6%	8%	14%
	Secondary allodynia (adjacent to primary area of pain).	Other pain qualities	**W**	2%	20%	20%	8%		29% (69%)	12%		8%
	Exhibits a nonlinear relationship between nociception and pain intensity (or stimulus and response).	Other pain qualities		2%	6%	29%		2%	35% (69%)	12%	4%	10%
	Latent or persistent pain after stimulus.	Other pain qualities		4%	10%	18%	2%		37% (65%)	20%	2%	6%
	Decreased threshold/heat hyperalgesia in areas remote to the area of primary pain.	Heat testing (REMOTE heat pain threshold OR NOXIOUS heat application)	**W**		8%	31%			27% (65%)		10%	24%
	Decreased acuity, mislocalisation of stimuli and/or sensory neglect.	Higher sensory function testing (tactile acuity test)			18%	20%			27% (65%)	4%	6%	24%
	Above cutoff (≥12).	Neuropathic questionnaires (Leeds assessment of neuropathic symptoms and signs (LANSS))			37%				29% (65%)		2%	33%
	Generally NOT responsive to tissue-based treatments.	Response to physical treatments	**W**	2%	16%	20%		2%	27% (63%)	4%	22%	6%
	Pricking, lancinating, stabbing, drilling, boring.	Subjective descriptors		2%	37%	2%	4%		24% (63%)	14%	4%	12%
	Hyperaesthesia.	Associated signs and symptoms			27%	8%			29% (63%)	24%	2%	10%
	Positive symptoms (eg, burning, paraesthesias, hyperalgesia, allodynia).	Neurological testing			24%		2%		39% (63%)	31%		4%
	Decreased threshold/hyperalgesia in areas remote to the area of primary pain.	Mechanical testing (REMOTE mechanical/pressure pain threshold OR NOXIOUS touch/pressure)	**W**	2%	2%	35%		4%	27% (63%)	12%		18%

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Table 4 (*continued*)

Feature/assessment finding	Method category (subcategory)		Contributor responses (%)								
			Nociceptive	Neuropathic	Nociplastic	Nociceptive + neuropathic	Nociceptive + nociplastic	Neuropathic + nociplastic	All nociceptive + neuropathic + nociplastic	None	Unsure
Above cutoff (>12).	Neuropathic questionnaires (Modified PainDETECT)			29%		2%		35% (63%)	2%	2%	31%
Positive findings (no cutoff proposed).	Neuropathic questionnaires (neuropathic pain Scale [NPS])			39%				24% (63%)		2%	35%
Secondary hyperalgesia (adjacent to primary area of pain).	Other pain qualities	W	2%	12%	20%	4%		29% (61%)	22%	2%	8%
Decreased threshold/heat allodynia in areas remote to the area of primary pain.	Heat testing (REMOTE heat detection threshold OR NON-NOXIOUS heat application)	W		6%	29%	2%	2%	27% (61%)	4%	12%	18%
Above cutoff (≥12).	Neuropathic questionnaires (Self-Administered LANSS [s-LANSS])			35%				27% (61%)	2%	2%	35%
Punishing, gruelling, cruel, vicious, killing.	Subjective descriptors			2%	33%			24% (59%)	20%	6%	14%
Primary allodynia.	Other pain qualities		10%	33%	4%	10%	2%	22% (59%)	10%		8%
Inefficient conditioned pain modulation (unchanged or decreased pain threshold).	Pain modulation testing (Conditioned pain modulation [eg, pressure cuff, cold pressor test])		4%	2%	24%		6%	33% (59%)	14%	2%	14%
Positive findings (no cutoff proposed).	Neuropathic questionnaires (neuropathic pain symptom Inventory [NPSI])			33%				27% (59%)		2%	39%
Increased TPD threshold (decreased tactile acuity or hypoaesthesia).	Higher sensory function testing (2-point discrimination testing)			22%	8%	2%		27% (57%)	8%	10%	22%
Generally responsive to anticonvulsants (eg, gabapentin, pregabalin).	Response to drugs	W		35%		2%		55%	6%		2%
Decreased threshold/hyperaesthesia.	Mechanical testing (LOCAL mechanical detection threshold OR NON-NOXIOUS touch/pressure)		2%	18%	6%	2%	2%	31% (55%)	27%	4%	8%
Stimulus-independent or spontaneous pain.	Other pain qualities		2%	4%	10%	2%	2%	53%	20%		6%
Decreased threshold/vibrational allodynia.	Vibration testing (LOCAL vibration detection threshold OR tuning fork application)			20%	14%	2%		18% (53%)	4%	20%	20%
Increased threshold/cold allodynia in areas remote to the area of primary pain.	Cold testing (REMOTE cold detection threshold OR NON-NOXIOUS cold application)	W	2%	10%	33%	2%		10% (53%)		8%	35%
Altered body perception.	Higher sensory function testing (Left-right discrimination task)			8%	29%			16% (53%)	4%	8%	35%
Demonstrates increased or altered activity in pain-processing brain regions in response to non-noxious stimuli.	Neuroimaging/electrophysiological testing (fMRI)				24%			29% (53%)	27%	4%	16%
Abnormal somatosensory-evoked potentials (SEPs).	Neuroimaging/electrophysiological testing (Electroencephalography [EEG])			22%	6%		2%	24% (53%)	8%	2%	35%
Sensory deficits (eg, numbness) in nondermatomal pattern.	Associated signs and symptoms	A		10%	33%		13%	8% (52%)	8%	13%	15%
Pain persists beyond expected tissue healing period or pathology recovery times.	Recovery/healing period				33%			51%	14%	2%	
Decreased threshold/allodynia localised to the area of primary pain.	Mechanical testing (LOCAL mechanical detection threshold OR NON-NOXIOUS touch/pressure)	W	4%	16%	4%	4%	2%	31% (51%)	31%	2%	6%

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Table 4 (*continued*)

Feature/assessment finding	Method category (subcategory)		Contributor responses (%)								
			Nociceptive	Neuropathic	Nociplastic	Nociceptive + neuropathic	Nociceptive + nociplastic	Neuropathic + nociplastic	All nociceptive + neuropathic + nociplastic	None	Unsure
Decreased threshold/heat allodynia localised to the area of primary pain.	Heat testing (LOCAL heat detection threshold OR NON-NOXIOUS heat application)	W	2%	14%	10%	2%	2%	27% (51%)	14%	8%	20%
Greater pain sensitvity to cold/cold hyperalgesia localised to the area of primary pain.	Cold testing (LOCAL cold pain threshold OR NOXIOUS cold application)	W	2%	18%	6%	2%	2%	27% (51%)	12%	6%	24%
Increased threshold/cold hyperalgesia in areas remote to the area of primary pain.	Cold testing (REMOTE cold pain threshold OR NOXIOUS cold application)	W	2%	8%	27%	4%	2%	16% (51%)		10%	31%
Altered body perception.	Higher sensory function testing (graphesthesia tests)			8%	22%	2%	2%	20% (51%)		6%	39%
Greater sensitvity to cold/cold allodynia localised to the area of primary pain.	Cold testing (LOCAL cold detection threshold OR NON-NOXIOUS cold application)	W		16%	10%	4%	2%	24% (51%)	8%	6%	29%
Temporal summation facilitation at remote areas	Pain modulation testing (Temporal summation [eg, repetitive mechanical/heat/cold/electrical stimuli using monofilaments, thermode, or electrodes])	A		4%	31%		4%	15% (50%)	15%	2%	29%
Generally NOT responsive to anti-inflammatory drugs (NSAIDs).	Response to drugs	W		18%	16%			49%	6%	6%	4%
Generally responsive to antidepressants (eg, duloxetine, amitriptyline).	Response to drugs	W		4%	14%			49%	29%		4%
Generally NOT responsive to opioid analgesics.	Response to drugs	W	2%	6%	24%			18% (49%)	10%	18%	20%
Symmetrical or bilateral distribution of pain.	Pain location			8%	18%	12%	6%	22% (49%)	12%	4%	16%
Spreading, radiating, penetrating, piercing.	Subjective descriptors			24%	4%	4%	4%	20% (49%)	31%	4%	8%
Intolerable sensations.	Subjective descriptors			14%	14%			20% (49%)	33%	8%	10%
Associated with high levels of functional disability.	Associated signs and symptoms		2%		27%		2%	22% (49%)	37%		10%
Abnormal laser-evoked potentials (LEPs).	Neuroimaging/electrophysiological testing (Electroencephalography [EEG])			16%	6%		2%	27% (49%)	8%	2%	39%
Abnormal changes, heightened response, or expanded receptive field.	Neuroimaging/electrophysiological testing (nociceptive withdrawal reflex)		2%	6%	20%	4%	2%	22% (49%)	18%	2%	22%
Nagging, nauseating, agonizing, dreadful, torturing.	Subjective descriptors			2%	27%			18% (47%)	33%	6%	14%
Temporal summation or wind-up/hyperpathia (abnormally painful reaction to a stimulus, especially a repetitive stimulus, as well as an increased threshold).	Other pain qualities			10%	20%			47%	20%	2%	
Decreased threshold/cold hypoaesthesia.	Cold testing (LOCAL cold detection threshold OR NON-NOXIOUS cold application)			35%	4%	2%		8% (47%)	4%	10%	37%
Decreased threshold/vibrational hyperaesthesia.	Vibration testing (LOCAL vibration detection threshold OR tuning fork application)			20%	14%	2%		12% (47%)	8%	18%	24%

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Table 4 (*continued*)

Feature/assessment finding	Method category (subcategory)		Contributor responses (%)								
			Nociceptive	Neuropathic	Nociplastic	Nociceptive + neuropathic	Nociceptive + nociplastic	Neuropathic + nociplastic	All nociceptive + neuropathic + nociplastic	None	Unsure
Increased threshold/vibrational hypoaesthesia.	Vibration testing (LOCAL vibration detection threshold OR tuning fork application)			39%		2%		8% (47%)	6%	14%	31%
Decreased threshold/vibrational allodynia in areas remote to the area of primary pain.	Vibration testing (REMOTE vibration detection threshold OR tuning fork application)	W		6%	27%			12% (45%)		22%	33%
Aftersensations or sensory aftereffects.	Other pain qualities			18%	4%	2%		45%	14%	2%	14%
Generally responsive to NMDA antagonists (eg, ketamine, memantine).	Response to drugs	W		4%	14%	8%		27% (45%)	12%	8%	27%
Fearful, frightful, terrifying.	Subjective descriptors			4%	27%	2%		14% (45%)	31%	6%	16%
Increased threshold/heat hypoaesthesia.	Heat testing (LOCAL heat detection threshold OR NON-NOXIOUS heat application)			37%		4%		8% (45%)	2%	18%	31%
Sickening, suffocating.	Subjective descriptors		2%	4%	24%		2%	16% (45%)	22%	8%	20%
Disproportionate, unpredictable pattern of pain provocation in response to multiple aggravating factors.	Aggravating factors			2%	43%			43%	6%	6%	
Increased deep tendon reflexes.	Neurological testing	A		31%	6%		2%	4% (42%)	2%	19%	35%
Enhanced temporal summation (wind-up).	Pain modulation testing (temporal summation [eg, repetitive mechanical/heat/cold/electrical stimuli using monofilaments, thermode, or electrodes])			4%	18%	2%	2%	41%	20%	4%	8%
Constant, continuous, or persisting pain even at rest.	Other pain qualities		2%	6%	6%	4%	4%	41%	29%	2%	6%
Presence of pain or worse pain during the night or disrupted sleep.	Aggravating factors		4%	8%	8%	4%	8%	24% (41%)	27%	2%	14%
Tight, numb, drawing, squeezing, tearing.	Subjective descriptors		4%	18%	8%	6%	4%	14% (41%)	22%	4%	18%
Wretched, blinding.	Subjective descriptors			4%	24%			12% (41%)	14%	12%	33%
Decreased threshold/vibrational hyperaesthesia in areas remote to the area of primary pain.	Vibration testing (REMOTE vibration detection threshold OR tuning fork application)	W		6%	22%			12% (41%)		24%	35%
Demonstrates increases in cortical event-related potential amplitudes (eg, increases in cortical pin prick-related potential amplitudes).	Neuroimaging/electrophysiological testing (electroencephalography [EEG])			2%	12%	2%		27% (41%)	16%	6%	35%

Features are ranked by percent of contributors in descending order. When a feature failed to reach the cutoff for Unique (present in 1 pain mechanism category) or Shared by 2, the combination of Unique and Shared by 2 pain mechanism categories were summed and are shown in brackets. If 2 pairs of Shared by 2 or the combination of Unique and Shared by 2 achieved the cutoff >40%, only the greater percentage is reported in brackets. If the values are equal, then both are reported in brackets. A = additional features proposed by contributors. W = wording changes proposed by contributors.

with ongoing nociceptive input. Absence of these features is unlikely to exclude nociceptive pain.

For neuropathic pain, unique features achieving greatest consensus related to nerve damage (eg, neurologically plausible distribution of pain, characteristic signs/symptoms such as numbness, and diagnostic tests confirming nerve damage). These findings are unsurprising and consistent with the NeuPSIG criteria[9,11] and definition[31] of neuropathic pain. When present, these findings can support the identification of neuropathic pain; however, if these cardinal signs are less definitive or absent, this would not exclude neuropathic pain because it presents variably.[31]

For nociplastic pain, the most agreed unique features were as follows: diffuse, widespread, or poorly localised pain, 82%; generalised hypersensitivity, 71%; and multiple somatic symptoms (eg, fatigue, memory/concentration/sleep disturbances), 65%. These features align with presentations that could be explained by sensitisation of central pain mechanisms and thus consistent with altered nociception/abnormal processing (eg, hypersensitivity and widespread pain[20]), which is included in the IASP definition[19] and the recently developed criteria/grading system for nociplastic pain.[18]

4.2. Unique or shared features of pain mechanism categories

Many features were identified as shared by 2 pain mechanism categories. Whether a feature is unique to 1 category or shared by 2 was the most common divergence of opinion amongst panelists. Of note, although a feature shared between 2 categories could not provide definitive identification of a likely category, it could aid in differentiation of those 2 categories from the third.

The potential for multiple mechanisms to coexist within an individual is likely to explain some divergence in opinion, particularly regarding features that are unique to, or shared by, neuropathic and nociplastic pain. It was common for features, typically considered to reflect sensitisation of central mechanisms (eg, remote/widespread mechanical hyperalgesia and paroxysmal pain attacks[28]), to be identified as shared by nociplastic and neuropathic pain. Whether these features primarily manifest from neuropathic pathology or reflect the addition of nociplastic mechanisms on the foundation of a neuropathic condition is likely to explain this divergence in opinion. It is plausible, if not universal, that conditions that begin as a consequence of neuropathic or nociceptive mechanisms, with some potential sensitisation of central mechanisms, progress to a greater contribution from nociplastic mechanisms. The prevalence of mixed mechanisms[12,30] is likely to explain why many experts consider some features to indicate both neuropathic and nociceptive pain. Any tool to discriminate between pain mechanism categories should aim to identify which category(-ies) contribute most to an individual's current presentation, rather than expecting to identify only 1.

4.3. Comparison with previous methods to discriminate between pain mechanism categories

Most features identified as unique to a pain mechanism category in this study agree with previous consensus studies.[23,28] For reasons outlined in the preceding section, some discrepancies primarily relate to features considered to be shared by 2 categories rather than unique to 1. Some features were supported by some panelists but not sufficient to reach the agreement threshold.

Some specific divergences require additional consideration. One issue relates to the criterion defined by Nijs et al.[23] in their mechanism-based classification of lower back pain that discriminates nociplastic from nociceptive mechanisms based on pain that is disproportionate to the nature and extent of injury or pathology. This is in general agreement with views expressed by panelists in this study, who agreed (53%) that no findings from imaging of body regions of potential relevance to the pain experience was a feature of nociplastic pain. However, Nijs et al.[23] argued that it is necessary to assess the patient's amount of injury, pathology, and objective dysfunctions capable of generating nociceptive input using imaging and clinical examination. Whether identification of a nociceptive source is necessary for confirmation of a nociceptive pain mechanism category is not yet clear.

Subtle distinction between presence and absence of a feature is relevant for comparison with the classification proposed by Smart et al.,[28] which emphasises a strong association between maladaptive psychological factors in the presentation of sensitised central pain mechanisms (ie, nociplastic mechanism). Agreement amongst panelists was not sufficient for the presence of psychological factors to be considered a unique feature of nociplastic pain. Rather, the absence of significant psychological features (ie, minimal or absent psychological features …) was agreed to suggest the presence of nociceptive or neuropathic mechanisms. Furthermore, in a consensus project conducted by Smart et al.[28], night pain/disrupted sleep was considered characteristic of nociplastic pain, and pain of moderate to high severity was considered to discriminate neuropathic pain. However, these features were considered by panelists in this study to be shared by all 3 pain mechanism categories.

4.4. Consideration of findings for the development of a tool to differentiate pain mechanism categories

A goal of this work is to set a foundation for developing a multidimensional tool to aid in the discrimination between pain mechanism categories in clinical practice and research. Several issues will be critical to consider. First, no single feature will be sufficient to discriminate between pain mechanism categories because many features are shared between 2 categories, and those that could provide more definitive identification of mechanisms are not present in all individuals with a specific category. Second, features may depend on the time course of the condition because the relative contribution of mechanisms is likely to change.[1] Third, the wording used in this study to describe some features will potentially require additional explanation to aid interpretation and utility. Fourth, challenges arise for features for which there are not well-defined methods or biomarkers (eg, genetics, biological markers, and brain imaging). Fifth, feasibility, accessibility, reliability, and validity of the methods to discriminate between pain mechanisms will be important to consider. Encouragingly, the domains with the greatest number of features were clinical examination (n = 134, 74%) and quantitative sensory testing (n = 34, 83%). The next step towards development of a tool(s) to differentiate between pain mechanism categories in individuals with musculoskeletal pain will be to seek expert opinion on the minimum set of features that are likely to lead to accurate interpretation.

4.5. Study strengths and limitations

The strengths of this study are the comprehensive process used to select candidate features/assessment findings, diversity of the expert group, a priori definitions for consensus, and clarification of outcomes with a second Delphi round. Limitations include most of the panelists being physiotherapists (29%) and from English-speaking countries (67%), although WHO regions were covered

well (North America, Europe, and Asia Pacific). Moreover, panelists may have interpreted the process of allocating the pain mechanism categories for each feature differently (ie, feature characteristic of or simply present in a category), which may have influenced allocation and outcomes. Furthermore, the threshold for retention of features was lenient and arbitrary, which led to retention of a large number of features.

5. Conclusion

This study aimed to identify consensus on features and assessment findings that could aid in discrimination between pain mechanism categories. The outcome is an agreed list of potential candidate measures that mostly involve clinical examination or quantitative sensory testing. This list of features that experts agree are unique to 1 category or shared between 2 categories provides a strong foundation to develop tools to aid evaluation of individuals experiencing pain in the musculoskeletal system.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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Appendix A. Supplemental digital content

Supplemental digital content associated with this article can be found online at http://links.lww.com/PAIN/B565.

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