



Screening and Measurement Tools for Neuropathic Pain: Their Role in Clinical Research and Practice

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ABSTRACT

Pain, which is an objective phenomenon, commonly originates from activation of primary nociceptive afferents by current or potential stimuli due to tissue damage and the processing of these activities within the nociceptive system. This is a complex experience of somatic mechanisms and psychological influence (affective & cognitive). Pain categorizes as nociceptive pain and neuropathic pain. Pain is a subjective condition that cannot be objectively measured; for this reason, self patient perspective is crucial. Neuropathic pain acts as an activation of pain pathway and it can occur due to the injury of peripheral nerves and posterior roots (peripheral neuropathic pain) and spinal cord and brain (central pain). Neuropathic pain is thought to a result of unique sensation, hence its makes more than sense to use verbal description for distinguishing neuropathic pain from tissue injury. For these reasons, screening and measurement tools were developed. Recently, several screening and measurement tools have been developed to discriminate the nociceptive and neuropathic pain. Screening tools (Douleair Neuropathique en 4 questions, ID-Pain) alert the clinician about possible presence of neuropathic pain mechanisms. Measurement tools assess the intensity of particular qualities of neuropathic pain. Both types of tools can improve measurement sensitivity within clinical trials and epidemiological research.

Keywords: Neuropathic, Nociceptive, Pain, Screening, Stimuli.

INTRODUCTION

Pain commonly originates from activation of primary nociceptive afferents by current or potential stimuli due to tissue damage and processing of these activities within the nociceptive system. It is complex experience of somatic mechanisms and psychological influence (affective & cognitive).¹ Recently, a fundamental mechanism based classification of pain has been proposed. Those pain categories are nociceptive pain and neuropathic pain. Neuropathy is the disturbance of function or pathological changes in a nerve. In the year 2008 The International Association for the Study of Pain (IASP) defined neuropathic pain as "pain arising as a direct consequence of a lesion or disease affecting the somatosensory system". It thought that neuropathic pain arises as an activation of pain pathway and it can occur due to the injury of peripheral nerves and posterior roots(peripheral neuropathic pain) and spinal cord and brain (central pain).¹

Signs of neuropathic pain can be related to the tingling, itching, and burning sensations. The locality of the pain is also an important indicator to determine the origin and the source of pain, which usually originates from the peripheral nerves and extends to the central nerves. However, these sensations of pain can be furthered analyzed on the molecular basis through signal transduction. Some key players involved during pain signaling may include the release of neurotransmitters and neuropeptides such as glutamate and substance P; receptors such as the AMPA, NMDA, and Glutamate receptors; the enzymes such as AMP-activated protein

kinase activators; and the gate keepers which include the sodium and calcium channels. In addition, brain-derived neurotrophic factors (BDNF), nerve growth factors (NGF), and glia-cell derived neurotrophic factors (GDNF) also influence neuropathic pain (Figure 1). Neurotrophins, which are usually involved in the development of sensory systems and neuronal plasticity, can mediate and indicate the underlying mechanisms of neuropathic pain. Moreover, a number of other neuropeptides such as endomorphins, dynorphin A, and galanin can also induce nerve stimulation. The modulation and alteration of each player in the signal transductions cascade contribute to the primary afferent hyper excitability; all in all, leading to the perception of neuropathic pain.²

Clinical Features of Neuropathic Pain

Neuropathic pain is highlighted by a number of common features at the time of clinical experience of pain like the symptoms and signs of spontaneous and evoked pains (Figure 2). None are pathognomonic but their presence may point out to a diagnosis of neuropathic pain. It is important to actively seek out these features, especially in patients with severe pain.

Spontaneous pain become continuous or paroxysmal and occurs without apparent stimulation. Examples of spontaneous pains that are continuous in nature include unpleasant or abnormal sensations felt in the skin (dysaesthesias) described as burning, tingling, itching or pins and needles. Deeper pain may be described as aching, gnawing, cramping or crushing. Paroxysmal



elements are often described as stabbing, shooting or electric shock-like pains.³

Evoked pains where an ordinary physical stimulus produces an unusual or exaggerated sensation of pain include allodynia and hyperalgesia. Allodynia is a kind of pain due to a stimulus which does not normally provoke pain. Temperature or physical stimuli can provoke allodynia, and it often occurs after injury to a site. Hyperalgesia is an increased sensitivity to pain, which

caused by damage of nociceptors or peripheral nerves. Sometimes temporarily increased sensitivity to pain occurs as part of sickness behavior, which may be an evolved response to infection.

Other symptoms that may support to diagnosis of neuropathic pain include descriptions of numbness areas or symptoms of concurrent motor or autonomic nerve involvement.³

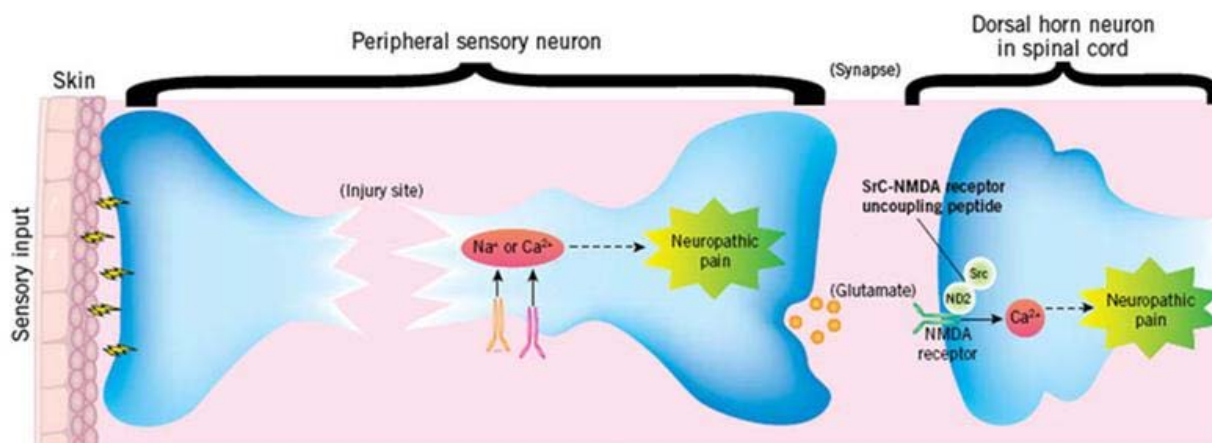


Figure 1: Neuropathic pain transmission pathway

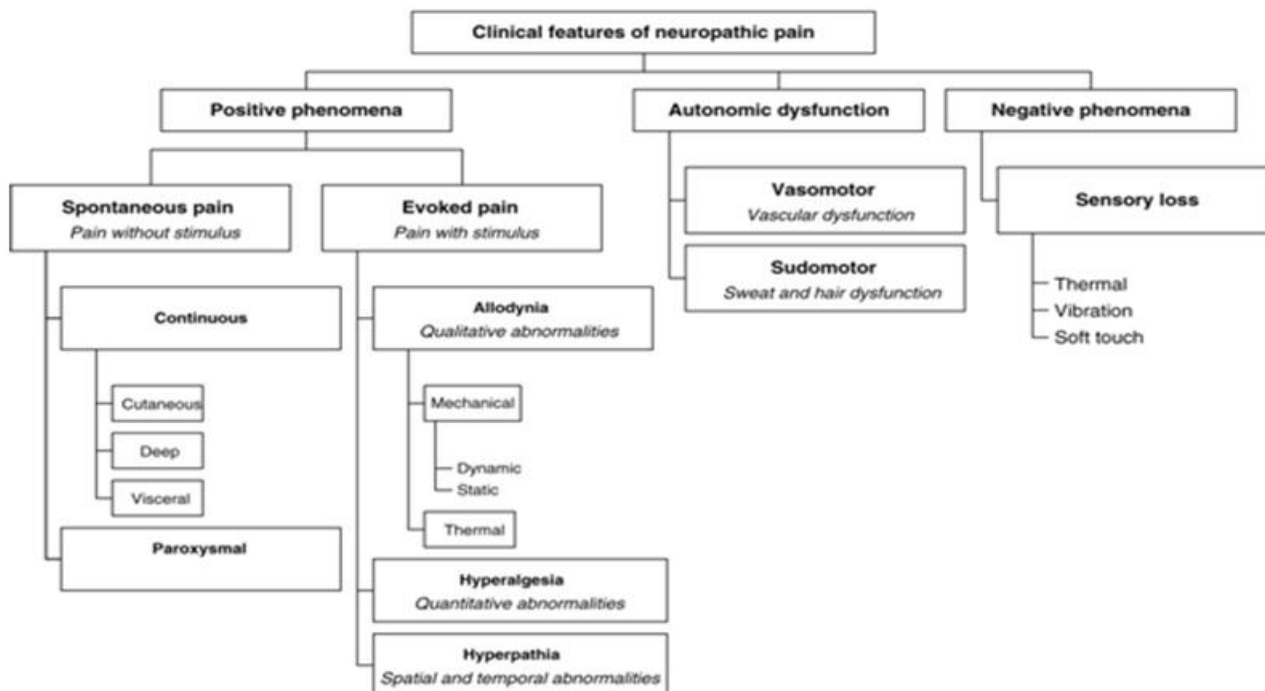


Figure 2: Organizational chart representing clinical features of neuropathic pain

Clinical Assessment

Pain is a complex sensation which strongly depends on cognitive, emotional, and educational influences. Identification of neuropathic pain in clinical practice is not always straightforward. At present, there are no recognized guidelines for the assessment of neuropathic pain. However, the International Association for the Study of Pain has been developing various diagnostic criterias which shall help to address this. Hence there is a pressing

need for tools which can measure pain objectively. We can distinguish four different levels of “objectivity”:

- (1) Laboratory tests that use quantitative tools and measure an objective response;
- (2) Quantitative sensory testing, a measure that despite using quantitative, graded stimuli inevitably relies on the patient’s evaluation;
- (3) Bedside examination, which relies on the physician’s experience and the patient’s ability and willingness to collaborate; and

(4) Pain questionnaires, tools that depend entirely on the patient.⁴

The term clinical assessment of neuropathic pain may be classified into two distinct types of assessment: - Assessing pain and Diagnosis of pain.³

Assessing pain

Here, all neuropathic pains can be projected. They are perceived within the innervation territory of the damaged nerve, root, or pathway due to the somatotopic organization of the primary somatosensory cortex (Figure 3) Pain drawings are a good tool to document the location of pain.^{5,6}

The intensity of pain can be assessed verbally (mild–moderate–severe–excruciating), numerically (on a 0–10 scale), or with a visual analogue scale (VAS) described latter. If there are several components of pain (e.g., continuous ongoing pain and superimposed lancinating pain), the intensity of both components should be assessed separately.⁷ Although neuropathic pain is often described as burning, tingling etc, no single feature of pain is diagnostic for neuropathic pain. However, combinations of certain symptoms, pain descriptors, and bedside findings increase the probabilities of diagnosis of neuropathic pain.¹

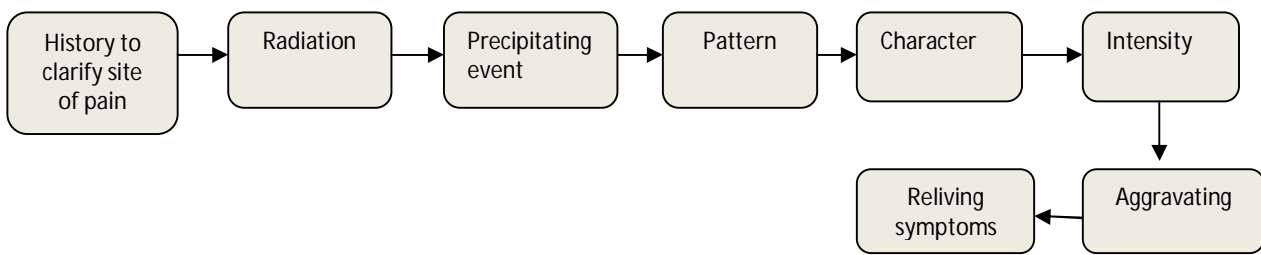


Figure 3: Assessment of pain generates process

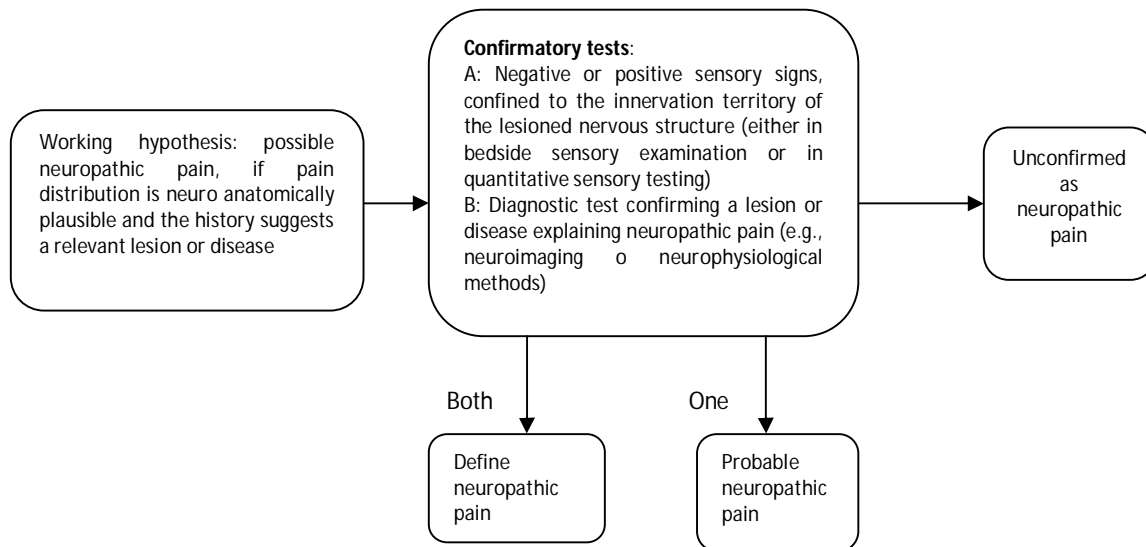


Figure 4: Flow chart of a grading system for neuropathic pain

Diagnosing neuropathic (as opposed to non-neuropathic) pain

Recognition of neuropathic pain is based on careful clinical examination. The history of such diagnosis should include questions about the location, intensity, character, and temporal profile of the pain, along with possible exacerbating factors. Concomitant symptoms should also be queried⁸. The procedure of diagnosing neuropathic pain can be defined as given in the below flowchart (Figure 4).

Assessment of somatosensory modalities beside examination

Location, quality and intensity of pain should included in the examination of pain during which information on

both spontaneous and evoked pains as well as all relevant clinical symptoms and signs should be recorded. Without detecting neuropathic signs in case of neuronal damage; a detail neurological examination is invaluable. There is a need to include assessment of motor and sensory function, reflexes, and some kind of autonomic function like skin perfusion or sweating. Sensory deficits should be neuroanatomically consistent before concluding the presence of neuropathic pain. Using simple equipment it is possible to assess both different types of sensory nerve fibres and their respective central channels in brain. Reports suggest that non-painful stimulus is mediated by thinly myelinated Aδ fibres that protect the brain.¹

Quantitative Sensory Testing (QST)

Quantitative sensory testing (QST) analyzes the perception in response to external stimuli of controlled intensity (Table 1). Pain thresholds are determined by applying stimuli to the skin in an ascending and descending order of magnitude. Mechanical sensitivity for tactile stimuli is measured with plastic filaments that produce graded pressures, such as the Von-Frey hairs, pinprick sensation with weighted needles, and vibration sensitivity with an electronic vibrometer. QST is subjective (psychophysical) method that requires cooperation of patient at the time of investigation. QST also mimics the

natural environmental stimulus like thermal, mechanical and chemical stimuli. The purpose of this test has been to observe the performance of the somatosensory system from the peripheral receptors located at nerve fibre terminals in the skin up to the brain. Thresholds can be quantified at the time of measuring sensitivity of patient towards stimuli at a specific intensity.

QST allows a large set of sensory examination procedures that provide all relevant submodalities of the somatosensory system (peripheral receptor, C, A δ , A β fibres, from central pathway to brain).^{1,9}

Table 1: Assessment of pain mediated by different peripheral and central somatosensory channels

Type of stimulus	Peripheral sensory channel	Central pathway	Bedside examination	QST
Thermal				
Cold	A δ	Spinothalamic	Cold reflex hammer, cold and warm Thermorollers or test-tubes device	Computer controlled thermal testing device
Warmth	C	Spinothalamic		
Cold Pain	A δ , C	Spinothalamic		
Heat pain	A δ , C	Spinothalamic		
Mechanical				
Static light touch	A β	Lemniscal	Q-Tip	Calibrated von Frey Hairs
Vibration	A β	Lemniscal	Tuning Fork (TF)	Vibrometer
Brushing	A β	Lemniscal	Brush/Cotton Swab	Brush
Pin Prick	A δ , C	Spinothalamic	Pin	Calibrated Pin
Blunt pressure	A δ , C	Spinothalamic	Examiner's thumb	Algometer

Screening Tools for Neuropathic Pain

Pain is essentially a subjective phenomenon described with patient-specific symptoms and expressed with certain intensity. Neuropathic pain is thought to be a result of unique sensation, so it makes sense to use verbal description for distinguishing neuropathic pain from tissue injury. Research activity of Dubuisson and Melzack (1976) and Boureau et al. (1990) supports the anecdotal opinion that key words may be helpful in screening of neuropathic pain.^{10,11} In the last few years, much research has been undertaken to develop screening and measurement tools for this purpose. These tools are based on verbal pain description with, or without, limited bedside testing.

Screening tools alert the clinician to the possible presence of neuropathic mechanism but they differ from clinical diagnosis. It's useful to identifying potential neuropathic pain in particularly primary care.

Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) pain scale

The LANSS was the first developed, published and used extensively worldwide of all the screening tools that

attempted to discriminate between neuropathic pain and nociceptive pain.

It contains five symptom based items and two clinical examination based items (allodynia and pinprick testing). It is quite fast procedure that takes five minutes to complete and easy to score within clinical settings¹². It has recently been validated as a self-reporting tool, known as S-LANSS.¹³ It has around 80% and 85% accuracy (sensitivity and specificity) when compared to expert clinician assessment. It helps to validate number of independent studies like cancer neuropathic pain, fibromyalgia, low back pain, and pain clinic population.

Although the LANSS was not designed as a measurement tool, it has also shown sensitivity to treatment effects; for example, patient with intractable neuropathic pain (trigeminal neuralgia or post-stroke pain) showed reduction in LANSS score after successful treatment, which does not appear in placebo. 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.

Douleur Neuropathique en 4 questions (DN4)

The French Neuropathic Pain Group (FNPG) developed a clinician-administered questionnaire called DN4 [Douleur neuropathique 4 questions" (i.e., "neuropathic pain four

questions,” in French, which is after being, translate into other languages)]. Bouhassira et al. (2005) in their study reported a comparison of pain syndromes associated with nervous or somatic lesions utilizing the DN4 tool.¹⁴ In their study, FNPG validated DN4 in 160 patients with either Neuropathic pain or nociceptive pain. The most common etiologies of Neropathic Pain (n= 89) were traumatic nerve injury, postherpetic neuralgia (PHN), and poststroke pain. Nonneurologic conditions included osteoarthritis, inflammatory arthropathies, and mechanical low back pain.

The DN4 contains 10 items for assessing pain. The first seven items are related to the quality of pain (burning, painful cold, electric shocks) and its association to abnormal sensations (tingling, pins and needles, numbness, itching). The other 3 items are related to neurological examination in the painful area (touch hypoesthesia, pinprick hypoesthesia, tactile allodynia).

During the questionnaire, a score of one is given to each positive item and a score of zero is given to each negative item. The total score is the sum of the ten question items. The 7 sensory descriptors can be used as a self-reportive questionnaire with similar results. The DN4 is easy to score, with a total score of 4 or more out of 10 suggesting Neuropathic pain. As compared with clinical diagnosis in the developmental study, the DN4 showed 83% sensitivity and 90% specificity.

painDETECT

Freyenhagen et al. (2005) reported a new screening tool referred to as *painDETECT*, which was developed and validated in Germany.¹⁵ PainDETECT incorporated an easy-to-use, patient-based (self-reportive) questionnaire with 9 items that do not require a clinical examination. There are 7 weighted sensory descriptor based items (“never” to “very strongly”) and 2 items relating to the spatial (“radiating”) and temporal characteristics of the individual pain pattern. The *painDETECT* questionnaire (PD-Q) was developed in cooperation with the German Research Network on Neuropathic Pain and validated in a prospective, multicenter study of 392 patients with either neuropathic pain ($n = 167$) or nociceptive pain ($n = 225$); and which was subsequently applied on a population of roughly 8000 patients with low back pain.

The PD-Q is a reliable screening tool with high sensitivity, specificity and positive predictive accuracy; these were 84% in a palm-top computerised version. The tool correctly classified 83% of patients to their diagnostic group with a sensitivity of 85% and a specificity of 80%.

Neuropathic Pain Questionnaire (NPQ)

Krause and Backonja (2003) published Neuropathic Pain Questionnaire (NPQ) which consists of 12 items, including 10 related to sensations or sensory responses and 2 related to affect.¹⁶ It was developed in 382 patients with a broad range of chronic pain diagnoses. The ability of the tool to discriminate the types of pain 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 when compared with clinical diagnosis in the validation of sample.

They further published a short form of the NPQ, which maintained similar discriminative properties with only 3 items:

- (1) Positive sensory phenomena (“increased pain due to touch”);
- (2) Negative sensory phenomena (“numbness”); and
- (3) Phenomena suggestive of paresthesia and dysesthesia (“tingling”).

ID-Pain

Portenoy (2006) developed ID-Pain in the USA which consists of five sensory descriptor items and one item relating to whether pain is located in the joints (used to identify nociceptive pain); which is not require in clinical examination.¹⁷

The tool was developed in 586 patients with chronic pain of nociceptive, mixed or neuropathic etiology, and was 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.

A cut off score of three or more on ID-pain suggested the possible presence of a neuropathic component to the patient pain. In the validation study, 22% of the nociceptive group, 39% of the mixed group, and 58% of the neuropathic group scored above this cut-off score.

The Standardized Evaluation of Pain (StEP)

Scholz et al. in a recent study developed a new pain assessment tool called StEP (Standardized Evaluation of Pain) that combines 6 interview questions and 10 physical tests. This novel tool assesses pain-related symptoms and signs.¹⁸

To differentiate between the distinct pain phenotypes which showed different reflecting mechanisms, Scholz et al. specifically evaluated the diagnostic usefulness of StEP in patients with low back pain; the most frequent (and often challenging) pain condition. Low back pain may comprise both nociceptive axial and neuropathic radicular pain. Differentiation between nociceptive and neuropathic pain is clinically important because these components require different pain management strategies; and also very important in pharmacological trials. By standardizing the assessment of pain-related symptoms and signs, StEP achieves more than 90% sensitivity and specificity in distinguishing neuropathic from nociceptive pain in patients.

Screening tool content and comparison

To discriminate between patients with neuropathic pain from others types of chronic pain with up to 80% sensitivity and specificity; there is a need that all these



screening tools make uniform usage of language. There is powerful evidence for the reliability and validity of this approach even though being developed in different languages (Table 2). Validation of these standardization

tools is needed across cultures and languages by others researchers to reach a consensus on which tool is most suited for a particular context.¹

Table 2: Comparison of the various questionnaires involved in the screening tools of neuropathic pain. The positive signs indicate items that increase the score while minus sign indicates items that reduce the score

Questionnaires	ID pain	NPQ	Pain DETECT	LANSS	DN4	StEP
Symptoms reported						
Ongoing pain						-
Pricking, tingling pins, needles (any dysesthesia)	+	+	+	+	+	+
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	-					
Itching					+	
Temporal patterns or temporal summation			+			-
Radiation of pain			+			
Autonomic changes	+					
Physical examination						
Abnormal response to cold temperature (decrease or allodynia)						+
Hyperalgesia						+
Abnormal response to blunt pressure (decreased or evoked pain)						+
Decreased response to vibration						+
Brush allodynia				+	+	-
Raised soft touch threshold					+	-
Raised pinprick threshold				+	+	+
Straight-leg-raising test						+
Skin changes						-

Measurement Tools for Neuropathic Pain

Measurement tools assess the intensity of particular qualities of neuropathic pain once a diagnosis has been made. These ancillary tools help in the assessment of pain characteristics by measuring instruments, i.e. pain scales, grading systems and questionnaires.

Unidimensional measurement of pain

Unidimensional scales are based on self-assessment of pain; they are easy to use, efficient and demand minimal effort from the examinee. In some instances it may not be possible to obtain reliable self-reports of pain (e.g. patients with impaired consciousness or cognitive impairment, young children, elderly patients, or where there are failures of communication due to language difficulties, inability to understand the measures,

unwillingness to cooperate or severe anxiety). In these circumstances other methods of pain assessment are needed.

There are no objective measures of 'pain' but associated factors such as hyperalgesia (e.g. mechanical withdrawal threshold), the stress response (e.g. plasma cortisol concentrations), behavioral responses (e.g. facial expression), functional impairment (e.g. coughing, ambulation) or physiological responses (e.g. changes in heart rate) may provide additional information. Analgesic requirements (e.g. patient-controlled opioid doses delivered) are commonly used as *post hoc* measures of pain experienced.¹⁹ Recording pain intensity as 'the fifth vital sign' aims to increase awareness and utilization of pain assessment and may lead to improved acute pain management.^{20,21} Regular and repeated measurements of

pain should be made to assess ongoing adequacy of analgesic therapy. An appropriate frequency of reassessment will be determined by the duration and severity of the pain, patient needs and response, and the type of drug or their intervention.

Visual Analogue Scale (VAS)

VAS consists of a 100 mm horizontal line with verbal anchors at both ends and no tick marks. The patient is asked to mark the line and the 'score' is the distance in millimeters from the left side of the scale to the mark. VAS are the most commonly used scales for rating pain intensity in research, with the words 'no pain' at the left end and 'worst pain imaginable' at the right. It is not suitable for older patients with vision and cognitive deficits.

VAS can also be used to measure other aspects of the pain experience (e.g. affective components, patient satisfaction, side effects). Assessment of pain immediately after surgery can be more difficult and lead to greater inter patient variability in pain scores because of transient anesthetic-related cognitive impairment and decreases in visual acuity.

A 'pain meter' (PAULA) which used five colored emoticon faces on the front of a ruler and corresponding VAS scores on the back, allowed patients to move a slider to mark the pain they were experiencing, resulted in less variance than pain scores obtained from a standard VAS.²²

VAS ratings of greater than 70 mm are considered to be indicative of 'severe pain' while readings of 0 to 5 mm meant 'no pain', 5 to 44 mm meant 'mild pain' and 45 to 74 mm meant 'moderate pain'.^{23,24} A reduction in pain intensity by 30% to 35% has been rated as clinically meaningful by patients with postoperative pain, acute pain in the emergency department, breakthrough cancer pain and chronic pain.²⁵⁻²⁸ These scales have the advantage of being simple and quick to use, allow for a wide choice of ratings and avoid imprecise descriptive terms.²⁹ However; these scales require more concentration and coordination, needing physical devices, are unsuitable for children under 5 years and may also be unsuitable in up to 26% of adult patients.³⁰

Verbal numerical rating scales (VNRS)

VNRS is often preferred because they are simpler to administer, give consistent results and correlate well with the VAS.³¹ Recall of pain intensity using the VNRS over the previous 24 hours usually showed that it can be a reasonable indicator of average pain experienced by the patient during same time duration.³²

In VNRS, patients are usually asked to rate their pain and pain relief on a 5-point standard Likert scale, prior to and after morphine administration as follows:

0 = no pain relief

1 = a little pain relief

2 = moderate pain relief

3 = a lot of pain relief and

4 = complete pain relief.

The VNRS reductions associated with these pain relief ratings were 9.0, 7.5, 3.9, 2.1 and -0.1 respectively.³³

The Functional Activity Scale score (FAS score)

It is a simple three-level ranked categorical score designed to be applied at the point of care²⁹. Its fundamental purpose is to assess whether the patient can undertake appropriate activity at their current state of pain control and act as a trigger for intervention. The patient is asked to perform the activity, or is taken through the activity in the case of structured physiotherapy (joint mobilization) or nurse-assisted care (e.g. ambulation, turned in bed) etc. The ability to complete the activity was then assessed by using the FAS as:

A — no limitation; the patient is able to undertake the activity without limitation due to pain (pain intensity score is typically 0 to 3)

B — mild limitation; the patient is able to undertake the activity but experiences moderate to severe pain (pain intensity score is typically 4 to 10) and

C — significant limitation; the patient is unable to complete the activity due to pain, or pain treatment-related side effects, in this pain intensity scores is independent.

This score is then used to track effectiveness of analgesia on function and trigger interventions if required. Disadvantages of the FAS score are that it has not been independently validated and clinical staff need to be educated in its application.

Descriptive scale

Descriptive scale is used to grade pain using descriptors, such as no pain, mild pain, and moderate, severe, extreme. If presented verbally, it is easily understandable even to patients with advanced stages of dementia.³⁴

Multidimensional Measurement of Pain

Multidimensional assessment of pain involves application of a range of different instruments and provides further information about the characteristics of the pain and its impact on the individual. Examples include the Brief Pain Inventory, which assesses pain intensity and associated disability and the McGill Pain Questionnaire, which assesses the sensory, affective and evaluative dimensions of pain.³⁵

Fibromyalgia Impact Questionnaires (FIQ)

It was designed to quantitate the overall impact of Fibromyalgia over many dimensions including function, pain levels, fatigue, sleep disturbance and psychological distress. This takes into account the pain history of the past week, so it would be suitable generation of a one-off assessment or as a weekly or monthly symptom diary.



The FIQ scores range from 0 to 100 with the latter number being the worst case: the average score for patients seen by specialist consultants is about 50. The FIQ is widely used to assess changes in Fibromyalgic status.³⁵

Neuropathic pain scale (NPS)

It was designed to assess the distinct pain qualities associated with neuropathic pain.³⁶ The NPS consists of 10 items. Seven of the ten items contain the words intense, sharp, hot, dull, cold, and itchy to characterize the patient's pain and the word sensitive to describe the patient's pain reaction to light touch or clothing. One item describes the time quality of the pain (all the time or some of the time). The ninth item describes the overall unpleasantness of the pain, whereas the last item indicates the intensity of the deep and surface pain.

All these items are rated on a 0 to 10 scale. Four items (sharp, sensitive, cold, itchy) distinguish postherpetic neuralgia from diabetic neuropathy and complex regional pain syndrome. As the characteristics of the pain sensation may indicate the underlying pathophysiologic mechanisms, these may suggest different neuropathic pain syndromes that may have different pathophysiologic mechanisms.

Postherpetic neuralgia may be secondary to neuronal damage and to the central and peripheral nervous systems; the acute inflammatory response results in injury to the cutaneous sensory nerves.³⁶ The investigators also noted that almost all of the NPS items were sensitive to the effects of treatment. The authors recommended that the NPS be used to examine the effects of treatment on the specific dimensions of pain experience of patients with neuropathic pain. In a subsequent publication, the authors confirmed the validity of the NPS in detecting changes in the pain symptoms after treatment and noted potential of the NPS for identifying the differential effects of analgesics on specific pain qualities.³⁷

Neuropathic Pain Symptom Inventory (NPSI)

This measurement tools was developed in France and Belgium, also evaluates the different symptoms of neuropathic pain.^{38, 39} The NPSI allows discrimination and quantification of the distinct and clinically relevant dimensions of neuropathic pain syndromes (spontaneous ongoing pain, spontaneous paroxysmal pain, evoked pain, and paresthesia/dysesthesia) that are sensitive to treatment. The pain may be burning, squeezing, or pressure in character.

The burning pain represents the superficial component, whereas pressure and squeezing pain represent the deep component of the spontaneous ongoing pain. The authors recommended usage of the psychometric properties of the NPSI to characterize subgroups of neuropathic pain patients and to verify the response of the patients to various pharmacologic agents or interventions. The final version of the NPSI includes 12 items; 10 are descriptors

of the different symptoms, and 2 assess the duration of spontaneous ongoing and paroxysmal pain.

A total intensity score is calculated as the sum of the scores of the 10 descriptors. Increases or decreases in the NPSI total score are related to changes in the patient's pain. An English version of the NPSI is also available

The NPS and NPSI evaluate the symptoms of patients with neuropathic pain, determine the efficacy of different treatments, and help to elucidate the mechanism(s) of effect of such treatments. The NPS and NPSI do not differentiate patients with neuropathic pain from patients with non neuropathic pain. The NPS and the NPSI are scales to determine the intensity of the neuropathic pain and follow the response of the patient's symptoms to treatment. The scales are slightly detailed and more applicable to research.

Brief Pain Inventory

The Brief Pain Inventory (BPI) measures the severity of pain and its interference with daily function but is not specifically for neuropathic pain. However, a modified version of the BPI was found to be a valid and reliable measure for the evaluation of painful diabetic peripheral neuropathy. Use 0-10 scales to assess pain at the time of assessment and during the preceding week, how distressing the pain is/was and how much it interferes with daily activities as well as how well treatments are working (Figure 5). They could provide a simple assessment for an effective weekly pain diary.^{38, 39}

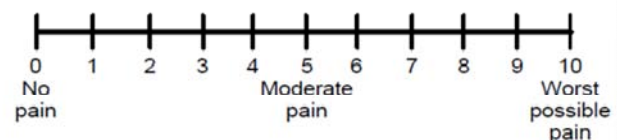


Figure 5: 0-10 Numeric Pain rating scale used in Brief pain inventory

Application Of Screening Tools In Clinical Practice And Research

Bridging the gap between definition and diagnosis

The definition of pain as defined by IASP appears simple to use in clinical practice, but in fact it describes two broad categories of potential underlying pain mechanisms but does not give any guidelines to recognize them. Patients typically present symptoms rather than easily recognizable neurological lesions. Clinicians then need to work through these verbal descriptions without a reference standard. In most cases of chronic pain, it is difficult to establish the presence or absence of nerve dysfunction, regardless of symptoms.³⁹

Many clinicians who manage patients with chronic pain, in both primary and secondary care, do not have adequate skill or time for a thorough neurological examination. They do not have easy access to quantitative sensory testing and so treatment decisions are supported by basic clinical evidence alone. Until

consensus is agreed upon 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.

Screening tools is not the replacement of clinical assessment

Screening tools helps to identify patients with neuropathic pain based on few available key symptom and signs. One of the potential shortcomings of this approach is that it may not detect any unusual presentation of neuropathic pain by patients. Clinicians need to be very careful to undertake further assessment, as this will subsequently influence management decisions.

Further, screening tools fail to identify about 10–20% of patients with clinician diagnosed neuropathic pain, indicating that they may only offer guidance for further diagnostic evaluation and pain management but clearly, they cannot replace clinical judgment.¹

Potential neuropathic pain identified in non specialist setting

This is based on the fact that the neuropathic pain may continue for some prolonged time period. Until consensus is agreed on a diagnostic approach to neuropathic pain, screening tools can only help to identify potential patients with neuropathic pain and this can be identified as the chief clinical strength of these tools, which may be particularly helpful in primary care like non specialist settings.

Screening tools can be used as standardized case identification tools in epidemiological studies. These can be used by non specialists and by patients themselves in clinic or other such settings, where these serve as chief source for providing immediate descriptive information. This can then alert clinicians to undertaken major assessment.¹

Improving sensitivity in clinical measurement

Research activities on neuropathic pain show that they consider clinician assessment as a golden standard reference. But there may be significant variance between, and within the study population which makes the data difficult to compare.

One of the important challenges is to reduce the gap between the rapid progressing basic science and clinical research. Without specific neuropathic pain screening tools, it may be difficult to separate patients into categories of diagnostic certainty.⁴⁰ Studies comparing the various tools indicate the need to standardize every tool on international basis.^{41, 42}

Screening tools in further research

There is a need for comprehensive evidence which shall identify patients with neuropathic pain. Studies have demonstrated that clinical examination may not always predict the outcome of therapy with imipramine or gabapentin in patients with suspected neuropathic pain.^{43,44} To identify possible presence and intensity of neuropathic pain these screening and measurement tools need to be optimized in various languages and combine them with the results of physical examination. StEP tool is one such example where physical examination is combined with patient's report. However, when a patient has been suffering from chronic pain for a prolonged time, the psychological attributes predominates, thereby decreasing the responsiveness to such treatment. In such cases ascertaining the correct pathway of diagnosis becomes an uphill task. In tools like BPI only impact of pain can be assessed irrespective of its origin and cause whereas in NPS, response to treatment can be monitored⁴⁴. There is a need to couple these findings with monitoring of response to treatment to ascertain the effectiveness of these tools.

CONCLUSION

The cause of neuropathic pain often remains unknown, and therefore careful assessment is needed before pain can be labeled as idiopathic or psychogenic. There is a need for development and optimization of various kinds of screening and measurement tools for diagnosing neuropathic pain associated with various levels of damaged nociceptives which shall accurately predict intensity of pain and define a treatment regimen. Ideally, these tools will also monitor the response of interventions, so that pain control can be further optimized. Upon critical analysis of various clinical trials one can conclude that despite the logic of a mechanism-based approach to therapy, 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. Further development of these tools will help to diagnose patients, identify the origin of pain and enable appropriate neuropathic analgesic therapy to be initiated as soon as possible for the mitigation of pain.

REFERENCES

1. Bennett MI, Attal N, Backonja MM, Baron R, Bouhassira D, Freynhagen R, Scholz J, Tölle TR, Wittchen HU, Jensen TS, Using screening tools to identify neuropathic pain, *Pain*, 127(3), 2007, 199–203.
2. Tillu DV, Melemedjian OK, Asiedu MN, Qu N, Felice MD, Dussor G, Price TJ, Resveratrol engages AMPK to attenuate ERK and mTOR signaling in sensory neurons and inhibits incision-induced acute and chronic pain, *Molecular Pain*, 8(5), 2012, doi: 10.1186/1744-8069-8-5 .
3. Callin S, Bennett MI, Assessment of neuropathic pain, *Continuing Education in Anaesthesia Critical Care and Pain*, 8(6), 2008, 210-213.



4. Cruccu G, Anand P, Attal N, Garcia-Larrea L, Haanpää M, Jørum E, Serra J, Jensen TS, EFNS guidelines on neuropathic pain assessment, *European Journal of Neurology*, 11, 2004, 153–162.
5. Bouhassira D, Lantéri-Minet M, Attal N, Laurent B, Touboul C, Prevalence of chronic pain with neuropathic characteristics in the general population, *Pain*, 136(3), 2008, 380-387.
6. Cruccu G, Sommera C, Anand P, Attal N, Baron R, Garcia-Larrea L, Haanpa M, Jensen TS, Serra J, Treede RD, EFNS guidelines on neuropathic pain assessment: revised 2009, *European Journal of Neurology*, 17(8), 2010, 1010-1018.
7. Treede RD, Jensen TS, Campbell JN, Cruccu G, Dostrovsky JO, Griffin JW, Hansson P, Hughes R, Nurmikko T, Serra J, Redefinition of neuropathic pain and a grading system for clinical use: consensus statement on clinical and research diagnostic criteria, *Neurology*, 70, 2008, 1630–1635.
8. Hansson P, Backonja M, Bouhassira D, Usefulness and limitations of quantitative sensory testing: Clinical and research application in neuropathic pain states, *Pain*, 129, 2007, 256–259.
9. Dubuisson D, Melzack R, Classification of clinical pain descriptions by multiple group discriminant analysis, *Experimental Neurology*, 51(2), 1976, 480–487.
10. Boureau F, Doubrere JF, Luu M, Study of verbal description in neuropathic pain, *Pain*, 42(2), 1990, 145-152.
11. Bennett MI, The LANSS Pain Scale: the Leeds assessment of neuropathic symptoms and signs, *Pain*, 92(1-2), 2001, 147–57.
12. 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, *Journal of Pain*, 6, 2005, 149–158.
13. Bouhassira D, Attal N, Fermanian J, Alchaar H, Gautron M, Masquelier E, Rostaing S, Lanteri-Minet M, Collin E, Grisare J, Boureau F, Development and validation of the Neuropathic Pain Symptom Inventory, *Pain* 108, 2004, 248–257.
14. Freynhagen R, Baron, Gockel U, Tölle TR, painDIRECT: A new screening questionnaire to identify neuropathic components in patients with back pain, *Current Medical Research and Opinion*, 22, 2006, 1911-1920.
15. Krause SJ, Backonja MM, Development of a neuropathic pain questionnaire, *The Clinical Journal of Pain*, 19, 2003, 306-314.
16. Portenoy R, Development and testing of a neuropathic pain screening questionnaire: ID Pain, *Current Medical Research and Opinion*, 22, 2006, 1555-1565.
17. Scholz J, Mannion RJ, Hord DE, Griffin RS, Rawal B, Zheng H, Scoffings D, Phillips A, Guo J, Laing RJC, Abdi S, Decosterd I, Woolf CJ, A novel tool for the assessment of pain: Validation in low back pain, *PLoS Med* 6(4), 2009, e1000047, doi: 10.1371/journal.pmed.1000047.
18. Cruccu G, Truini A, Tools for Assessing Neuropathic Pain, *PLoS Med* 6(4), 2009, e1000045. doi:10.1371/journal.pmed.1000045.
19. JCAHO and NPC (2001) Pain: Current Understanding of Assessment, Management and Treatments. www.jcaho.org/news+room/health+care+issues/pm+mono+graphs.htm Joint Commission on Accreditation of Healthcare Organisations and the National Pharmaceutical Council, Inc.
20. Von Korff M, Ormel J, Keefe FJ, Dworkin SF, Grading the severity of chronic pain, *Pain*, 50, 1992, 133–149.
21. Gould TH, Crosby DL, Harmer M, Lloyd SM, Lunn JN, Rees GA, Roberts DE, Webster JA, Policy for controlling pain after surgery: effect of sequential changes in management, *British Medical Journal*, 305(6863), 1992, 1187–1193.
22. Machata AM, Kabon B, Willschke H, A new instrument for pain assessment in the immediate postoperative period, *Anaesthesia*, 64(4), 2009, 392–398.
23. Badariah AAC, Kamalrujan HS, Non-Verbal Pain Assessment: A Literature Review, *The International Medical Journal*, 9(1), 2010, 67-71.
24. Jensen MP, Chen C, Brugger AM, Interpretation of visual analog scale ratings and change scores: a reanalysis of two clinical trials of postoperative pain, *Journal of Pain*, 4(7), 2003, 407–414.
25. Cepeda MS, Africano JM, Polo R, Alcalá R, Carr DB, What decline in pain intensity is meaningful to patients with acute pain, *Pain*, 105(1-2), 2003, 151–157.
26. Lee JS, Hobden E, Stiell IG, Wells GA, Clinically important change in the visual analog scale after adequate pain control, *Academic Emergency Medicine*, 10(10), 2003, 1128–1130.
27. Farrar JT, Portenoy RK, Berlin JA, Kinman JL, Strom BL, Defining the clinically important difference in pain outcome measures, *Pain*, 88, 2000, 287–294.
28. Farrar JT, Young JP, LaMoreaux L, Werth JL, Michael PR, Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale, *Pain*, 94, 2001, 149–158.
29. Gray P, Acute neuropathic pain: diagnosis and treatment, *Current Opinion in Anaesthesiology*, 21(5), 2008, 590-595.
30. Cook AK, Niven CA, Downs MG, Assessing the pain of people with cognitive impairment, *International Journal of Geriatric Psychiatry*, 14(6), 1999, 421–425.
31. Murphy DF, McDonald A, Power C, Measurement of pain: A comparison of the visual analogue with a nonvisual analogue scale, *The Clinical Journal of Pain*, 3(4), 1988 191–97.
32. Jensen MP, Mardekian J, Lakshminarayanan M, Boye ME, Validity of 24-h recall ratings of pain severity: biasing effects of “Peak” and “End” pain, *Pain*, 137(2), 2008, 422–427.
33. Bernstein SL, Bijur PE, Gallagher EJ, Relationship between intensity and relief in patients with acute severe pain, *The American Journal of Emergency Medicine*, 24(2), 2006, 162–166.
34. 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*, 122, 2006, 289–94.

35. Daut RL, Cleeland CS, Flanery RC, Development of the Wisconsin Brief Pain Questionnaire to assess pain in cancer and other diseases, *Pain*, 17(2), 1983, 197–210.
36. Galer B, Jensen M, Development and preliminary validation of a pain measure specific to neuropathic pain, *The neuropathic pain scale*, *Neurology*, 48, 1997, 332–338.
37. Jensen M, Dworkin RH, Gammaitoni AR, Olaleye DO, Oleka N, Galer B, Assessment of pain quality in chronic neuropathic pain and nociceptive pain clinical trials with the neuropathic pain scale, *Journal of Pain*, 6, 2005, 98–106.
38. Melzack R, The short-form McGill Pain Questionnaire, *Pain*, 30(2), 1987, 191–197.
39. 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, *International Journal of Epidemiology*, 35, 2006, 468–476.
40. Rasmussen PV, Sindrup SH, Jensen TS, Bach FW, Symptoms and signs in patients with suspected neuropathic pain, *Pain* 110, 2004, 461–469.
41. Galer BS, Jensen MP, Development and preliminary validation of a pain measure specific to neuropathic pain: the Neuropathic Pain Scale, *Neurology*, 48, 1997, 332–338.
42. Bennett G, Can we distinguish between inflammatory and neuropathic pain, *Pain Research and Management*, 11, 2006, 11A–5A.
43. Rasmussen PV, Sindrup SH, Jensen TS, Bach FW, Therapeutic outcome in neuropathic pain: relationship to evidence of nervous system lesion, *European Journal of Neurology*, 11, 2004, 545–553.

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