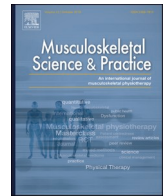




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Professional issue

Neuropathic pain questionnaires for back pain, what do we know?

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ABSTRACT

Introduction: Low back pain is a global public health concern, with an estimated lifetime prevalence of 84%. Axial low back pain refers to pain confined to an area in the low back and is different to radicular pain which radiates to extremities. Axial low back pain has traditionally been considered as nociceptive. However, research suggests it may have neuropathic components. Neuropathic axial low back pain is an unresolved, hotly contested topic due to controversies surrounding its aetiology, diagnosis, clinical course, prognosis and treatment options.

Purpose: The reference standard for diagnosing neuropathic pain is by medical history and clinical assessment (i. e., sensory testing), with optional neuropathic screening tools and selective, further diagnostic tests when clinically needed. Neuropathic screening tools are not always specific for neuropathic radiating low back pain, let alone neuropathic axial low back pain. Additionally, not all have been validated for the English language (e.g., PainDETECT). Research also suggests the percentage of patients identified as having neuropathic radiating low back pain may be dependent on the combination of reference standards used.

Implications: There is a need for research that works towards improving understanding of neuropathic axial low back pain and developing a standardised, validated and reliable system for assessing and identifying this condition. This body of research will promote earlier stratification and more rapid referral for appropriate treatment, and improve awareness, assessment and visibility of this condition amongst healthcare practitioners and in healthcare settings. This will lead to transformations in Pathways and health guidelines, ultimately improving patient outcomes.

1. Introduction: neuropathic axial low back pain

Most individuals will experience pain in the lower back at some point during their life. The lifetime prevalence of low back pain has been estimated to be as high as 84% (Airaksinen et al., 2006), and it occurs in high-, middle- and low-income countries and all age groups (Hartvigsen et al., 2018). Low back pain is associated with profound burden on healthcare and social support systems and high economic costs (Hartvigsen et al., 2018). Globally, the age-standardised point-prevalence of low back pain has been reported as 7.50% (95% CI: 6.75–8.27%) and low back pain was the leading cause of years lived with disability in 2017 (Wu et al., 2020). Low back pain is therefore a global public health concern (Buchbinder et al., 2018).

Axial low back pain refers to pain that is confined to the low back

area and it can feel sharp or dull and can come and go or be constant. It is different to radicular pain where the pain radiates to extremities with tingling or burning sensations. Although most cases of acute axial low back pain will recover, for others their pain does not improve. For instance, in a large study with 973 individuals with acute axial low back pain in Australian Primary Care, 28% had not fully recovered 12 months after the baseline consultation (Henschke et al., 2008). A number of factors were associated with a longer time to recovery, including older age, higher pain intensity, longer duration of back pain prior to consultation, more days of reduced activity due to low back pain prior to consultation, compensation cases, feelings of depression and perceived risk of persistence (Henschke et al., 2008). Additionally, in a systematic review of 11 studies, whilst recovery from axial low back pain was observed in 33% of patients in the first three months, the percentage of

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people recovering only increased slightly to 35% at one year after onset (Itz et al., 2013). This therefore demonstrates there is a substantial percentage of individuals whose axial low back pain does not improve, progressing to chronic axial low back pain.

Axial low back pain has traditionally been considered as nociceptive but research suggests that it may have a neuropathic component (Freemont, 2008). Neuropathic pain is defined by the International Association for the Study of Pain (IASP) as 'pain caused by a lesion or disease of the somatosensory nervous system' (International Association for the Study of Pain, 2017). Features that are associated with this type of pain can include hypoaesthesia, allodynia and hyperalgesia. Hypoaesthesia is defined by the IASP as 'decreased sensitivity to stimulation, excluding the special senses' and indicates a decrease or loss of somatosensory function mediated by nerves (International Association for the Study of Pain, 2017). It is thought that hypoaesthesia is one of the most sensitive and reliable indications of neuropathic pain (Backonja and Schmidt RF, 2007). Unlike hypoaesthesia, allodynia or hyperalgesia are considered positive sensory phenomena. Allodynia is defined by the IASP as 'pain due to a stimulus that does not normally provoke pain' (International Association for the Study of Pain, 2017), and can be 'static' if it arises from slight pressure on the skin, or 'dynamic' if it arises from light stimuli moving on the skin (Truini et al., 2013). For instance, a light touch (static allodynia) or brush (dynamic allodynia) of the back can feel very painful. It is estimated that 18–54% of patients with neuropathic pain may have dynamic mechanical allodynia (Bouhassira et al., 2005; Koroschetz et al., 2011). Hyperalgesia is defined by the IASP as 'increased pain from a stimulus that normally provokes pain' (International Association for the Study of Pain, 2017). For instance, someone may feel extreme pain when a previously injured area of the back comes into contact with an object, such as the back of the chair.

The prevalence of pain with neuropathic features is thought to range from 7 to 10% (Fayaz et al., 2016; van Hecke et al., 2014). Since neuropathic back pain with radiating pain into the arm or leg is considered one of the most common presentations of neuropathic back pain (Freyhagen and Baron, 2009), the prevalence of neuropathic axial low back is not known. This is confounded by controversy in the literature regarding whether it is a specific diagnosis or an early stage of low back pain with neuropathic features (e.g., radiating pain to extremities), and is therefore unresolved.

As a result, there is little literature on the costs of neuropathic axial low back pain. This contrasts with research investigating the costs associated with neuropathic radiating back pain where research among patients with persistent back pain in Germany suggested that the healthcare costs were approximately 67% higher for an individual thought to have neuropathic radiating back pain (ascertained by the PainDETECT neuropathic screening tool) than those for an individual thought to have nociceptive back pain (Schmidt et al., 2009). In addition, findings from a retrospective, observational study conducted in the United States of America showed that chronic low back pain with a neuropathic pain component was associated with approximately US \$4000 in direct costs to subjects, US\$6000 in direct costs to payers, US \$22,500 in direct costs and a grand total of US\$34,000 (Sadosky et al., 2014). Although the authors stated that the neuropathic pain component was confirmed based on results from validated neuropathic pain screening tools, it is unclear which tools were used, whether they were combined with other assessment techniques and whether neuropathic axial low back pain was included.

2. Assessing neuropathic pain

In the UK, there is currently no diagnostic gold standard for neuropathic pain. According to research and recent guidelines by the European Federation of Neurological Societies (EFNS) (Crucchu et al., 2010), IASP's Neuropathic Pain Special Interest Group (NeuPSIG) (Finnerup et al., 2016) and the Australian and New Zealand College of Anaesthetists (ANZCA, 2018) an assessment for neuropathic pain should include.

1. An assessment of the patient's medical history to assess the character and distribution of the pain in accordance with neuropathic criteria, and whether a relevant disease or lesion may be responsible for the pain.
2. Clinical examination to determine the presence of loss of function (e.g., hypoaesthesia with diminished perception to a range of mechanical or thermal stimuli including warm, cold, touch, brush, pressure and vibration by sensory tests) and gain of function (e.g., allodynia and/or hyperalgesia with cotton wool, touch, pinprick/cocktail stick, cold stimulus and warm stimulus during sensory testing) and their relevance to the underlying disease or lesion.
3. Further diagnostic tests to either document the presence of a specific underlying neurological disease or to confirm a sensory lesion within the pain distribution. Further diagnostic tests could include (Crucchu et al., 2010):
 - a. Quantitative sensory testing (QST) where response to external stimuli of controlled intensity is assessed.
 - b. Nerve conduction studies which measure the speed of an electrical impulse through nerves to identify damaged nerves.
 - c. Laser-evoked potentials which are brain responses to laser-related heat and provide a means of studying the nociceptive pathway in individuals with neuropathic pain.
 - d. Microneurography which records single-fibres to provide information on the physiology and pathophysiology of nerve groups.
 - e. Functional neuroimaging (e.g., positron emission tomography [PET] and functional magnetic resonance imaging [fMRI]) to explore differences in cerebral blood flow or metabolic changes in different brain regions.
 - f. Skin biopsy.

It should be noted that many of these further diagnostic tests may not be available in most clinical settings, potentially presenting a challenge for mixed pain syndromes in particular. As chronic axial low back pain can have both non-neuropathic and neuropathic features and can come with gain of function, neuropathic axial low back pain can be challenging to diagnose and is controversial.

As part of the process for diagnosing neuropathic pain, research also recommends using screening tools such as pain questionnaires and pain drawings (Crucchu et al., 2010; Freyhagen et al., 2011). Neuropathic screening tools have become increasingly popular in both clinical practice and research to aid with discriminating neuropathic from non-neuropathic pain. These screening tools are typically completed by patients to provide an indication of whether their back pain has neuropathic features. Neuropathic screening tools include the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS), Douleur Neuropathique (en) 4 Questions (DN4), PainDETECT and Standardized Evaluation of Pain (StEP). Table 1 provides a summary of these four neuropathic screening tools.

Whilst these screening questionnaires are quick to complete (usually 5–8 min), they were designed to be used by non-specialists and are thought to show limited sensitivity and specificity when used in mixed pain syndromes (axial low back pain can have both non-neuropathic and neuropathic features) (Haanpää et al., 2011). Furthermore, a number of variables are thought to potentially influence scores from screening tools. For instance, in a retrospective review of 652 patients attending an outpatient pain centre, pain catastrophising, depression, anxiety and stress contributed to higher PainDETECT scores (Tampin et al., 2019). In addition, the presence of anxiety was associated with a high false positive neuropathic pain classification, leading to incorrect identification of individuals as having neuropathic pain (Tampin et al., 2019). The authors postulate that this may have occurred due to the PainDETECT including weighted sensory descriptors (e.g., never/hardly noticed/slightly/moderately/strongly/very strongly) (Tampin et al., 2019) rather than binary sensory descriptors (e.g., yes/no as used in the LANSS). Furthermore, since some of these screening tools require patients to rate the severity and not just the presence/absence of their

Table 1
Summary of neuropathic screening tools.

Neuropathic screening tool	Purpose	Initial validation	Design and scoring
Leeds Assessment of Neuropathic Symptoms and Signs (LANSS)	The LANSS is a validated questionnaire that was developed to identify patients in whom neuropathic pain dominates their pain experience (Bennett, 2001) (i.e., not specific to neuropathic radiating low back pain or neuropathic axial low back pain).	The initial validation studies recruited patients with a variety of diagnoses, including low back pain, visceral pain, complex regional pain syndrome and so on (Bennett, 2001).	LANSS comprises seven questions; five (yes/no) questions which consider the characteristics of the pain and are completed by the patient, with the remaining two questions requiring sensory testing of cotton wool and pinprick tests conducted by a clinician. There is also a self-reported LANSS version (S-LANSS) which does not include the sensory testing by a clinician. For both the LANSS and S-LANSS, responses are scored and a score ≥ 12 out of a total score of 24 suggests pain of predominantly neuropathic origin.
Douleur Neuropathique (en) 4 Questions (DN4)	The DN4 is a validated questionnaire that was developed to discriminate between neuropathic and non-neuropathic pain (Bouhassira et al., 2005) (i.e., not specific to neuropathic radiating low back pain or neuropathic axial low back pain).	The tool was originally developed and validated in French. Although it has been translated into numerous languages, including Spanish, Portuguese, Korean, Arabic, Turkish, Dutch, Greek and Thai, there is little validation evidence of the English translation (see (Timmerman et al., 2017) for an overview). The initial validation studies recruited patients with a variety of diagnoses, including traumatic nerve injury, post-herpetic neuralgia, post-stroke pain, osteoarthritis, inflammatory arthropathies and mechanical low back pain (Bouhassira et al., 2005).	The tool comprises seven interview questions (completed by the patient) and three physical tests (completed by the physician). The patient questions pertain to the characteristics of the pain (e.g., burning, painful cold, electric shocks, tingling, pins and needles, numbness and itching). The clinician questions concern evidence of hypoesthesia to touch and pinprick, and whether brushing causes or increases pain. Responses are then scored and a score ≥ 4 out of a total score of 10 is considered to reflect neuropathic pain. There is also a self-reported version of the DN4, which comprises the

Table 1 (continued)

Neuropathic screening tool	Purpose	Initial validation	Design and scoring
PainDETECT	The PainDETECT is a validated questionnaire that was developed as a screening tool for neuropathic pain components specifically in patients with low back pain (Freyhagen et al., 2006).	The tool was developed and validated in German and has not been validated in English (only reliability data for the English version exist (Tampin et al., 2017)). The questionnaire has been shown to have high discriminant validity between patients with and without neuropathic low back pain (Gudala et al., 2017).	seven interview questions (completed by the patient). A score ≥ 3 is considered to reflect neuropathic pain (Bouhassira et al., 2005). Questions require patients to: assess their current pain and their pain during the past four weeks on an 11-point scale from 0 (none) to 10 (maximum); assess the temporal pattern of their pain using a diagram to best reflect the course of their pain; and the characteristics of their pain (including burning, tingling or prickling sensations, sudden pain attacks, numbness, whether cold, heat or pressure cause pain and whether the pain radiates to other regions of the body). The responses are then scored out of a total score of 38 where 0–12 is thought to reflect nociceptive pain, 13–18 is unclear and scores of 19–38 are considered to reflect neuropathic pain.
Standardized Evaluation of Pain (StEP)	This is a validated questionnaire that assesses pain-related symptoms and signs that differentiate pain phenotypes according to pain mechanisms (Scholz et al., 2009).	The StEP was originally developed in patients with diabetic polyneuropathy, postherpetic neuralgia, and chronic low back pain (radicular and axial) in the United States of America, and validated in patients with radicular low back pain and axial low back pain in the UK (Scholz et al., 2009).	The StEP comprises three yes/no interview questions (e.g., pain all the time, pain quality, non-painful sensations) and eight yes/no physical tests (e.g., skin changes, blunt pressure, brush movement, decreased response to vibration, pinprick, cold temperature, temporal summation and radicular pain produced in the straight-leg-

(continued on next page)

Table 1 (continued)

Neuropathic screening tool	Purpose	Initial validation	Design and scoring
			raising test). The responses are then scored where a score ≥ 4 out of a total of 15 indicates the low back pain is likely to be neuropathic (i.e., radicular).

symptoms, it is possible that only severe cases of neuropathic pain were identified with less severe cases getting missed. This reinforces the importance of using a combination of the reference standards to ascertain the presence of neuropathic pain. Indeed, when the DN4 was administered alone, the percentage of patients with neuropathic radiating back pain was 11.2% (Enthoven et al., 2013). However, when the DN4 was combined with a physical examination, the percentage of patients considered to have neuropathic radiating back pain decreased to 2% (Enthoven et al., 2013). Also, in our centre, the self-administered version of the LANSS (S-LANSS) pointed to patients having non-neuropathic back pain whilst the clinical assessment (comprising medical history and sensory tests by cotton wool, touch and pinprick), identified patients having neuropathic components in their back pain (Baranidharan et al., 2021). Therefore, although there is currently no reliable gold standard for diagnosing neuropathic pain, it is important to heed recommendations for conducting a medical history and clinical assessment, with the option of neuropathic screening questionnaires and a follow-up of selective, further diagnostic testing when clinically needed.

3. Implications for research and practice

Working with colleagues in the community, our service has seen and treated patients who have started with acute axial low back pain with nociceptive features and who have then gone on to develop chronic neuropathic axial low back pain without radiating pain (as determined by medical history plus clinical examination with sensory testing of hypoaesthesia, allodynia and hyperalgesia). Neuropathic pain is hard to treat and the evidence of positive treatment response to simple community and physiotherapy management is unclear (Akyuz and Kenis, 2014). This can lead to patients being referred to specialist centres or seeking numerous medical opinions and sometimes undergoing unnecessary surgery which may be of no benefit and carries significant risks (Weir et al., 2017). In turn, this may delay treatment, potentially escalating symptoms and for some treatments, the rate of success may be inversely related to the duration of time between the beginning of neuropathic pain and time of treatment. For instance, spinal cord stimulation (SCS) is a National Institute for Health Care and Excellence (NICE) approved treatment for adults who have had chronic pain of neuropathic origin for more than six months with a visual analogue scale score >50 mm despite conservative treatment (NICE TA 159, 2008). It involves activating the spinal cord using mild electrical stimulation that is generated by a battery and delivered by one or two leads that are placed in the epidural space. Research has demonstrated that the longer a patient has had neuropathic pain before receiving SCS, the lower the chance of future success with this treatment (Kumar et al., 1998, 2006). Although this initial research has been conducted in SCS, it highlights the importance of accurate and timely diagnosis of neuropathic pain in order to identify appropriate treatment and enhance the chances of positive response.

There is considerable research investigating effective treatments for neuropathic pain and increasing interest in identifying new, potential therapeutic options for neuropathic axial low back pain, including SCS

(Deer et al., 2014). Although there is little research investigating SCS in neuropathic axial low back pain, randomised controlled trials have demonstrated analgesic effects and a promising safety profile in persistent spinal pain syndrome, failed neck surgery syndrome, painful diabetic neuropathy and complex regional pain syndrome (Al-Kaisy et al., 2018; De Ridder et al., 2013; de Vos et al., 2014; Kemler et al., 2000). However, it should be noted that a recent Cochrane Review demonstrated mixed evidence for the efficacy, effectiveness, adverse events and cost-effectiveness of SCS (O'Connell et al., 2021). Furthermore, SCS in patients with chronic radicular pain after lumbar surgery reported no significant difference in change from baseline for self-reported disability during stimulation compared to placebo stimulation (Hara et al., 2022). However, shortcomings with this study included limited details on the placebo stimulation, no statistical analysis of the effect of SCS and placebo stimulation over time (the study was performed over 12 months, but only three timepoints were statistically analysed) and the minimal clinically important differences (MCID) were based on outdated recommendations. Furthermore, a prior study (Eldabe et al., 2021) had shown that the waveform used by Hara et al. (2022) was as good as sham and we would therefore argue that it was not ethical to carry on the study when it was deemed a placebo previously. As a consequence, there is a need for well-designed and -delivered placebo-controlled, blinded trials investigating SCS in neuropathic pain conditions. In trials with patients with 'neuropathic axial low back pain', the presentation should be carefully considered and detailed, as patients who have mainly gain of function sensory signs (allodynia and hyperalgesia) and no loss of function (hypoaesthesia) may in fact have nociplastic axial low back.

Research identifying new, potential therapeutic options for neuropathic axial low back pain has been facilitated by the development and evolution of the bio-psycho-social model of chronic pain. The bio-psycho-social model views chronic pain as a dynamic and intricate interaction between biological, psychological and social factors that can antagonise or calm pain, with chronic pain requiring multidisciplinary treatment that addresses all these elements (Waddell, 2004; Kamper et al., 2014). A Cochrane Review examining the evidence on the effectiveness of multidisciplinary bio-psycho-social rehabilitation programs in patients with chronic low back pain showed that those who underwent multidisciplinary bio-psycho-social rehabilitation were likely to experience less pain and disability than those receiving usual care or a physical treatment (Kamper et al., 2014). Furthermore, this form of management for chronic low back pain had a positive influence on work status compared to physical treatment (Kamper et al., 2014). Although there is some research demonstrating promising findings with multidisciplinary bio-psycho-social rehabilitation (Kotsougiani-Fischer et al., 2020; Rome, 2016), there is little research investigating the effectiveness of this approach in many other neuropathic pain conditions including neuropathic axial low back pain.

Despite a variety of screening tools for neuropathic pain, of the four tools explored here, only PainDETECT and STEP were developed as a screening tool for neuropathic components in low back pain. However, disadvantages are associated with both. Firstly, the PainDETECT has not been validated in the English language. Secondly, the STEP is a relatively new tool and although there is increasing research investigating and applying the tool, it may not be as established as other neuropathic screening tools. Finally, since these screening tools consider radiating pain to be a key characteristic of neuropathic pain and neuropathic axial low back pain presents in the low back area only (without radiating pain) (Henschke et al., 2008; Itz et al., 2013), the reliability and validity of applying the tools to assess neuropathic axial low back pain is unclear and therefore deserving of further research.

4. Conclusion

Although neuropathic axial low back pain is a hotly contested topic in the literature due to controversies surrounding its aetiology, diagnosis, clinical course, prognosis and treatment options, it presents a

challenge to practitioners and should be carefully considered when a patient presents with localised acute or chronic low back pain. In particular, care should be taken when patients present with gain of function sensory signs and no loss of function, as it is possible this may be nociceptive axial low back pain rather than neuropathic axial low back pain. Application of the possibility for acute axial low back pain to progress to neuropathic axial low back pain should be embedded in a body of research that works towards developing a standardised, validated and reliable system for assessing and identifying neuropathic axial low back pain, including robust investigation of neuropathic screening tools when applied in neuropathic axial low back pain. This is important for patients, as this research would work towards facilitating earlier stratification and promoting more rapid referral for appropriate treatment in specialist centres for neuropathic axial low back pain with biopsychosocial and multidisciplinary involvement. Of course, this should be combined with educational studies that aim to improve awareness of this condition, so that an individual presenting with neuropathic axial low back pain is not missed. In turn, this will improve awareness, assessment and visibility of neuropathic axial low back pain in community settings, ultimately leading to changes in practice and behaviour amongst healthcare professionals which will bring positive benefit to patients.

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Declaration of competing interest

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