

For the Primer, visit [doi:10.1038/nrdp.2017.2](https://doi.org/10.1038/nrdp.2017.2)

➔ **Neuropathic pain is caused by lesions or diseases of the somatosensory system, including peripheral fibres (A $\beta$ , A $\delta$  and C fibres) and central neurons, and is associated with allodynia, burning and tingling sensations. Conditions associated with neuropathic pain include trigeminal neuralgia, postherpetic neuralgia, radiculopathy, diabetic neuropathy, HIV infection, stroke and amputation.**

## EPIDEMIOLOGY

Estimating the incidence and prevalence of neuropathic pain has been difficult owing to the lack of simple diagnostic criteria that can be used for large epidemiological surveys of the general population. However, new screening tools have been developed; the population prevalence of chronic neuropathic pain has been estimated to be 7–10%.

! The available data indicate that chronic neuropathic pain is more frequent in women than in men and in individuals >50 years of age

## QUALITY OF LIFE

Neuropathic pain can substantially impair quality of life, as it is often associated with other problems such as anxiety, depression, disturbed sleep and high prescription drug use. Patient-reported scores in, for example, physical functioning and emotional role functioning can be significantly lower in those with neuropathic pain than in the general population.



## DIAGNOSIS

! Determining whether the pain in question is neuropathic (as opposed to, for example, nociceptive caused by damage to body tissue or other chronic pain syndromes) is important to provide appropriate treatments

**Possible neuropathic pain**

- Fits with the patient's history
- Neuroanatomically plausible

**EXAMINATION**  
Quantitative sensory tests use standardized mechanical and thermal stimuli to test the afferent nociceptive and non-nociceptive systems, assessing loss and gain of function of the nerves



**Probable neuropathic pain**

- Requires clinical evidence

**Definite neuropathic pain**

- Requires objective evidence that confirms the lesion or disease of the somatosensory system

## OUTLOOK

The development of novel interventions with improved efficacy and tolerability is paramount to reduce

polypharmacy in patients with neuropathic pain. Drug discovery relies on improved understanding of the mechanisms underlying

the pain and improved clinical trial designs that incorporate and stratify patients according to their genotypic and phenotypic profiles.

## PATIENT HISTORY



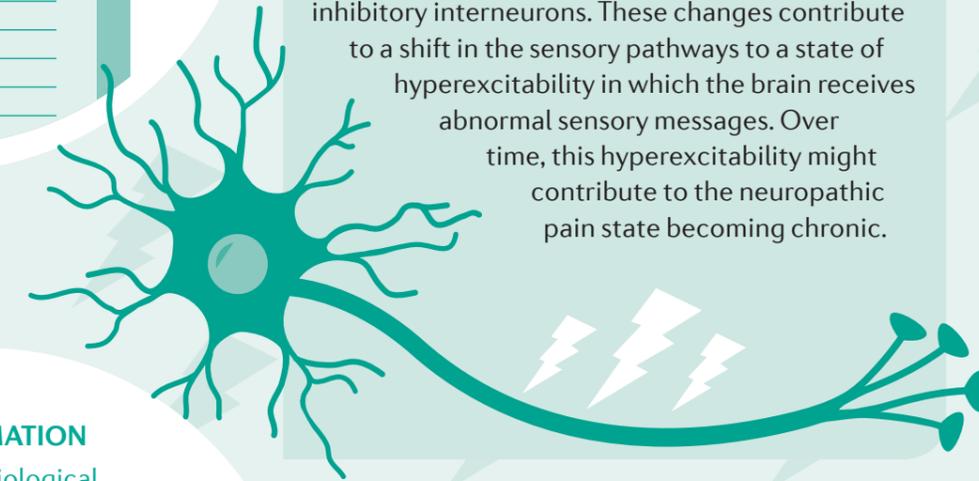
## CONFIRMATION

Neurophysiological tests can be used to identify damage along the somatosensory pathways and skin biopsies can be used to diagnose small-fibre neuropathies



## MECHANISMS

In neuropathic pain, peripheral sensory and central neurons show a gain of excitation and facilitation and a loss of inhibition. Several mechanisms can contribute to the neuropathy, including changes in the function and expression of voltage-gated sodium, calcium and potassium channels; in the function of second-order nociceptive neurons (which convey sensory information to the thalamus for further processing); and in the function of inhibitory interneurons. These changes contribute to a shift in the sensory pathways to a state of hyperexcitability in which the brain receives abnormal sensory messages. Over time, this hyperexcitability might contribute to the neuropathic pain state becoming chronic.



## MANAGEMENT

Typically, patients with neuropathic pain undergo conservative pharmacological and integrative treatments (such as cognitive-behavioural therapy and physical therapy) before interventional treatments are attempted. Medical treatments include  $\gamma$ -aminobutyric acid (GABA; an inhibitory neurotransmitter) analogues, serotonin-noradrenaline reuptake inhibitors and tricyclic antidepressants. The effects of these agents are mediated by their actions on descending inhibitory control systems. Interventional treatments are largely surgical and include spinal cord stimulation and implanted intrathecal pumps, which provide targeted drug delivery, as well as repetitive transcranial magnetic stimulation.