Using screening tools to identify neuropathic pain

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1. Introduction

It is widely accepted that the unique painful and non-painful sensations in neuropathic pain are the result of particular mechanisms, and that specific management strategies for neuropathic pain should be applied to tackle them. Ideally, the treatment of chronic pain should be directed at eliminating the cause of pain, but in reality this is rarely possible. The management of chronic pain is therefore often limited to reducing the intensity of such pain and associated symptoms.

Pain is essentially a subjective phenomenon described with patient-specific symptoms and expressed with a certain intensity. It therefore makes sense to examine the value of verbal descriptors and pain qualities as a basis for distinguishing neuropathic pain from other types of chronic pain. Work by Dubuisson and Melzack (1976) and later by Boureau et al. (1990) supported anecdotal opinion that key words might be discriminatory for neuropathic pain. In the last 5 years, much research has been undertaken to develop screening tools for this purpose. These tools are based on verbal pain description with, or without, limited bedside testing. This paper reviews the strengths and weaknesses of such tools.

2. Current screening tools for neuropathic pain

2.1. Leeds Assessment of Neuropathic Symptoms and Signs (LANSS)

The LANSS was the first tool to be developed and contains 5 symptom items and 2 clinical examination items, and is easy to score within clinical settings (Bennett, 2001). It has recently been validated as a self-report tool, the S-LANSS (Bennett et al., 2005). The original LANSS was developed in a sample of 60 patients with chronic nociceptive or neuropathic pain and validated in a further sample of 40 patients. Sensitivity and specificity in the latter group were 85% and 80%, respectively, compared to clinical diagnosis.

The LANSS has subsequently been tested and validated in several settings (e.g. Potter et al., 2003; Yucel et al., 2004; Kaki et al., 2005) with sensitivity and specificity ranging from 82% to 91% and 80% to 94% respectively, compared to clinical diagnosis. Although the LANSS was not designed as a measurement tool, it has also shown sensitivity to treatment effects (Khedr et al., 2005). Positive scores on the LANSS or S-LANSS identify patients with pain of predominantly neuropathic origin (POPNO) i.e., pain that is dominated by neuropathic mechanisms.

2.2. Neuropathic Pain Questionnaire (NPQ)

The NPQ consists of 12 items that include 10 related to sensations or sensory responses, and 2 related to affect (Krause and Backonja, 2003). It was developed in 382 patients with a broad range of chronic pain diagnoses. The discriminant function was initially calculated on a random sample of 75% of the patients, and then cross-validated in the remaining 25%. The NPQ demonstrated 66% sensitivity and 74% specificity compared to clinical diagnosis in the validation sample. The short form of the NPQ maintained similar discriminative properties with only 3 items (numbness, tingling and pain increase in response to touch) (Backonja and Krause, 2003).

2.3. Douleur Neuropathique en 4 questions (DN4)

The DN4 was developed in 160 patients with either neuropathic or nociceptive pain and consists of 7 items related to symptoms and 3 related to clinical examination (Bouhassira et al., 2005). The DN4 is easy to score and a total score of 4 out of 10 or more suggests neuropathic pain. The DN4 showed 83% sensitivity and 90% specificity when compared to clinical diagnosis in the development study. The 7 sensory descriptors can be used as a self-report questionnaire with similar results (Bouhassira et al., 2005). The tool was developed and validated in French and is being translated into other languages.

2.4. painDETECT

painDETECT was developed and validated in German (Freynhagen et al., 2005, 2006) and incorporates an easy to use patient-based (self-report) questionnaire with 9 items that do not require a clinical examination. There are 7 weighted sensory descriptor items (never to very strongly) and 2 items relating to the spatial (radiating) and temporal characteristics of the individual pain pattern. This questionnaire was validated in a multicentre study of 392 patients with either neuropathic (n = 167) or nociceptive pain (n = 225), as well as a population of patients with low back pain. The tool correctly classified 83% of patients to their diagnostic group with a sensitivity of 85% and a specificity of 80%. It is also available in English.

2.5. ID-Pain

ID-Pain consists of 5 sensory descriptor items and 1 item relating to whether pain is located in the joints (used to identify nociceptive pain); it also does not require a clinical examination (Portenoy, 2006). The tool was developed in 586 patients with chronic pain of nociceptive, mixed or neuropathic etiology, and validated in 308 patients with similar pain classification. The tool was designed to screen for the likely presence of a neuropathic component to the patient's pain. In the validation study, 22% of the nociceptive group, 39% of the mixed group, and 58% of the neuropathic group scored above 3 points, the recommended cut-off score.

2.6. Screening tool content

Despite the differences in development of these tools, all five make use of similar language to discriminate patients with neuropathic pain from those with other types of chronic pain with up to 80% sensitivity and specificity (see Table 1). This is powerful evidence for the reliability and validity of this approach, though further validation of these standardized tools is needed across cultures and languages. Their use by other clinicians and researchers is needed to reach consensus on which tool is most suited for a particular context or task.

3. Limitations

3.1. Independent validation

The conceptual basis of these tools is that they standardize distinguishing features associated with neuropathic pain and attempt to reduce a comprehensive clinical evaluation to few key criteria in order to make this process more reproducible. The inevitable overlap with the gold standard clinical assessment introduces a bias that restricts the evaluation of a tool's validity and is probably a limitation of their use. However, studies which used demonstrable nerve lesion as a gold standard ended with questionnaires with similar content to those that did not (Bennett et al., 2005; Bouhassira et al., 2005).

3.2. Complex relationship between symptoms and pain mechanisms

A complex relationship exists between disease etiology and pain mechanisms, such that any symptoms or signs that indicate the presence of neuropathic pain do not readily translate into particular pain mechanisms (Scholz and Woolf, 2002; Jensen and Baron, 2003; Backonja and Argoff, 2005; Baron, 2006). This is illustrated by a recent study that compared the results of detailed sensory testing and verbal pain description using the short form McGill Pain Questionnaire (Rasmussen et al., 2004a). The authors proposed clinical criteria for neuropathic pain-based on pain etiology and presence of sensory loss, and labeled patients as having 'unlikely', 'possible' and 'definite' neuropathic pain. The authors found no differences in verbal description across the groups, and demonstrated considerable variation in sensory abnormalities (e.g. 57% of the 'unlikely' neuropathic pain group had sensory abnormalities).

4. Role of screening tools in clinical practice and research

4.1. Bridging the gap between definition and diagnosis

The International Association for the Study of Pain (IASP) defines neuropathic pain as 'pain initiated or caused by a primary lesion or dysfunction in the nervous system' (Merskey and Bogduk, 1994). This definition appears simple to use in clinical practice, but in fact it describes two broad categories of potential underlying pain mechanisms and not how to recognize them. Patients typically present with symptoms rather than easily recognizable neurological lesions. Clinicians then have to work through these verbal descriptions without a reference standard for what is a symptom of neuropathic pain because none were included in the IASP definition.

In most cases of chronic pain, it is difficult to establish the presence or absence of nerve dysfunction, regardless of symptoms (Aggarwal et al., 2006). Many clinicians that manage patients with chronic pain, in both primary and secondary care, do not have adequate skill or

time for a thorough neurological examination. Neither do they have easy access to quantitative sensory testing and so treatment decisions are supported by basic clinical evidence alone.

Until consensus is agreed on a diagnostic approach to neuropathic pain, screening tools will serve to identify potential patients with neuropathic pain, particularly by non-specialists and this is probably their chief clinical strength. Their ease of use by professionals and patients alike, in clinic or via telephone or internet, makes these screening tools attractive because they provide immediately available information. Clinicians should then be alerted to undertake further assessment, which may subsequently influence management decisions. Screening tools fail to identify about 10–20% of patients with clinician diagnosed neuropathic pain indicating that they may offer guidance for further diagnostic evaluation and pain management but clearly, they do not replace clinical judgment.

4.2. Standardizing identification of patients in research studies

The lack of clinical criteria that result from the IASP definition is likely to result in significant variance between clinicians when recruiting patients to research studies and makes study populations difficult to compare. Commonly, authors of research studies either focus on single disease groups or present lists of etiologies to support their classification of neuropathic pain. Although this approach offers some face validity, it does not allow for standardized comparisons regarding the impact of any specific intervention on pain qualities.

Screening tools can be used as standardized case identification tools in epidemiological studies, and this is probably their chief research strength. The lack of reliable epidemiological data has hampered progress in understanding the clinical impact of neuropathic pain and associated features. Studies using the S-LANSS (Torrance et al., 2006) and painDETECT (Freynhagen et al., 2006) indicate that standardized tools improve the quality of epidemiological data, and similar ongoing studies using DN4 will report soon. Standardized screening tools for neuropathic pain may also be useful in future trials of new therapies because they might help assess treatment efficacy for a specific symptom, or symptom combination, rather than to a disease entity (Jensen, 2005).

4.3. Improving sensitivity in clinical measurement

An important challenge facing clinical research is to reduce the gap between the rapid progress made by basic science, which has revealed a multitude of underlying mechanisms, and the slow progress in clinical practice, where standardizing measurement approaches has been difficult.

Without specific neuropathic pain screening tools, it may be difficult to separate patients into categories of diagnostic certainty (Rasmussen et al., 2004a). One study compared responses to the S-LANSS and the Neuropathic Pain Scale (a measurement tool rather than a screening tool (Galer and Jensen, 1997) with clinician ratings of certainty in 200 chronic pain patients and illustrates the need for a standardized approach (Bennett et al., 2006). In this study, three groups of ‘unlikely’, ‘possible’ and ‘definite’ neuropathic pain were formed and significant differences in S-LANSS and Neuropathic Pain Scale scores were found between the groups. Using more sensitive tools for verbal description, a spectrum phenomenon was demonstrated for chronic pain, with various expressions of neuropathic features. The concept that chronic pain may be more or less neuropathic is novel, and relatively untested, but seems to have

construct validity (Backonja, 2003; Attal and Bouhassira, 2004; Bennett et al., 2006) and fits well with basic science opinion regarding chronic pain mechanisms (Bennett, 2006).

4.4. Screening tools in further research

Despite the widespread acceptance of the need to identify patients with neuropathic pain, what evidence exists to support this approach? One study demonstrated that clinical examination did not predict the outcome of therapy with imipramine or gabapentin in patients with suspected neuropathic pain. (Rasmussen et al., 2004b). A critical analysis of previous clinical trials concluded that despite the logic of a mechanism-based approach to therapy, evidence supporting its success remains inconclusive (Finnerup and Jensen, 2006). An intriguing research question is therefore ‘do patients that score positively on these screening tools respond differentially to therapy from those that do not, regardless of exact pathological mechanism?’

Meanwhile, it is likely that neuropathic pain screening tools will gain increasing acceptance and their common features may indeed form the basis of forthcoming clinical diagnostic criteria.

Table 1
Comparison of items within five neuropathic pain screening tools (*shaded boxes highlight features shared by two or more tools*)

	LANSS ^a	DN4 ^a	NPQ	painDETECT	ID Pain
<i>Symptoms</i>					
Pricking, tingling, pins and needles	+	+	+	+	+
Electric shocks or shooting	+	+	+	+	+
Hot or burning	+	+	+	+	+
Numbness		+	+	+	+
Pain evoked by light touching	+		+	+	+
Painful cold or freezing pain		+	+		
Pain evoked by mild pressure				+	
Pain evoked by heat or cold				+	
Pain evoked by changes in weather			+		
Pain limited to joints ^b					•
Itching		+			
Temporal patterns				+	
Radiation of pain				+	
Autonomic changes	+				
<i>Clinical examination</i>					
Brush allodynia	+	+			
Raised soft touch threshold		+			
Raised pin prick threshold	+	+			

^a Tools that involve clinical examination.

^b Used to identify non-neuropathic pain.

Acknowledgements

The authors acknowledge support from Pfizer Global Pharmaceuticals in sponsoring a workshop ‘Neuropathic pain screening tools’ held in Frankfurt, Germany, in February 2006. This paper reflects the independent views of the authors and not necessarily those of Pfizer. M.I.B. will act as guarantor.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.pain. 2006.10.034.

References

- Aggarwal VR, McBeth J, Zakrzewska JM, Lunt M, Macfarlane GJ. The epidemiology of chronic syndromes that are frequently unexplained: do they have common associated factors? *Int J Epidemiol* 2006;35:468–76.
- Attal N, Bouhassira D. Can pain be more or less neuropathic? (Editorial). *Pain* 2004;110:510–1.
- Backonja MM. Defining neuropathic pain. *Anesth Analg* 2003;97:785–90.
- Backonja MM, Krause SJ. Neuropathic Pain Questionnaire – short form. *Clin J Pain* 2003;19:315–6.
- Backonja MM, Argoff CE. Neuropathic pain: definition and implications for research and therapy. *Journal of Neuropathic Pain and Symptom Palliation* 2005;1:11–7.
- Baron R. Mechanisms of disease: neuropathic pain – a clinical perspective. *Nat Clin Pract Neurol* 2006;2:95–106.
- Bennett G. Can we distinguish between inflammatory and neuropathic pain? *Pain Res Manag* 2006;11:11A–5A.
- Bennett MI. The LANSS Pain Scale: the Leeds assessment of neuropathic symptoms and signs. *Pain* 2001;92:147–57.
- Bennett MI, Smith BH, Torrance N, Potter J. The S-LANSS score for identifying pain of predominantly neuropathic origin: validation for use in clinical and postal research. *J Pain* 2005;6:149–58.
- Bennett MI, Smith BH, Torrance N, Lee AJ. Can pain be more or less neuropathic? Comparison of symptom assessment tools with ratings of certainty by clinicians. *Pain* 2006;122:289–94.
- Bouhassira D, Attal N, Alchaar H, Boureau F, Bruxelles J, Cunin G, et al. Comparison of pain syndromes associated with nervous or somatic lesions and development of a new neuropathic pain diagnostic questionnaire (DN4). *Pain* 2005;114:29–36.
- Boureau F, Doubre JF, Luu M. Study of verbal description in neuropathic pain. *Pain* 1990;42:145–52.
- Dubuisson D, Melzack R. Classification of clinical pain descriptions by multiple group discriminant analysis. *Exp Neurol* 1976;51:480–7.
- Finnerup NB, Jensen TS. Mechanisms of disease: mechanism-based classification of neuropathic pain – a critical analysis. *Nat Clin Pract Neurol* 2006;2:107–15.
- Freynhagen R, Tölle TR, Baron R. painDETECT – ein Palmtopbasiertes Verfahren für Versorgungsforschung, Qualitätsmanagement und Screening bei chronischen Schmerzen. *Akt. Neurol* 2005;34:641.
- Freynhagen R, Baron R, Gockel U, Tölle T. painDetect: a new screening questionnaire to detect neuropathic components in patients with back pain. *Curr Med Res Opin* 2006;22:1911–20.
- Galer BS, Jensen MP. Development and preliminary validation of a pain measure specific to neuropathic pain: the Neuropathic Pain Scale. *Neurology* 1997;48:332–8.
- Jensen MP. Using pain quality assessment measures for selecting analgesic agents. *Clin J Pain* 2005;22:S9–S13.
- Jensen TS, Baron R. Translation of symptoms and signs into mechanisms in neuropathic pain. *Pain* 2003;102:1–8.
- Kaki AM, El-Yaski AZ, Youseif E. Identifying neuropathic pain among patients with chronic low-back pain: use of the Leeds Assessment of Neuropathic Symptoms and Signs pain scale. *Reg Anesth Pain Med* 2005;30:422–8.
- Khedr EM, Kotb H, Kamel NF, Ahmed MA, Sadek R, Rothwell JC. Long lasting antalgic effects of daily sessions of repetitive transcranial magnetic stimulation in central and peripheral neuropathic pain. *J Neurol Neurosurg Psychiatry* 2005;76:833–8.
- Krause SJ, Backonja MM. Development of a Neuropathic Pain Questionnaire. *Clin J Pain* 2003;19:306–14.
- Merskey H, Bogduk N. Classification of chronic pain. Seattle: IASP Press; 1994.

- Portenoy R. for the ID Pain Steering Committee. Development and testing of a neuropathic pain screening questionnaire: ID Pain. *Curr Med Res Opin* 2006;22:1555–65.
- Potter J, Higginson IJ, Scadding JW, Quigley CW. Identifying neuropathic pain in patients with head and neck cancer: use of the Leeds Assessment of Neuropathic Symptoms and Signs Scale. *J R Soc Med*. 2003;96:379–83.
- Rasmussen PV, Sindrup SH, Jensen TS, Bach FW. Symptoms and signs in patients with suspected neuropathic pain. *Pain* 2004a;110:461–9.
- Rasmussen PV, Sindrup SH, Jensen TS, Bach FW. Therapeutic outcome in neuropathic pain: relationship to evidence of nervous system lesion. *Eur J Neurol* 2004b;11:545–53.
- Scholz J, Woolf CJ. Can we conquer pain? *Nat Neurosci* 2002;5:1062–7.
- Torrance N, Smith BH, Bennett MI, Lee AJ. The epidemiology of chronic pain of predominantly neuropathic origin. Results from a general population survey. *J Pain* 2006;7:281–9.
- Yucel A, Senocak M, Kocasoy Orhan E, Cimen A, Ertas M. Results of the Leeds assessment of neuropathic symptoms and signs pain scale in Turkey: a validation study. *J Pain* 2004;5:427–32.