

Clinical Examination of a Patient with Possible Neuropathic Pain

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Educational Objectives

1. State the definition of neuropathic pain and describe grading methods to determine clinical certainty of neuropathic pain.
2. Give an overview of the clinical examination for diagnosing neuropathic pain.
3. Discuss the limitations and challenges of clinical examination in diagnosing neuropathic pain and in differentiating it from other types of pain.

The Rationale for Diagnosing Neuropathic Pain

Neuropathic pain causes suffering and disability for many patients and is a well-known public health problem. Neuropathic pain differs from nociceptive pain in terms of symptoms, mechanisms, and therapeutic management [2]. Early diagnosis is a prerequisite for adequate management. Hence, the basics of clinical examination of a patient with suspected neuropathic pain should be familiar to all clinicians treating pain patients. In specialized pain centers, more extensive skills should be available for diagnosing pain conditions, including skilled clinical examination and the availability of laboratory examinations needed to confirm or exclude suspected cause of the pain state.

This chapter explains the crucial role and practical performance of the bedside examination of a pain patient with suspected neuropathic pain. Despite the development of neurophysiological and neuroimaging methods, taking a history and performing a clinical examination of a patient, using simple tools, remain the most important step in the diagnostic process. Basic knowledge of neuroanatomy, sufficient practical training in neurological examination, and an analytic approach in the patient are needed. The accompanying chapters by Truini and Meier review laboratory tools, quantitative sensory testing, and confocal corneal microscopy in assessing patients with possible neuropathic pain.

Definition of Neuropathic Pain

IASP defines neuropathic pain as “pain caused by a lesion or disease of the somatosensory system.” Compared to the former definition, “pain initiated or caused by a primary lesion or dysfunction of the nervous system,” the current definition is more restrictive and precise by necessitating “a lesion or disease” instead of the obscure “dysfunction” and by locating it in the “somatosensory system” instead of the broader “nervous system.” For example, the new definition excludes pain secondary to increased muscle tone in pyramidal or extrapyramidal motor system diseases from neuropathic

pain [9,14]. The lack of structural abnormalities in pain states such as fibromyalgia or complex regional pain syndrome, type I, currently excludes them from neuropathic pain, although there may be subgroups in these diagnostic categories that fulfill the requirement of a recognized lesion in the nervous system [20]. With advances in neuroscience, new conditions are now included in the concept of neuropathic pain, such as primary erythromelalgia, a painful condition caused by a mutation in the *SCCN9A* gene that codes for the voltage-gated sodium channel $Na_v1.7$ [6].

Neuropathic pain is a syndrome caused by a range of different diseases or lesions. Neuropathic pain can arise from damage to the nerve pathways at any point from the terminals of the peripheral nociceptors to the cortical neurons in the brain. It is not known why the same condition is painful in some patients and painless in others. Neuropathic pain is classified as central (originating from damage to the brain or spinal cord) or peripheral (originating from damage to a peripheral nerve, plexus, dorsal root ganglion, or root). Of note, the term “central pain” should never be used to describe chronification of an acute pain (despite producing central changes), as it is reserved for neuropathic pain associated with lesion(s) in the central nervous system.

Neuroanatomy of Neuropathic Pain

The somatosensory system comprises mechanoreception, thermoreception, nociception, proprioception, and visceroreception functions, providing conscious perception of sensory information from the skin, the musculoskeletal system, and the viscera [5]. The somatosensory system can be divided into the dorsal column-lemniscal system and the spinothalamic tract system. The former subserves mechanoreception and proprioception, and the latter thermoreception, nociception, and visceroreception. The two systems project via the ventrobasal and intralaminar groups of thalamic nuclei into a network of somatosensory cortex areas, which include the primary and secondary somatosensory cortex, posterior parietal cortex, posterior and mid-insula, and mid-cingulate cortex. Besides these two main systems, other pathways have been suggested to be involved in mediating somatosensory functions, such as the dorsal spinocerebellar tract (lower limb proprioception), postsynaptic dorsal column pathway (pelvic organ pain), and vagus nerve

(non-painful visceral percepts). Descending tracts are also part of the somatosensory system. These tracts originate in cortical, subcortical, and brainstem regions, importantly including the midbrain periaqueductal gray and rostroventral medial medulla. The projections from the brainstem are both inhibitory and facilitatory. The variable nature of neuropathic pain is not surprising, considering the complexity of the somatosensory system and the myriad of ways it may be affected by disease or injury. The literature on neuropathic pain overemphasizes conscious perception of sensory information from the skin. However, we lack standardized methodology for the assessment of pain from deep tissues (such as muscles and joints) and from viscera, which are the more dominant areas of complaint from patients. [11]

Aims and General Principles of Assessment of a Pain Patient

Assessment of a patient with possible neuropathic pain aims at (1) recognizing what type of pain the patient has—nociceptive pain, neuropathic pain, a combination of them (called “mixed pain”) [2], or neither of them; (2) diagnosing the disease(s) or event(s) that caused the pain; and (3) recognizing the functional limitations, possible comorbidities, and other important aspects related to tailoring the management of the patient. The best clinical tools in pain assessment are the clinician’s capacity to listen to patients as they tell their story, careful observation, and thorough physical examination.

Medical history. It is best to initiate the medical history by permitting patients to fully describe their pain experience as they understand it. The history should include questions about the location, intensity, character, temporal profile, and possible exacerbating factors of the pain. Concomitant symptoms should also be queried. Past medical and surgical history, psychosocial history, and functional history (i.e., the impact of symptoms on level of mobility, activities of daily living, relation with others, sleep, and mood) are also important.

Conscious observation of patients from the very first moment of the appointment—their way of expressing themselves, cognition, movement, gait, and general behavior—is important in giving the physician a general impression and clues about any functional impairment they may have. During the history the

physician formulates hypotheses about the type of pain the patient has and the possible causes of pain.

Physical examination then tests these hypotheses and hence verifies or rejects the suggested explanations for the pain. In neurological examination the findings should be consistent when tested multiple times in multiple ways, and they should be consistent with the pre-examination observation of behavior. If there is any discrepancy between the patient's performance during the history and clinical examination, testing needs to be repeated or modulated so that the clinician can titrate out the real impairment from possible functional variation due to malingering or conversion syndrome.

In addition to general examination, the pain area is inspected and palpated. Next, neurological examination is performed to an adequate extent. Assessment of cranial nerves, motor function, deep tendon reflexes, muscle tone, coordination, gait, and balance is performed in the usual sequence. Sensory examination, which is the most important part of the examination in case of suspected neuropathic pain, is performed next. Touch can be assessed by gently applying cotton wool to the skin, pinprick sensation by the response to sharp pinprick stimuli, thermal sensation by warm and cold objects (e.g., water-filled tubes), and vibration sensation by a 128-Hz tuning fork. The findings in the painful area are compared with the findings in the contralateral area in unilateral pain and in other sites on the proximal-distal axis in bilateral pain. The relation between a stimulus and the perceived sensation may be changed quantitatively (hypo- or hyperphenomena), qualitatively, spatially, and temporally (Table II), and in an individual patient the somatosensory findings are a mosaic of aberrations in different modalities. Sensory loss should be specified with respect to the somatosensory submodalities involved—tactile, thermoreceptive, or nociceptive—to pinpoint the type of somatosensory pathways that are damaged. Sensory gain (hyperphenomena) is basically limited to

the nociceptive submodality. In addition, allodynia to light moving tactile stimuli (dynamic mechanical allodynia), gentle pressure (static mechanical allodynia), innocuous warmth (heat allodynia), or cold (cold allodynia) may occur. It is helpful to document the extent of each abnormal sensory finding on a body template.

Depending on the patient's symptoms, specific tests such as straight leg testing or Tinel's test are performed. Guidelines and review articles are recommended for specific clinical entities such as low back pain [15,16], facial pain [21,25], or peripheral neuropathy [7].

Character of Neuropathic Pain

Neuropathic pain is characterized by spontaneous and provoked pain and negative signs (sensory deficits) reflecting neural damage. Many patients with neural damage only have negative symptoms, but some patients also have positive symptoms such as paresthesias and dysesthesias, because particular pathological processes are engaged that increase pain sensitivity or drive spontaneous activation of the nociceptive pathway. It is not possible to draw conclusions about the etiology of neuropathic pain from the clinical characteristics of the pain [1]. Additionally, there may be other symptoms and clinical findings (e.g., motor paresis, muscle cramps, and autonomic nervous symptoms) depending on the site of the lesion.

Although neuropathic pain is often described as burning, no single feature of pain is diagnostic for neuropathic pain. However, combinations of certain symptoms, pain descriptors, and bedside findings increase the likelihood of neuropathic pain. Screening tools, comprising simple questionnaires, either patient- or clinician-completed, can be used to alert a clinician to the need for careful examination in search of neuropathic pain [3] (Table I). However, a screening tool cannot replace careful clinical examination [11].

Grading of Level of Certainty of the Diagnosis of Neuropathic Pain

The neuropathic pain grading system, summarized in Fig. 1 (modified from [23]), provides for three levels of certainty regarding the presence or absence of neuropathic pain in an individual patient. In all cases, there should be a neuroanatomically plausible

Table II
Sensory abnormalities found in patients with neuropathic pain

Quantitative	Qualitative	Spatial	Temporal
Hypoesthesia	Allodynia	Poor localization	Abnormal latency
Hyperesthesia	Paresthesia	Abnormal radiation	Aftersensation
Hypoalgesia	Dysesthesia		Summation
Hyperalgesia			

Source: Modified from [18].

Table I
Common items in neuropathic pain screening tools

Item	LANSS	DN4	NPQ	painDETECT	ID Pain
Pricking, tingling	x	x	x	x	x
Electric shocks, shooting	x	x	x	x	x
Hot, burning	x	x	x	x	x
Numbness		x	x	x	x
Pain evoked by light touch	x		x	x	x
Painful cold, freezing pain		x	x		
Autonomic changes	x				
Brush allodynia	x	x			
Raised soft touch threshold		x			
Raised pinprick threshold	x	x			

Source: Modified from [3].

Abbreviations: DN4, Douleur neuropathique 4 questions ; LANSS, Leeds Assessment of Neuropathic Symptoms and Signs; NPQ, Neuropathic Pain Questionnaire.

pain distribution and a clinical history suggesting a relevant lesion or disease. For definite neuropathic pain, the abnormal sensory findings are confined to the innervation territory of the lesioned nervous system structure, AND diagnostic test(s) confirm a nervous system lesion or disease that could explain neuropathic pain. If only one prerequisite is fulfilled, neuropathic pain is probable, and if neither of them is fulfilled, the certainty level of neuropathic pain is unconfirmed. The levels “definite” and “probable” indicate that the presence of neuropathic pain has been established. The level of “possible” implies that the presence of neuropathic pain has not yet been established.

Is the Location of Pain Neuroanatomically Plausible?

All neuropathic pains are projected; they are perceived within the innervation territory of the damaged nerve, root, or pathway owing to the somatotopic organization of the primary somatosensory cortex. Pain drawings are a good tool to document the distribution of pain (Fig. 2). The area of pain does not necessarily need to be identical to the innervation territory of a peripheral nerve or root, but it should be in a distribution that is typical for the underlying disorder. A patient with a distal nerve entrapment may also complain of pain proximally to the entrapment site because of referred pain.

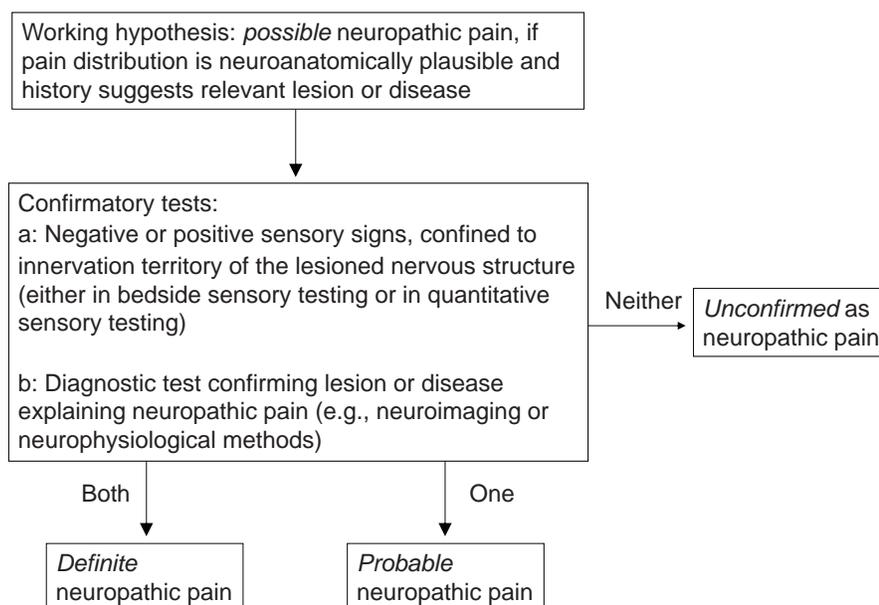


Fig. 1. Grading system for neuropathic pain (modified from [23]).

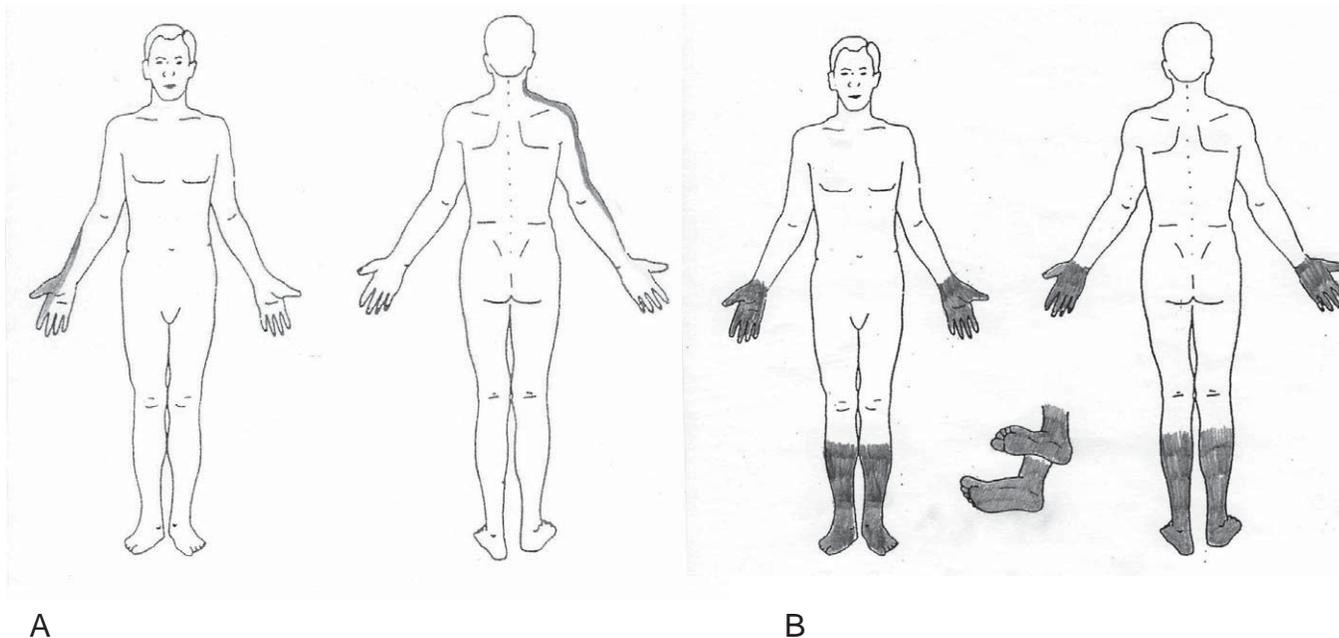


Fig. 2. Examples of pain drawings of neuropathic pain patients. (A) Radicular pain of the right C6 dermatome. (B) Painful polyneuropathy.

It is not always easy to recognize the neuroanatomical plausibility of the pain. This difficulty may result from the coexistence of different pains; the patient draws several pains in the body template, and the location of pain is not neuroanatomically logical. Further questions about the character and occurrence of the pain in different areas and careful clinical examination can clarify the situation. In some cases the pain area may be small with regard to the site of the lesion and extent of sensory abnormality. A patient may complain of pain in the left hand and knee, whereas clinical examination reveals hemibody sensory loss and MRI scan shows vascular lesions in the right hemisphere [24]. This example highlights the importance of full neurological examination instead examining only the pain area.

Are There Sensory Abnormalities, and Are They Neuroanatomically Plausible?

When performing sensory testing and interpreting sensory findings, the clinician should be aware of the complexity of sensory aberrations. Regional areas of numbness are commonly associated with regional soft tissue pain, especially in the presence of muscle tightness and spasm. These features do not necessarily mean that there is a neurological dysfunction related to pain. Negative sensory phenomena (hypoesthesia and hypoalgesia) have been reported in non-neuropathic pain, such as muscular pain [17]. It is crucial to survey the borders of sensory dysfunction to differentiate diffusely located

non-neuropathic pains from neuroanatomically plausible distribution of neuropathic pain. In addition, repeated testing may be helpful; the outcome of repeated testing during one session should be reproducible. Positive sensory phenomena (allodynia and hyperalgesia) are common in nociceptive pain states, especially in inflammatory conditions. Even in neuropathic conditions, the area of allodynia may be extensive compared with areas of other sensory findings, reflecting central sensitization. In addition, the clinical evidence of thermal and nociceptive hypoesthesia may be difficult to detect at the bedside because it is frequently hidden by tactile allodynia.

In some cases sensory findings on bedside examination may be normal (although quantitative sensory testing may reveal mild abnormality). Classical trigeminal neuralgia is an example; abnormal findings on bedside sensory testing strongly raise the suspicion of secondary trigeminal neuralgia [10]. Clinical examination alone is less sensitive than several complementary tests to document the presence of a somatosensory lesion [7,8]. For example, electroneuromyography is superior to clinical examination alone for the diagnosis of peripheral neuropathy. Overlap of dermatomes, especially in the trunk, explains normal sensory findings in a lesion of a single intercostal nerve. In cases where neuropathic pain is caused by somatosensory pathways lacking a cutaneous distribution, bedside examination is unable to show sensory aberration. Currently, validated methods to test sensitivity in deeper tissues are lacking.

The location of sensory abnormalities may not perfectly resemble published diagrams of an innervated territory. There are several reasons. First, there is great variance in nerve distribution among individuals. Second, the area of pain and abnormal sensations can vary at different appointments depending on pain intensity [19], which reflects the dynamic modulation of sensory function. In addition, bilateral sensory abnormalities are possible in neuropathic pain conditions regarded as unilateral, such as postherpetic neuralgia [12,13].

Is There a Need for Further Examination?

Finally, it is important to emphasize that the clinical examination can never prove any pain to be of neuropathic origin, but can only provide supporting evidence for altered function of the nervous system. The final diagnosis is always a result of the interpretation of all available information.

The need for further investigations is considered individually, depending on the clinical question and available consultation services. Tests in a specialized center may include conventional electrophysiological procedures, quantitative somatosensory testing, neuroimaging, blood and cerebrospinal fluid samples, and less conventional laboratory tools to assess the nociceptive pathways in the peripheral as well as central nervous system.

Even after relevant clinical examination and further examinations, pain may remain without a specific explanation. Medically unexplained symptoms refer to symptoms for which no clear or consistent organic pathology can be demonstrated (although organ dysfunction may be an integral part of the symptom) [4]. The term is purely descriptive and does not imply psychogenesis. In these cases it is important to find a balance between excluding and treating organic causes and overinvestigating. Supportive care is mandatory, and it is important to acknowledge the patient's suffering, as is the case for all pain patients [22].

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