Revista Médica del
Hospital General de México

PERMANYER

Check for updates

EDITORIAL

Neuropathic pain: from concept to multimodal treatment

José D. Carrillo-Ruiz[1,2], José R. Carrillo-Márquez[3], and Ma. Fernanda Carrillo-Márquez[4]*

[1]Research Direction and Stereotactic, and Functional Neurosurgery Service, Hospital General de México Dr. Eduardo Liceaga, Secretaría de Salud; [2]Coordination of Neurosciences, Faculty of Psychology, Universidad Anáhuac México; [3]School of Medicine, Universidad West Hill; [4]Faculty of Health Sciences, Universidad Anáhuac México. Mexico City, Mexico

Introduction

Pain has been considered one of the main reasons why a patient goes to the doctor, being regarded as one of the most unpleasant experiences: anyone has experienced pain at some point, knowing that it can present itself as something whose intensity can be annoying and tolerable to something that can become completely disabling for daily life. This preface deals with neuropathic pain where the nervous system is the main actor both in its injury and in its reaction, understanding its concept, anatomy, physiology, pathophysiology, classification, and the consequent therapy involved in its resolution.

Concept

Pain is described as an unpleasant sensation and is considered by the WHO as another vital sign to be taken into consideration, so its importance is fundamental, since in a general consultation more than 90% of patients go to the doctor for pain. The International Association for the Study of Pain (IASP) has recently modified its definition by establishing that pain is: "an unpleasant sensory and emotional experience associated with or similar to that associated with an actual or potential tissue injury"[1]. The definition covers a specifically physiological part where there is an injury to the body with an immediate basic neurological response, which is highly objective; but that also encompasses another nervous part involving the limbic circuits on emotions, whose meaning is highly subjective for the patient.

Physiology and pathophysiology

The physiology of pain involves the external or internal stimulation of receptors for this modality, its transmission to the higher centers, its regulation, and later the understanding of it with its immediate response to pain by the individual. Then, four phases are described: (1) transduction: it is the conversion of the external or internal stimulus (mechanical, chemical, or temperature fashion, through any of the receptors, in this case, nociceptive) (2) transmission: it is known as the transfer of the action potential in each fiber of the receptors recruiting in the nerve bundles of the peripheral nerves to the spinal cord (3) modulation: it is the inhibition or excitation of the fibers that enhance the sensation of pain by means of neurotransmitters (4) perception: once the electrical stimulus ascends to the primary sensory cortex, it can be transferred to the cingulate and prefrontal cortex to give it meaning[2] (Fig. 1).

It should be remembered that there are different classifications to understand pain, including its etiology: somatic, neuropathic, psychogenic, or mixed. Neuropathic pain shows clinical characteristics of the injury to the nerve, which corresponds to a burning and scratching pain, sometimes described as "smearing chili," which is paroxysmal, abrupt, and covers a dermatome of an altered nerve[3]. Although it can be acute, the pain becomes subacute or downright chronic (for more than 3 months). The fibers involved in pain transmission correspond to the A-delta fibers for the transmission of acute pain, as the speed is moderately fast,

***Correspondence:**
José D. Carrillo-Ruiz
E-mail: josecarrilloruiz@yahoo.com

Date of reception: 27-01-2025
Date of acceptance: 29-01-2025
DOI: 10.24875/HGMX.M25000050

Available online: 01-04-2025
Rev Med Hosp Gen Mex. 2025;88(2):57-61
www.hospitalgeneral.mx

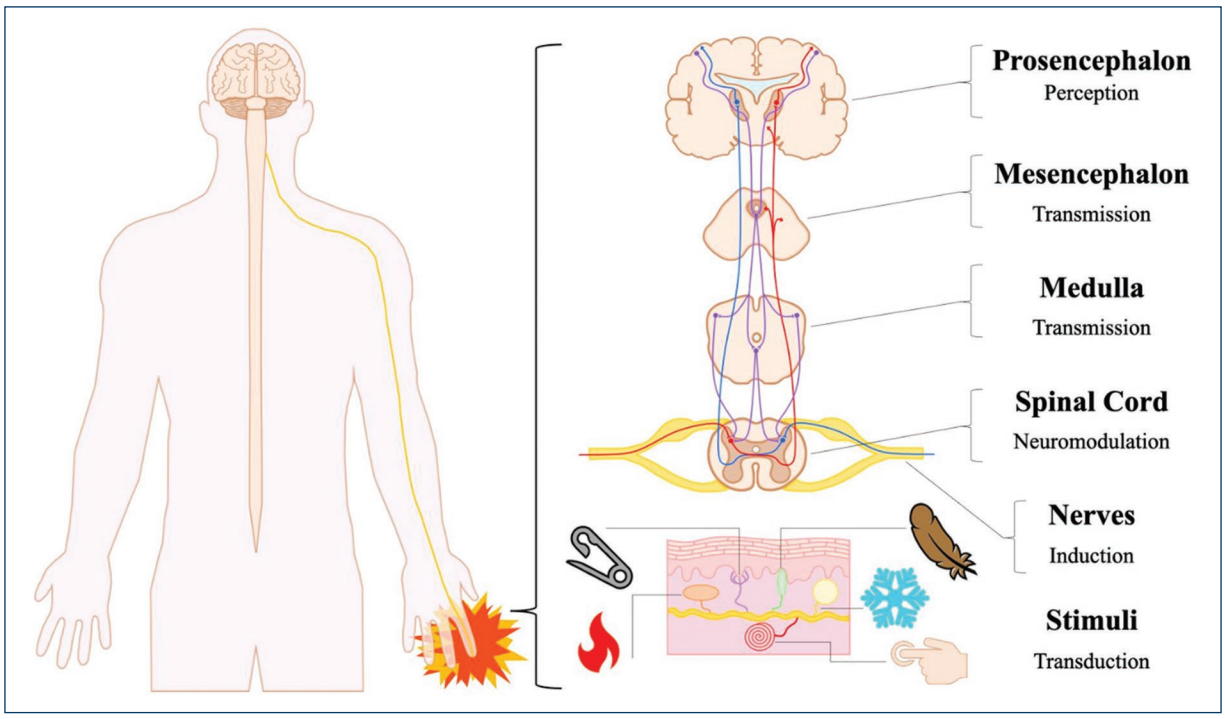

Figure 1. Anatomy and physiology of neuropathic pain.

and the C fibers, with a slower speed, for sustained pain. The neurotransmitters involved would be of a different nature depending on their origin. The main substances are tachykinins such as substance P (Pain), or prostaglandins, glutamate and aspartate, bradykinin, or ions such as chlorine[2,3]. Figure 2 shows these components.

Therapeutics

The understanding of anatomy together with physiology marks the way to achieve a multimodal treatment to be followed: rehabilitation is established in those patients in whom pain is tolerable, otherwise it increases with movements. Therapies can be performed (use of infrared rays, ultrasound, magnetic fields; TENS among others) on the relaxation of nearby muscles that improve compressive symptoms in a duct through which the nerves pass[4,5]. The second type is the use of different GABA-enhancing drugs as an inhibitory drug, or the use of glutamatergic antagonists, as they are excitatory. In this way, the main neuromodulators are antiepileptics (interacting with sodium, calcium, or chlorine channels) or antidepressants (promoting the increase of serotonin or norepinephrine in the synaptic terminals). New neuromodulatory drugs may have a dual action for both improving neuropathic pain and depression (breaking a pain-anxiety-depression cycle) ultimately improving pain[2]. Normally, the algology service can collaborate in an important way when performing nerve blocks, in which the nerve is infiltrated through the use of steroidal anti-inflammatory drugs alone or in combination with local anesthetics such as xylocaine or bupivacaine, either isolated or in combination with the possible modification of medications or doses[2,6]. An escalation can be made in cases where the pain is very intense using morphine or one of its derivatives such as buprenorphine or oxycodone following the WHO promotion scheme. Finally, the use of neurosurgery for pain is a last option, in which lesional or neuromodulatory procedures are found in the peripheral nerve, spinal cord, or at the brain level[3,6]. Among the interventions on the nerve are total or partial neurotomies, which are currently not recommended. Although neurolysis can be performed with good results for the plexus or some nerves, electrodes have also been placed on the peripheral nerve or cranial nerve, with satisfactory results[7,8]. Special consideration is the decompression of cranial nerves from vascular insult over the V of IX facial nerves[9], and the use of radiofrequency or radiosurgery is well effective in pain amelioration[10,11]. On the other hand, spinal cord injury has been beneficial with the use of cordotomies, medial myelotomies, or posterior rhizotomies, with their current use being

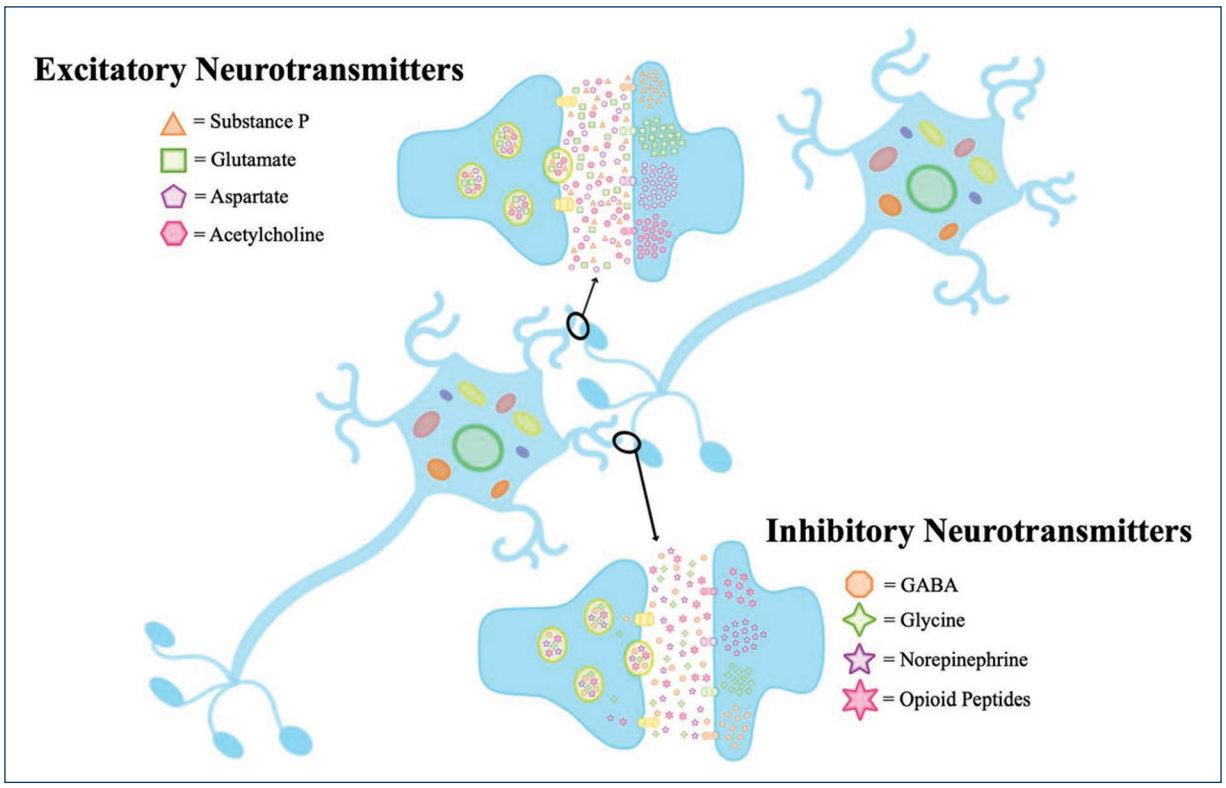

Figure 2. Neurotransmitters in production and abolition of pain.

Table 1. Lesional procedures for pain syndromes

Anatomical site	Procedure	Indication
Peripheral nerve	Neurotomy Neurolysis	Neurofibroma, neuroma, and compressive nerve pain
Cranial nerve	Baloon, glycerol, and RFR MVD Radiosurgery	V Neuralgia
	RFR and MVD Radiosurgery	IX Neuralgia
Spinal cord	DREZotomy	Deafferentation pain, brachial plexus injury, and spasticity
	Cordotomy	Cancer pain
	Medial myelotomy	Limb pain and spasticity
Brain	Thalamotomy	Deafferentation pain, cancer, and central pain. Contralateral limb pain
	Mesencephalic tracheotomy	Unilateral head pain, facial, and neck pain

RFR: radiofrequency rhizotomy; MVD: microvascular decompression.

very limited. The DREZotomy (Dorsal Root Entry Zone), which is a dorsolateral myelotomy, has been found to be more effective in patients with neuropathic pain[3]. As for neuromodulatory procedures, there are two: stimulation of the spinal cord percutaneously or by surgery, with good to very good results in close to 70% of cases. There is also the implantation of programmable infusion pumps where morphine, bupivacaine, and clonidine among other drugs are infused directly into the subarachnoid space, being effective in their use[6].

Table 2. Neuromodulation procedures for pain syndromes

Anatomical site	Procedure	Indication
Peripheral nerve	Nerve stimulation	Deafferentation pain and nerve tumor
Cranial nerve	Nerve stimulation	V, IX Neuralgia
Spinal cord	Posterior stimulation	Herpes Zoster, RCS, and spasticity
	Infusion pump	Cancer pain, RCS, and spasticity
Brain	Mesencephalic stimulation	Facial pain and post-ictus pain
	Hypothalamic nucleus	Aggressive cluster headache
	Thalamic stimulation	Contralateral limb pain and Dejerine–Roussy syndrome
	Motor cortex stimulation	Herpetic pain, phantom limb, and atypical facial pain

RCS: regional complex syndrome.

As for brain procedures, which are the last step when the others have failed, there is a radiofrequency injury to the thalamic nuclei such as the parafascicular or the centromedian nucleus. It has also been done on the cingulate with multiple lesions, or on the mesencephalic periaqueductal gray matter to abolish neuropathic pain. In addition, pituitary adenolysis is used in patients with mixed pain in terminal cancer conditions. With respect to neuromodulation, there is deep brain stimulation in the same sites mentioned for the injury[12], but also stimulation of the motor cortex has very good results[13,14]. Tables 1 and 2 summarize the above.

Conclusions

Understanding the concept of neuropathic pain, and its pathophysiology with the initial response of the receptors, with transmission, neuromodulation, and sensory perception is fundamental in medicine. It involves both fibers and neurotransmitters, and this applies to therapeutics that involve rehabilitation, medications, blocks, or in the latter case, lesional or neuromodulatory surgical interventions on the nerve, spinal cord, or brain.

Funding

The authors declare that they have not received funding.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality, informed consent, and ethical approval. The study does not involve patient personal data nor requires ethical approval. The SAGER guidelines do not apply.

Declaration on the use of artificial intelligence. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript.

References

1. Raja SN, Carr DB, Cohen M, Finnerup NB, Flor H, Gibson S, et al. The revised international association for the study of pain definition of pain: concepts, challenges, and compromises. Pain. 2020;161: 1976-82.
2. González-Hermosillo DC, González-Hermosillo LM, Villaseñor-Almaraz M, Ballesteros-Herrera D, Moreno-Jimenez S, Corona-Cedillo R, et al. Current concepts of pain pathways: a brief review of anatomy, physiology, and medical imaging. Curr Med Imaging. 2024;(20):1-17. DOI:10.2174/1573405620666230519144112
3. Carrillo-Ruiz JD. La neuromodulación en el tratamiento del dolor. Dol Clin Ter. 2003;11:9-14.
4. Carrillo-Ruiz JD, Cortés-Contreras AP, Salazar AA, Cid-Rodríguez FX, González-Morales HF, García-Jerónimo AI, et al. Positive sensory symptoms, in surgically managed patients with carpal tunnel syndrome: a long term follow-up. Exp Ther Med. 2024;28:401.
5. González-Echeverría KE, Esqueda-Liquidano MA, Ariñez-Barahona E, Latorre-Dávila CA, Carrillo-Ruiz JD. Changes of neuropathic pain in two patients with thoracic outlet syndrome due to accessory cervical rib. Rev Mex Neuroc. 2018;19:39-48.
6. Deer TR, Prager J, Levy R, Rathmell J, Buchser E, Burton A, et al. Polyanalgesic consensus conference 2012: recommendations for the management of pain by intrathecal (intraspinal) drug delivery: report of an interdisciplinary expert panel. Neuromodulation. 2012;15(5):436-66. Erratum in: Neuromodulation. 2013; 16(4):38.
7. Armas-Salazar A, Téllez-León N, García-Jerónimo AI, Villegas-López FA Navarro-Olvera JL, Carrillo-Ruiz JD. Neuropathic pain relief after surgical neurolysis in patients with traumatic brachial plexus injuries: a preliminary report. Pain Res Manag. 2022;2022: 5660462.

8. García-Jerónimo AI, Armas-Salazar A, García-Muñoz L, Navarro-Olvera JL, Esqueda-Liquidano MA, Carrillo-Ruiz JD. Neuropathic pain and positive sensory symptoms in brachial plexus neuropathy: an exploratory study of outcomes after surgical decompression and proposal of a new sensory frequency of symptoms scale. J Integr Neurosci. 2023;22:25.
9. Carrillo-Ruiz JD, Covaleda-Rodriguez JC, Díaz-Martínez JA, Vallejo-Estrella A, Navarro-Olvera JL, Velasco-Campos F, et al. Minimally invasive retrosigmoidal parasterional burr-hole approach: technique and neuropathic pain amelioration after microvascular decompression of the trigeminal nerve. Biomedicines. 2023;11:2707.
10. Altamirano JM, Jimenez-Olvera M, Moreno-Jimenez S, Gutierrez-Aceves GA, Velasco-Campos F, Navarro-Olvera JL, et al. Comparison of microvascular decompression, percutaneous radiofrequency rhizotomy, and stereotactic radiosurgery in the treatment of trigeminal neuralgia: a long term quasi-experimental study. Pain Pract. 2024;24:514-24.
11. Gomes-da Silva De Rosenzweig P, Pastrana-Brandes S, Merikansky GS, Victoria-Garcia LO, Curtius-Caruso MS, Carrillo-Ruiz JD. Factors associated with outcomes following microvascular decompression for the treatment of primary trigeminal neuralgia in adults: a systematic review and meta-analysis. J Dent Anesth Pain Med. 2024;24:227-43.
12. Carrillo-Ruiz JD, Carrillo-Márquez JR, Beltrán JQ, Jiménez-Ponce F, García-Muñoz L, Navarro-Olvera JL, et al. Innovative perspectives in limbic surgery using deep brain stimulation. Front Neurosci. 2023;17:1167244.
13. Velasco F, Argüelles C, Carrillo-Ruiz JD, Castro G, Velasco AL, Jiménez F, et al. Efficacy of motor cortex stimulation in the treatment of neuropathic pain: a randomized double-blind trial. J Neurosurg. 2008;108:698-706.
14. Velasco F, Carrillo-Ruiz JD, Castro G, Argüelles C, Velasco M, Kassian A, et al. Motor cortex electrical stimulation applied to patients with complex regional pain syndrome. Pain. 2009;147:91-8.