Sensory Descriptors which identify Neuropathic Pain Mechanisms in Low Back Pain: A Systematic Review

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Abstract

Objective: Descriptors provided by patients with neuropathic low back pain (NLBP) with or without spinally referred leg pain are frequently used by clinicians to help to identify the predominant pain mechanisms. Indeed, many neuropathic screening tools are primarily based on subjective descriptors to determine the presence of neuropathic pain. There is a need to systematically review and analyse the existing evidence to determine the validity of such descriptors in this cohort.

Methods: Ten databases were systematically searched. The review adhered to PRISMA and CRD guidelines and included a risk of bias assessment using QUADAS-2. Studies were included if they contained symptom descriptors from a group of NLBP patients +/-leg pain. Studies had to include a reference test to identity neuropathic pain from other pain mechanisms.

Results: Eight studies of 3,099 NLBP patients were included. Allodynia and numbness were found to discriminate between NLBP and nociceptive LBP in 4 studies. Autonomic dysfunction, (changes in the colour or appearance of the skin), was also found to discriminate between the groups in 2 studies. Dysesthesia identified NLBP in 5/7 respectively. Results from studies were equivocal regarding pain described as hot/burning cold and paroxysmal pain in people with NLBP.

Conclusion: Subjectively reported allodynia and numbness would suggest a neuropathic pain mechanism in LBP. Dysesthesia would raise the suspicion of NLBP. More research is needed to determine if descriptors suggesting autonomic dysfunction can identify NLBP. There is poor consensus on whether other descriptors can identify NLBP.

Key words: Sensory descriptors; Descriptors; Neuropathic Pain; Low Back Pain

Introduction

Neuropathic low back pain (NLBP) with or without spinally referred leg pain is an ongoing problem for clinicians to diagnose and a costly experience for patients. It has been reported that people with NLBP +/- leg pain have higher levels of pain, depression, anxiety and poorer quality of life outcomes than people with nociceptive low back +/- leg pain [1,2,3,4]. People seeking treatment for NLBP and leg pain account for a disproportionately high cost of medical care and disability compensation [5]. Neuropathic pain (NP) is defined as "pain arising as a direct consequence of a lesion or disease affecting the somatosensory system" [6]. The identification and classification of NLBP +/- leg pain is difficult due to its heterogeneity and remains one of the most challenging chronic pain disorders to treat [7,8,3,9]. At present, patients are still generally classified on a trial and error basis influenced by which clinician they have attended, and there is a suggestion that clinicians fail to identify significant NLBP +/- leg pain [3,10]. For successful and cost-effective treatment of NLBP +/- leg pain there needs to be accurate diagnosis. For example, current NICE guidelines recommend non-steroidal anti-inflammatory medications for nociceptive LBP but a choice of amitriptyline, duloxetine, gabapentin or pregabalin as initial treatment for NLBP [11,12].

For many years, it has been suggested that verbal descriptors are important in the identification of pain mechanisms, such as NP [13]. In current Covid times, where many face to face consultations have been replaced by virtual means and physical examination is more difficult, descriptors have an even greater role in identification of mechanisms at play. However, there is conflicting evidence about the value of descriptors in identifying NP and it remains unclear if there is sufficient evidence to recommend their use. Boureau et al. [13], Rasmussen et al. [14] and Dworkin et al. [15] examined if NP could be differentiated from non-NP by the use of individual descriptors in people with a variety of pain conditions. Boureau et al. [13] and Dworkin et al. [15] both concluded that sensory descriptors could identify NP, but the specific descriptors identified were different in each study. In contrast, Ramussen et al. [14] concluded that descriptors could not identify NP. These studies investigated NP in a number of conditions such as post-herpetic neuropathy, post-surgical nerve trauma and diabetic neuropathy but did not examine NLBP exclusively. Most research into descriptors has been carried

out to facilitate the development of screening tools, with a dramatic increase in the use of screening tools to diagnose NP [16,17]. These tools use clusters of descriptors to identify NLBP +/- leg pain. With this increased use, there is a need to clarify the ability of descriptors to identify NP. Perhaps more importantly, in clinical practice patients are asked to describe their symptoms and may only use one or two descriptors, therefore there is a need to examine if individual descriptors can be used to raise the index of suspicion of NLBP.

There appears to be a paucity of literature analysing the value of individual sensory descriptors of NLBP +/- leg, and to the authors' knowledge, no systematic review has been found to address this gap. The aim of this integrative review was to conduct a systematic search of the literature, to assess whether subjective sensory descriptors are valid in identifying NLBP in people with or without leg pain.

Methods

Study Design

An integrative review, a specific systematic review method, was carried out, as it has the advantage of being able to analyse and synthesize nonexperimental study designs [18] and provide comprehensive understanding of health care problems [19]. The Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines for reporting Systematic Reviews [20] was used to guide and report the integrative review. These guidelines, with the help of a checklist, are intended to improve the quality of reporting of systematic reviews (Appendix 1). The complexity inherent in combining non-randomised control trials can contribute to a lack of rigour, inaccuracy and bias, so to address this the five methodological stages for integrative reviews, as recommended by Whittemore and Knafl [19] were used. The review protocol was registered with PROSPERO, the International prospective register of systematic reviews, and can be accessed via www.crd.york.ac.uk/prospero/display_record.php?RecordID=81497.

Search strategy

A systematic search of electronic databases (AMED, CINAHL, Cochrane and DARE, Embase, MEDLINE, PEDRO, PubMed) was initiated on 18th July 2017 and final search carried out on 2nd May 2019. Grey literature was searched through Google scholar and Cochrane. A research registry database, Web of Science, was also searched. Hand searching of reference lists of relevant studies was carried out to further identify studies. The search strategy was developed and conducted by the authors and included MeSH terms and keyword searches, with combinations of all being used (Table 1). There was no limit on publication date. For full search strategy, see Appendix 2.

Eligibility Criteria

A study was included when it met all of the following criteria:

(1) Verbal descriptors of symptoms were collected from patients, which included a group of NLBP patients +/- spinally referred leg pain. Studies that collected descriptors via a questionnaire were included. Studies were required to have analyses of descriptors or data available that would facilitate analysis. Authors were contacted when some analysis of descriptors were supplied but further information was needed for analysis.

 (2) Performed a reference test to distinguish NLBP from other pain mechanisms. Questionnaires to identify NP were accepted

(3) English language text

(4) Study design appropriate for diagnostic accuracy including cohort, cross-sectional, longitudinal, Delphi and case series studies

Articles were excluded if they:

(1) Were studies performed on animals

(2) Included participants with LBP due to serious spinal pathology or specific LBP populations without a confirmed neuropathic mechanism

(3) Did not include a reference test to identify NP

Study Selection and Data Extraction

Titles of studies retrieved were initially reviewed using the eligibility criteria by one researcher (MH), to remove those with no uncertainty about their exclusion[21]. After this, eligibility assessment was performed independently by two reviewers (MH and CR) at each phase: title, abstract and full text review. Any discrepancies were discussed until a consensus was reached.

A data extraction form was developed to help reduce bias and improve reliability and validity [22]. If two studies analysed the same cohort of subjects, the study with the most information on descriptors or NLBP was chosen, to avoid duplication bias [20]. Information was extracted from each included study on aim, subject characteristics, study design with methodological considerations including eligibility criteria, withdrawals, sample sizes, index and reference test including who conducted tests, timelines and sensitivity, specificity or likelihood ratios, study funding and results relevant to descriptors. Meta-analysis was not possible due to the heterogeneity of the studies and it has not been recommended for pooling results from diverse non-randomised control study types [22]. The analysis of the data was performed using the constant comparison method. Initial analysis was performed on each individual study using the data extraction form, which facilitated the ability to systematically compare the studies to enhance methodological rigour [19]. The data extracted was analysed to identify themes, patterns, relationships and similarities. Results were synthesised using a narrative summary.

Risk of bias assessment

Assessment of risk of bias of eligible studies was performed using the Quality Assessment of Diagnostic Accuracy Studies tool 2 (QUADAS-2), which analyses risk within four key domains (patients' selection, index test, reference standard and flow and timing) [23] and has shown adequate agreement between items [24]. Signalling questions were used to assess the risk of bias, which were answered Yes, No or Unclear. These facilitated the reviewer to answer an anchor question which assessed risk as Low, High or Unclear in each domain. Applicability of three of the domains, patients'

selection, index test and reference standard, were assessed in the same way. Unclear was used when insufficient data was reported to permit judgement or data was missing [25]. All eligible studies were assessed by two reviewers (MH and CR) working independently. After reviewing the studies, the reviewers discussed disagreements until a consensus was reached.

Results

Study Selection

Electronic searching of databases and research registry retrieved 5,207 results. The process of study selection is represented in figure 1 in a PRISMA flowchart. If full-text could not be retrieved, it was requested from the author of the study. The full text of 94 articles were assessed by 2 independent reviewers. Kappa co-efficient for inter-rater agreement on inclusion of articles from full text was 0.82, with scores from 0.80 – 1.00 indicating almost perfect agreement [27]. Eight studies were identified for inclusion in the integrative review.

Risk of bias across studies

QUADAS-2 item inter-rater agreement was calculated using the Kappa statistic as 0.42, which indicated moderate agreement [27]. Table 2 details the results of QUADAS-2. Three studies Fishbain et al. [30], Gierthmuhlen et al. [31] and Schloz et al. [34] were at lowest risk of bias, scoring 5 low risks and 2 unclear risks. The 2 unclear risks indicated insufficient reporting. The index test and reference standard test domains were most commonly at risk of bias in all studies. Consideration was taken of there being no gold standard to identify NLBP. If a study had utilised multiple methods for the reference standard, they were deemed to have a low risk of bias. Generally, flow and timing and applicability concerns were low, with a few exceptions (see table 2).

Study Characteristics

The individual characteristics of the included studies are reported in table 3. All studies used a cross-sectional design except Ljunggren [32], which employed a mixed methods design. No study reported sensitivity or specificity or likelihood ratio data for sensory descriptors. Eight studies gathered and analysed descriptors from a total population of 3,099 NLBP patients, with or without spinally referred leg pain [28,29,30,31,32,33,34,35]. Five of these compared descriptors from 849 patients with NLBP to patients with nociceptive LBP [29,30,31,34,35]. One study [33] reported the percentages of descriptors chosen by NLBP patients and created and compared subgroups of descriptors from 2,094 NLBP patients, to subgroups of descriptors from patients with other painful neuropathies; diabetes and post-herpetic neuralgia. The two remaining studies [28,32] looked at the consistency with which 156 NLBP patients chose particular descriptors or the frequency which NLBP patients chose a descriptor from a questionnaire. The most common method of obtaining descriptors from NLBP patients was the painDETECT questionnaire, used by 3 studies [28,31,33]. Other questionnaires used included an adapted McGill questionnaire [32], the LANSS questionnaire [29,35], the DN4 questionnaire [35] and NPS questionnaire [30].

Individual Descriptors used to discriminate NLBP from nociceptive LBP

Whilst there were similarities in the types of sensory descriptors used across studies, different terms were often used to describe them, which complicated analysis. For the purpose of presenting comprehensive results, similar descriptors were grouped together, with the precise descriptor used in each study identified. Sivas et al. [35] used 2 questionnaires, DN4 and LANSS, to gather different descriptors from the same group of patients and these will be presented as 2 sets of results, one for each of the questionnaires. Three studies [29,33,35] gathered percentages of descriptors chosen by patients with NLBP and these are presented in table 4.

Allodynia, pain to light tough and evoked pain

Pain to light touch, described in some studies as allodynia and others as evoked pain, was gathered in 4 studies [28,29,31,35]. Whilst pain to light touch is classically considered to be a physical test

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procedure, it was classified as a descriptor in these studies, as participants were asked if this was something they experienced. Allodynia was found to discriminate between those with and without NLBP in the 4 studies that investigated it [28,29,31,35]. Gierthmuhlen et al. [31] found a statistically significant higher percentage of participants in the radiculopathy group selected allodynia from a list of descriptors compared to nociceptive LBP group. Cappelleri et al. [28] reported allodynia demonstrated adequate item discrimination (≥0.4) between groups and El Sissi et al. [29] found allodynia was more statistically significantly associated with NLBP group compared to nociceptive group. Sivas et al. [35] found patients with NLBP chose this descriptor more frequently than patients with nociceptive LBP, this being statistically significant, with 61% of their NLBP patients choosing this descriptor on LANSS compared to 11% of nociceptive LBP patients. The specific area on the body that participants experienced allodynia (i.e. leg or back) was only possible to ascertain in one study [31], since all other studies did not report the specific area that symptoms were explored. Gierthmuhlen et al. [31] found that those with NLBP reported a higher frequency of allodynia in the back compared to the leg but despite it being over double than reported in the leg, this did not reach statistical significance. Of these studies, Gierthmuhlen et al. [31] was of high methodological quality whilst Cappelleri et al. [28], El Sissi et al. [29] and Sivas et al. [35] were of low methodological quality.

Numbness

Four studies investigated numbness as a descriptor [28,31,32,35]. Gierthmuhlen et al. [31] found a higher percentage of participants in the radiculopathy group selected numbness from a list of descriptors compared to nociceptive LBP group ($p<0.05$) (with no significant difference between leg and back sites), Cappelleri et al. [28] report adequate discriminative item to total correlation for numbness (0.47) for NLBP. Sivas et al. [35] found statistically significant number of patients with NLBP chose numbness compared with nociceptive LBP ($p<0.001$). Ljunggren [32] found 100% of the 50 patients with NLBP who they interviewed reported numbness in the foot or low back. Sivas et al. [35] report 97% of patients with NLBP chose this descriptor on DN4 which was statistically significant compared to 54% of nociceptive LBP patients. When the methodological quality was

considered Gierthmuhlen et al. [29] was of high quality and Cappelleri et al. [26], Ljunggren [30] and Sivas et al. [33] were of low quality.

Autonomic dysfunction

Two studies which used LANSS to classify NLBP looked at subjectively reported autonomic dysfunction, described by LANSS as "the changes in the colour or appearance of the skin in the painful area". Both El Sissi et al. [28] and Sivas et al. [35] found more patients (p<0.05) with NLBP (70% and 15% respectively) chose autonomic dysfunction compared to 0% of those with nociceptive LBP.

Dysesthesia

Seven studies examined dysesthesia, also described as tingling or prickling, as an individual descriptor or in combination [28,29,30,31,32,34,35]. Gierthmuhlen et al. [31] found a statistically significant higher percentage of participants in the radiculopathy group selected prickling in both the back and leg from a list of descriptors compared to nociceptive LBP group, with no statistical difference between the 2 sites. Fishbain et al. [30] reported the mean scores on a 10 point scale were statistically significantly higher for dysesthesia in the NLBP group compared to nociceptive LBP group (p <0.001). El Sissi et al. [29] found dysesthesia was chosen by 96% of NLBP patients and was more statistically significantly associated with NLBP compared to nociceptive LBP. Cappelleri et al. [28] reported tingling or prickling demonstrated adequate item discrimination (≥0.4) between groups. Sivas et al. [35] found NLBP patients chose dysesthesia statistically significantly more frequently compared to nociceptive LBP. They report 85% of patients with NLBP on DN4 chose tingling and 100% of patients with NLBP on the LANSS chose dysesthesia

However, in contrast to these studies, Ljunggren [32] and Scholz et al. [34] found a lack of consistency for dysesthesia descriptors to discriminate between NLBP +/- leg pain patients and nociceptive LBP. Of the studies reporting in favour of dysesthesia Fishbain et al. [30] and Gierthmuhlen et al. [31] were of high methodological quality and Cappelleri et al. [28], El Sissi et al. [29] and Sivas et al. [35] were of low methodological quality, which neither strengthens or negates the

evidence to support the use of dysesthesia to identify NLBP. Of the studies that found dysesthesia could not discriminate between NLBP and nociceptive pain, Scholz et al. [34] had high methodological quality and Ljungreen [32] was low methodological quality. Overall there were 5 studies [28,29,30,31,35] which found dysesthesia could discriminate between those with NLBP and 2 which found it could not [32,34]

Itching, generally considered to be a form of dysesthesia, was investigated as a separate descriptor to dysesthesia in 2 studies [30,35]. Fishbain et al. [30] found the mean score on a 10 point scale was statistically significantly higher for itching in the NLBP group compared to nociceptive LBP and Sivas et al. [35] found 42% of patients with NLBP on DN4 reported itching, which was statistically significant compared to the 3% of nociceptive LBP who chose it.

Temperature pain

Thermal pain was reported in 7 studies [28,29,30,31,32,34,35]. However, the question was phrased quite differently in studies. The 2 studies using painDETECT [28,31] asked both "Is cold or hot in this area painful", suggesting thermal hyperalgesia, in addition to whether they would describe their pain as a burning sensation. The other 5 studies [29,30,32,34,35] used phrasing such as if the patient had felt pain in the area that would be described as hot or burning or cold. For this reason, the results for temperature related pain are presented in two separate sub sections.

- *Thermal Hyperalgesia*

Gierthmuhlen et al. [31] found no statistically significant difference for the thermal pain threshold between NLBP and nociceptive LBP groups. When they examined thermal hyperalgesia for the low back versus the leg area, the found no difference between the areas for heat hyperalgesia however cold hyperalgesia was reported more (p<0.05) in the low back compared to the leg in patients with NLBP. Cappelleri et al. [28] reported that thermal pain did not show adequate item discrimination (≥0.4) between NLBP and nociceptive LBP.

- *Pain described as hot/burning/cold*

El Sissi et al. [29], Cappelleri et al. [28] and Gierthmuhlen et al. [31] found pain described as hot/burning was significantly associated with NLBP group compared to nociceptive group. No statistically significant differences in burning pain were found between the low back area and the leg area by Gierthmuhlen et al. [31]. Sivas et al. [35] found both hot and cold was chosen more (P<0.05) by the NLBP than the nociceptive LBP group. Fishbain et al. [30] found the mean score on a 10 point scale was statistically significantly higher for hot but not cold pain in the NLBP group compared to nociceptive LBP group. El Sissi et al. [29] found 83% of NLBP participants chose thermal pain compared to 38% of nociceptive pain which was statistically significant. Sivas et al. [35] report 83% of NLBP patients chose hot/cold on LANSS and 64% chose burning and 49% painful cold on DN4.

In contrast, Lunggreen [32] and Scholz et al. [34] found pain described as burning/hot did not discriminate between NLBP and nociceptive LBP groups. Overall there were 4 studies [28,29,31,35] supporting and 2 [32,34] negating the ability of pain described as hot/burning and cold to identify NLBP and 1 study [30] which found pain described as hot but not cold could identify NLBP.

Paroxysmal pain

Paroxysmal pain, also described in studies as pain attacks, electric shocks, jumping, bursting and spontaneous pain were reported in 5 studies [28,29,31,32,35]. Of these, Cappelleri et al. [28], El Sissi et al. [29] and Sivas et al. [35] found that paroxysmal pain discriminated between NLBP from nociceptive LBP groups. Cappelleri et al. [28] found adequate item discrimination (≥0.4) for pain attacks, while El Sissi et al. [29] found that paroxysmal pain was significantly associated with NLBP group compared to nociceptive group. Sivas et al. [35] found 78% of patients with NLBP chose paroxysmal pain using the LANSS and 45% with NLBP on DN4 chose electrical shocks as a descriptor (table 4).

Conversely, Gierthmuhlen et al. [31] reported no statistically significant difference for paroxysmal pain between NLBP and nociceptive LBP groups and Ljunggren [32] did not find paroxysmal pain to be discriminatory for NLBP.

Spontaneous pain, described as sudden-onset spontaneous pain, was looked at as a separate descriptor by Gierthmuhlen et al. [31] to paroxysmal pain, described as sudden onset pain like electric shocks. They found a statistically significant higher percentage of participants with NLBP selected spontaneous pain descriptor than those with nociceptive LBP, which was in contrast to their finding for paroxysmal pain.

Dull and Sharp pain

Dull pain was not found to be a discriminatory descriptor between those with NLBP and with nociceptive LBP [30,34]. Fishbain et al. [30] found a statistically significant difference on a 10 point mean scale for sharp pain between those with radiculopathy and the nociceptive LBP group. However, Scholz et al. [34] found sharp pain did not discriminate between NLBP and nociceptive LBP.

Pins and needles

Pins and needles were reported in 2 studies [34,35]. There were contrasting results with Sholz et al. [32] finding pins and needles did not discriminate between NLBP and nociceptive LBP but Sivas et al. [35] reporting that 78%, of NLBP patients chose this descriptor compared to 20% of nociceptive LBP patients (p<0.001).

Feeling of deep pressure or muscle hardening

Gierthmuhlen et al. [31] examined feeling of deep pressure or muscle hardening and found no statistical difference for this descriptor between those with NLBP +/- leg pain and nociceptive LBP. However within the NLBP group, there was a statistically significant higher frequency of muscle hardening in the LBP region than in the leg region.

Results of cluster group analysis

Mahn et al. [33] compared the sensory descriptors of 2094 patients with NLBP +/- leg pain to those with painful diabetic neuropathy and post herpetic neuralgia. A cluster analysis using the sensory descriptors found 1 distinct subgroup for NLBP +/- leg pain, when compared to diabetic and post

herpetic patients. This sub-group was characterised predominantly with combined severe painful attacks and pressure induced pain.

Discussion

Summary of evidence

Whilst there is not universal consensus in the literature that descriptors can distinguish NLBP from nociceptive LBP, overall 5 studies [28,29,30,31,35] found that descriptors were able to distinguish NLBP from nociceptive LBP, whereas 2 studies [32,34] did not. However, there was a lack of agreement between studies as to which specific descriptors are most accurate in distinguishing between the 2 LBP groups.

Evidence supporting individual descriptors to identify NLBP

For individual specific descriptors, there was evidence that subjectively reported allodynia could discriminate between NLBP and nociceptive LBP in the 4 studies that examined it Cappelleri et al. [28], El Sissi et al. [29], Gierthmuhlen et al. [31] and Sivas et al. [35]. All 4 studies [28,31,32,35] which examined numbness indicated found that it could also discriminate between those with and without NLBP. It is unclear whether there is a difference in the presence of allodynia or numbness between regions (back or leg) since only one paper distinguished between the 2 regions [31] and found no significant difference between them.

Both studies that looked at autonomic dysfunction [29,35], described as changes in the colour or appearance of the skin, found it could identify NLBP. However, due to the low number of studies examining this descriptor it is not possible to confidently recommend the description of autonomic symptoms to identify NLBP.

Five [28,29,30,31,35] of the 7 studies [32,34] investigating dysesthesia found it could discriminate NLBP, indicating it would raise the suspicion of NLBP. Two of these studies [30,35] also investigated itching, which frequently comes under the umbrella term dysesthesia, and found it discriminated between NLBP compared to nociceptive LBP.

Equivocal evidence for individual descriptors to identify NLBP

Three studies supported paroxysmal pain [28,29,35] as a useful descriptor to identify NLBP and 2 negated this descriptor [31,32], indicating overall that there is equivocal evidence for this descriptor to identify NLBP. However, whilst Gierthmuhlen et al [31] did not find paroxysmal pain (described as pain attacks) to be a useful discriminating descriptor, they did find that sudden onset spontaneous pain discriminated between NLBP and nociceptive pain. Such a description may suggest this is more related to paroxysmal pain, than another commonly reported descriptor; spontaneous ongoing pain[36]. This may suggest that the way in which this descriptor is derived may lead to a different response from participants, and likely warrants more investigation. In addition, Mahn et al. [33] found a unique cluster in those patients with painful radiculopathy from a cluster analysis of descriptors taken from patients with neuropathic pain conditions. The prime feature of this cluster was painful attacks. All of the patients in this study [33] had a predominance of leg pain over low back pain, and therefore it makes comparisons to other studies difficult. Interestingly numbness was almost never reported in this group. It may suggest that there are sub-groups of patients with NLBP who have a different pattern of descriptors, potentially indicating different mechanisms for their pain (Mahn et al. [33].

There were 4 studies [28,29,31,35] supporting and 2 [32,34] negating the ability of pain described as hot/burning and cold to identify NLBP and 1 study [30] which found pain described as hot but not cold could identify NLBP. Neither of the studies [28,31] which looked at thermal hyperalgesia found that it differentiated between NLBP and nociceptive LBP

There were equivalent numbers of studies finding evidence for and against pins and needles [34,35] and sharp pain [29,34] in people with NLBP, suggesting that at this time, there is insufficient evidence to support these items to identify NLBP.

One consideration when looking at these results is the method in which descriptors were gathered in each of the studies. Of the studies that used questionnaires to gather descriptors, five [28,29,30,31,35] found a statistically significant difference between the frequency of descriptors chosen by the NLBP

group when compared to nociceptive LBP or other painful neuropathies, whereas only 1 study [32] found no consistency in the frequency of descriptors chosen by NLBP patients. The only study which asked patients for their own descriptors first before using a pre-selected list of descriptors, Scholz et al. [34], found that sensory descriptors did not discriminate between NLBP and nociceptive LBP groups. It is possible that not using specified pain descriptors in the first instance introduced considerable variability in the words that patients chose to describe their symptoms. Subsequently giving pre-selected words may have then altered their perception of their own symptoms. It is not possible to know if participants in the study [32] subsequently changed their descriptors after being given the list, or indeed were only given the list if they could not find their own words. Either may have affected the ability to compare descriptors between individuals. This may explain why studies which used questionnaires had more positive findings for the use of descriptors to identify NLBP. The disadvantage of use of NP screening tools, with limited options of specific descriptors, is that it could potentially have led patients to falsely select descriptors if the descriptor which best suited their symptoms was not available, which may have influenced the outcome of the studies. It is unclear if there was an option for participants to state that there were no descriptors available to match their symptoms in the studies, which could potentially introduce response bias [37].

Three of the studies [28,29,35] used questionnaires to determine if the predominant pain presentation was neuropathic pain and the same questionnaire results to analyse descriptors. As the index and reference tests were the same questionnaire, there was potential for common method bias [38]. It is also possible that different phrasing or emphasis of the question asked of the patient may have led to different responses. For example, thermal pain in the painDETECT is phrased "Is cold or heat in this area occasionally painful" while LANSS phrases the thermal question "Does your pain feel as if the skin temperature in the painful area has changed abnormally". While both these questions area related to temperature change and are reported as a thermal descriptor in papers, they suggest quite different mechanisms. The length of time patients were given to consider their symptoms also may have led to differences between studies. The LANSS questionnaire asks patients for their symptoms for the last week while the painDETECT looks for response for symptoms from the last 4 weeks. Any of the

above factors could have influenced the difference in outcomes between the studies that used different data gathering methods.

The reference standard test potentially contributed to the lack of consensus of this integrative review. To date, there is a lack of a gold standard reference test to identify NLBP [39,10]. Studies using multiple methods to classify NLBP +/- leg pain were considered by the authors to have made reasonable effort to classify NLBP. Those which used multiple methods found conflicting results with respect to the ability of descriptors to identify NLBP; Ljunggren [32] and Scholz et al. [34] found poor discriminatory ability of descriptors, while Fishbain et al. [30] and Gierthmuhlen et al. [31] found the descriptors to be discriminatory. Of these four studies, 2 [31,32] used similar methods to identify NLBP, that would have been sufficient to comply with the NeuPSIG committee guidelines for diagnosing definite NP published in 2016 [40]. If a reference standard is controversial or the condition difficult to identify, there is risk of bias and potential for inaccurate findings [37]. As the included studies used differing methods to identify NLBP +/- leg pain, it is unlikely that the studies compared identical groups. If studies had followed recommended guidelines to identify NLBP, the interpretations made from the synthesis of the results would be stronger.

To the authors' knowledge no other systematic reviews have specifically looked at sensory descriptors which identify NLBP, and therefore the results of the current review are compared to literature which has examined this in other NP conditions. Boureau et al. [13] found 5 descriptors (burning, electric shocks, tingling, prickling, itchy and cold) which differentiated between people with a number of peripheral NP conditions and those without NP. In agreement, Dworkin et al. [15] found some similar descriptors to Boureau et al. [13] (hot (burning), cold and itchy) could discriminate between those patients with neuropathic pain compared to those without neuropathic pain, but in addition the descriptors skin sensitivity and dull pain. Dworkin et al. [15] did not give their patients the choice of tingling or prickling. In the current review, both studies that examined the descriptor "itchy" found it could identify NLBP and there was more evidence supporting dysesthesia (tingling and prickling) than negating it. There was marginally more evidence supporting paroxysmal descriptors such as

electric shock or pain attacks and burning/cold than negating as a descriptor that could identifying NLBP.

In contrast to Dworkin et al. [15] and Boureau et al. [13], Rasmussen et al. [14] found both NP and non-NP groups used similar descriptors to describe their pain. Patients with low back pain were included in both NP and non-NP groups, though it was not possible to identify the descriptors chosen by this group [14]. As in the studies in this integrative review, the 3 studies used different methods to classify NP. These 3 studies present conflicting results on whether subjective descriptors can identify NP and are in keeping with the findings of this integrative review.

Relevance to practice

The findings of this integrative review are relevant to all practitioners who work with LBP patients. The subjective interview is an essential first encounter with the patient, where hypotheses regarding the presenting symptoms are processed. Indeed, as many interactions between patients and clinicians are now occurring virtually or via telephone [41] , the subjective interview may be the only means to decide whether a patient has neuropathic or non-neuropathic LBP. The results of this systematic review suggest that the clinicians' index of suspicion of neuropathic pain contributing to the patient pain mechanism may be raised if patients report the descriptors allodynia and numbness. The results of 2 studies suggest autonomic dysfunction descriptors such as changes in the colour or appearance of the skin may also be useful, but more research is required to support this finding. In addition, if the patient reports dysesthesia, this is suggestive of a neuropathic pain mechanism in LBP. While these descriptors can aid in the decision indicating that the patient is presenting with NLBP, clinicians should undertake further assessment to evaluate if there is NLBP where possible.

Strengths and limitations

The search strategy for this study was a strength as it was well defined, incorporating a broad range of terms. It included multiple databases, registries and also hand searching, to identify the maximum number of potentially relevant studies. However, the search was limited to English which may have

introduced publication bias, as studies with significant results conducted in other languages may be more likely to be translated and published than those with non-significant results [2].

All studies included collected data on sensory descriptors in patients with NLBP +/- leg pain, however the primary aim of the majority of studies was not to validate their use in identifying NLBP +/- leg pain, and therefore data had to often be extrapolated for this review. QUADAS-2 provided a comprehensive risk of bias assessment, however some subjectivity was required for decisions. For this reason piloting work was undertaken to improve the standardisation of using the tool between the 2 reviewers.

Recommendations for future research

For future research, it would be recommended to address the areas that have contributed to the limitations of this integrative review. Studies are required whose primary aim is to investigate if subjective descriptors can identify NLBP +/- leg pain. It is recommended they use recognised criteria to classify NLBP, such as the NeuPSIG committee guidelines for diagnosing definite NP [40] to improve reliability of the classification of patients. Future studies could explore if there is a difference in results when participants are asked for their descriptors in their own words, compared to choosing descriptors from a questionnaire, to examine if this influences results.

Conclusion

A systematic search of the literature found 8 studies that collected sensory descriptors from NLBP +/- leg pain patients. The current evidence is insufficient to support or refute the use of sensory descriptors to identify NLBP with or without spinally referred leg pain, though there was stronger evidence for the use of allodynia and numbness. Autonomic dysfunction may help identify NLBP but there have only been 2 studies that have investigated it to date. There is conflicting evidence, with more studies supporting than negating, the benefit in the use of dysesthesia/itching to distinguish between NLBP and nociceptive LBP.

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Table 1 Search keywords and MeSH terms

"Low Back Pain*", Sciatic*, "Radicular pain*", Radiculopath*, Lumbago, "Lumbar pain*","Sciatic Neuralgia","Low Back Ache*","Low Back Pain*, Recurrent" ,"Low Backache*","Lower Back Pain*","Recurrent Low Back Pain*","Nerve Root Disorder*",Radiculitis, Radiculitides, "Nerve Root Inflammation*","Inflammation, Nerve Root", "Nerve Root Compression", "Compression, Nerve Root"

AND

"Neuropathic pain*", "Nerve Pain*", "Pain*, Nerve", "Neural Pain*", "Pain*, Neural", "Nervous System Pain*", "Pain*, Nervous system", "Neuralgia, Atypical", Neuralgia*, Neurodynia*, "Paroxysmal Nerve Pain*", "Pain*, Paroxysmal Nerve", Neuropath*, "Pain*, Neuropathic"

AND

Descript*, Term*, "Patient account", Explanation*, Sign, Signs, Symptom, Symptoms, "Pain quality descript*", "Verbal descript*", Subjective, Word*, "Patient experience*", "Pain Qualit*", "Pain measure*", "Pain intensity", "Pain Perception*"

NOT

Rat, Rats, Mouse, Mice, Rodent*, "Animal Stud*", "Animal Model"

Table 2 Results from QUADAS-2

Study	Risk of bias				Applicability Concerns		
	Patient Selection	**Index Test**	**Reference Standard**	**Flow and Timing**	**Patient Selection**	**Index Test**	**Reference Standard**
Cappelleri et al. [28]	High	Unclear	Unclear	High	Unclear	Low	Unclear
El Sissi et al. [29]	Low	High	High	Low	Low	Low	High
Fishbain et al. [30]	Low	Unclear	Unclear	Low	Low	Low	Low
Gierthmuhlen et al. [231]	Low	Unclear	Unclear	Low	Low	Low	Low
Ljunggren [32]	High	High	Low	Low	Low	Low	Low
Mahn et al. [33]	Low	Unclear	High	Low	Unclear	Low	High
Scholz et al. [34]	Low	Unclear	Unclear	Low	Low	Low	Low
Sivas et al. [35]	Unclear	High	High	Low	Low	Low	Unclear

Table 3 Individual Characteristics

	Inclusion	Exclusion	Mean Age Gender Pain duration Numerical Rating Scale (NRS)	Sample Size Group information	Index standard Test	Reference standard test	Withdrawals	Funding	Results relevant to sensory descriptors
Cappelleri et al. [28]	≥ 18 yrs Diagnosis of NP condition Pain ≥ 3/12	Participation in drug study in past 6/12 Unstable medical or psychological condition or concomitant illness unrelated to NP that may confound assessment.	55.5 years Male 55.4% Female 44.6% Ave. Duration 9.5 years NRS 5.2 - 6	NLBP 106 Painful Diabetic Neuropathy 112 Spinal Cord Injury related NP 103 Neuropathic HIV 103 Post-trauma/Surgical neuropathy 100 Small fiber neuropathy 100	PainDETECT ≥ 19 NLBP, ≤ 12 NLBP unlikely. Scores from 13 – 18 unclear	Validated NP screening tool, the name of which was not supplied but stated that was not painDETECT	3 due to missing data Unclear NP group removed	Study funded by drug company. Authors employees or received funding from drug company for this study	Assessment of item-level discrimination was performed overall and a value of ≥ 0.4 was considered adequate discriminatory level for a descriptor. Prickling, allodynia, thermal pain, pain attacks, numbness, pressure trigger pain had adequate discrimination. No adequate discrimination of burning.
El Sissi et al. [29]	LBP > 3/12 >18 yrs	Affective disease or mental disorder	45 years Male 59.7% Female 40.3%	628 NLBP +/- leg pain 506 Nociceptive LBP	Descriptors on LANSS questionnaire	LANSS questionnaire ≥ 12 for NLBP diagnosis	Complete data not available for all patients reported but no numbers of same	Two authors employed by drug companies. Authors declare no conflicts of interest	Significant odds ratios between groups calculated descriptors. All found to be significant with the highest odds ratio at 27.5 was for

			Ave duration 2.9 years NRS Not reported						dysesthesia, the 17.5 for evoked pain, 17.2 for autonomic dysfunction, 2.6 for pain described as thermal and 2.5 for paroxysmal pain
Fishbain et al. [30]	Pain > 6/12		55.8 years 50% Males and Females Duration > 6/12 Not reported	305 patients NLBP +/- leg pain 44. LBP 51. Other groups included CRPS, Epidural fibrosis, failed back surgery syndrome, spinal stenosis, fibromyalgia and myofascial pain syndrome	Neuropathic pain scale Threshold 5.53/10	Chronic Radiculopathy with A) Pain and abnormal sensory symptoms in association with hypoesthesia or allodynia B) Pain and abnormal sensation with indications of motor or autonomic dysfunction	60 excluded with A) frequencies too low for stat analysis or deemed not relevant. B) Chronic radiculopathy without NLBP or spondylolysis/degenerative arthritis with NLBP	No declaration on conflicts of interest	Statistically significant difference between groups for intense, sharp, hot, cold, sensitive, itchy, unpleasant, deep and superficial pain No statistical significance between groups for dull pain
Gierthmuhlen et al. [31]	LBP > 3/12 > 18 yrs	Former alcohol or drug abuse. Strong opioid treatment	61.3 years 51% Male 49% Female Duration > 3/12 NRS 4.5	NLBP with radiculopathy 16 nociceptive LBP 32	PainDETECT Questionnaire ≥ 19 probable NLBP, ≤ 12 NLBP unlikely, 13-18 result unclear. Descriptors ≥ 3 clinically relevant	Radicular pain pattern, typical signs for radicular pain with compatible MRI finding.	None reported	Authors received speaker fees, travel support, consultancy fees, grants research support from drug companies	Statistical significance between groups for burning, prickling, allodynia, numbness, spontaneous pain. No statistical significance between groups for pain attacks, cold or heat hyperalgesia, light or deep pressure pain

									and feeling of muscle hardening
Ljunggren [32]	Lumbago-sciatica patients, with normal intellectual ability		40 years 17 men, 33 women Duration < 1 year	50 NLBP	Norwegian translation of McGill pain questionnaire	Neurological examination indicating nerve root involvement with radiographic findings of disc herniation	Not reported	Funding from Norsk Hydro, an aluminium and renewable energy company	A lack of constancy in pain descriptors was revealed in NLBP +/- leg pain patients except numbness which was choosen by 100% of participants
Mahn et al. [33]	≥18 yrs NP		59.4 years Males 41.5% Female 58.4% Duration not reported NRS 5.8	2094 NLBP 1623 Painful diabetic neuropathy 498 Post herpetic neuralgia	painDETECT questionnaire Descriptors >3 clinically relevant	Leg pain dominant with LBP absent/minor intensity.	None reported	Study received grant from drug company. Authors employed, received research support, consulting or speakers fees from drug companies	Cluster analysis found 1 distinct subgroup of NLBP +/- leg pain with combined severe painful attacks and pressure induced pain. % of descriptors chosen by NLBP were: Allodynia 10% Prickling 26% Pressure 21% Burning 25% Thermal 8% Pain attacks 32% Numbness 16%
Scholz et al. [34]	Pain > 3/12 NRS >6 >18 yrs	Severe medical or psychiatric illness Another painful disorder or neurological disease that might interfere	Age 55 Women 51% Men 49%, Duration 4 yr NRS 5	57 NLBP +/- leg pain 57 nociceptive LBP 50 Diabetic polyneuropathy, 23 post herpetic neuralgia,	Patients asked to characterise pain in their own words, then offered list of: throbbing, pounding, pulsating, shooting, radiating, cramping,	Clinical signs of nerve root involvement including sensory or motor deficits or reduced reflexes. Diagnostic test MRI/EMG	32 ineligible	Authors sit on advisory boards, consultancy, received speaker fees and grants from drug companies	Differentiation of groups based only on symptoms was weak and did not discriminate between neuropathic and non-neuropathic pain

		with assessment, local infection			squeezing, stabbing, sharp, aching, dull, painful pins and needles, stinging, burning or hot.	considered if available			
Sivas et al. [35]	LBP > 3 months 18-60 yrs	Malignancy, compression fractures, pain unknown origin, AS, FMS, Severe mental illness, Substance or alcohol abuse, Unable to fill out questionnaire, low back surgery, metabolic or endocrine disorder	42 years Males 35.6% Females 64.4% Duration ave 36 months	101 LBP patients with radiating leg pain NLBP DN4 group 65.3% LANSS group 40.6%	Descriptors on the DN4 and LANSS	DN4 65.3% 2. LANSS 40.6%	None reported	Declaration of no conflicts of interest	All descriptors investigated found to be statistically significantly more frequently chosen by NLBP than non-NLBP. NP% V non-LBP% DN4 Results: Numbness 97% V 54% Tingling 84.8% V 54% Pins + Needles 78% V 20% Burning 64% v 23% Pain to cold 48% V 11% Electric Shocks 45% V 8% Itching 42% V 2% Of NP by LANSS Dysesthesia 100% V 58% Autonomic Dysfunction 15% V 0% Evoked pain 61% V 11% Paroxysmal pain 78% V 25%

									Thermal pain 83% V 38%

Table 4 Percentages of descriptors chosen by NLBP and nociceptive LBP

Descriptor	El Sissi et al. [29]		Mahn et al. [33]		Sivas et al. [35] LANSS		Sivas et al. [35] DN4	
	NLBP	Non	NLBP	Non	NLBP	Non	NLBP	Non
Allodynia	81	20	10		61	11		
Autonomic Dysfunction	69	0.3			15	0		
Dysesthesia	97	50	26		100	58	85 Itching 42	54 Itching 3
Numbness			16				97	54
Deep Pressure/Muscle Hardening			21					
Paroxysmal	79	60	32		78	25	45	9
Thermal Hyperalgesia			8					
Hot/Burning/Cold	56	32	25		83	38	Cold 48 Burning 64	11 23
Pins and Needles							79	22