MINI REVIEW

Descending modulation and neuropathic pain

Eshubella Clarks

Clarks E. Descending modulation and neuropathic pain. Anesthesiol: Case Rep. 2022; 5(3):8-9.

ABSTRACT

Acute pain serves a physiological purpose in preventing tissue damage, but chronic pain can linger as a complication of a wide range of illnesses due to maladaptive plasticity in the peripheral and central nervous systems. It is obvious that many patients treated as a homogeneous patient population fail to control their pain successfully, hence new treatment algorithms are urgently required. Early groundbreaking research showed that midbrain microstimulation resulted in a potent analgesia. Later research revealed that this modulation can be used to either augment or reduce spinal sensory transmission. These descending controls are balanced to optimize sensory acquisition when at rest, but they can quickly change based on the situation, the expectation, and the emotional state. Important examples are conditioned pain modulation, attentional analgesia, offset analgesia/onset hyperalgesia, and offset analgesia/onset hyperalgesia. All of these coexist inside the descending pain modulatory system (DPMS) and rely on signalling pathways and systems that partially overlap. For instance, conditioned pain modulation is mediated primarily by noradrenergic signalling and partially by opioidergic signaling, whereas attentional analgesia, stressinduced analgesia/hyperalgesia, and offset analgesia are linked to the periaqueductal grey-dorsal raphe axis and require descending opioidergic pathways, respectively.

Key Words: Pain modulation; chronic pain; Guidelines; Neuropathic pain; Analgesia

INTRODUCTION

A substantial body of preclinical data links impaired descending A substantial body of preciment and control to the emergence and maintenance of neuropathic pain states [1], and clinical investigations based on imaging or psychophysical testing corroborate these findings. Conditioned Pain Modulation (CPM), also known as diffuse noxious inhibitory controls, is the most frequently examined in patients and may serve as a translatable endpoint connecting pre-clinical and clinical research [2]. This type of dynamic quantitative sensory assessment, which may be summed up as "pain blocks pain" when two far-off noxious stimuli cause analgesia, probably serves as a proxy for measuring the net balance of descending facilitatory and inhibitory signaling. Ineffective CPM has been noted in neuropathic and chronic pain syndromes, and it offers insight into pathophysiological causes [3]. As tapentadol/duloxetine efficacy is inversely correlated with CPM efficiency in neuropathic patients, inefficient CPM has also been linked to "pain vulnerability" for postoperative pain [4]. This suggests that inefficient CPM may be useful as a sensory biomarker for mechanism-led treatment selection [5].

DESCENDING PAIN MODULATION

The descending modulation of nociceptive transmission in the spinal cord sets pain thresholds in part as a consequence of emotional and psychological states. It is believed that Rostral Ventromedial Medulla (RVM) neurons play a crucial role in this process, but it is yet unclear how specific populations of RVM neurons influence pain through neuronal circuits and synaptic mechanisms [6-8]. The modulation of somatosensory information processing at the spinal cord level by the brain has long been known to significantly impact pain thresholds. Underlying variations in pain thresholds as a consequence of mood. expectations and interior states is a phenomenon known as the descending regulation of pain. Acute stress and the anticipation of pain alleviation, for instance, might provide analgesia, whereas longterm stress and anxiety, as seen in post-traumatic stress disorder or pain catastrophizing, can make the pain worse [9]. Traditional extracellular recording techniques revealed the existence of on-cells, off-cells, and neutral cells as three classes of RVM neurons projecting to the spinal cord [10]. On-cells are believed to play a key role in descending pain regulation by promoting nociception, most likely through glutamatergic neurotransmission and the stimulation of excitatory dorsal horn neurons and primary afferent terminals. Oncells' molecular identity remains unclear, though. Furthermore, little is known about how RVM spinal cord networks are structured and how RVM neurons affect neuronal activity and nociception at the spinal level [11-13]. To control nociception, the endogenous opioid system modifies the excitability and neurotransmission in the RVM and spinal cord. Exogenous opioid analgesics, like morphine, work by blocking the Mu-Opioid Receptors (MORs) on on-cells, which decreases pain facilitation, and the MORs and Delta-Opioid Receptors (DORs), which are located on the spinal terminals of

Managing Editor, Anesthesiology: Case Report, Berkshire, UK

Correspondence: Eshubella Clarks, Managing Editor, Anesthesiology: Case Report, Berkshire, UK, E-mail: anesthesiology.editorialoffice@gmail.com

Received:03 May, 2022, Manuscript No. pulacr-22-5138, Editor assigned:05 May, 2022, Pre QC No. pulacr-22-5138 (PQ), Reviewed:19 May, 2022, QC No. pulacr-22-5138 (Q), Revised: 23 May, 2022, Manuscript No. pulacr-22-5138 (R), Published:26 May, 2022, DOI: 10.37532. pulacr.22.5.3.8-9.

ACCESS This open-access article is distributed under the terms of the Creative Commons Attribution Non-Commercial License (CC BY-NC) (http://creativecommons.org/licenses/by-nc/4.0/), which permits reuse, distribution and reproduction of the article, provided that the original work is properly cited and the reuse is restricted to noncommercial purposes. For commercial reuse, contact reprints@pulsus.com

OPEN

Clarks

Dorsal Root Ganglion (DRG) neurons, which decrease nociception [14]. On the other hand, it is yet unclear how endogenous opioids modulate pain. The pentapeptides enkephalins, which are highly abundant in the dorsal horn and both high-affinity agonists for DORs and MORs, are particularly interesting. Enkephalinergic neuromodulation in the spine plays a crucial part in the regulation of pain, as shown by the reduction of pain by enkephalin-degrading enzyme inhibitors and the analgesic effects of intrathecal injection of enkephalins. According to electrophysiological recordings in spinal cord slices, exogenous opioids can operate on DORs and MORs to presynaptically block neurotransmitter release from DRG axon terminalsIsIt is unknown if endogenous enkephalins secreted from spinal neurons behave similarly or help to determine pain thresholds.

NEUROPATHIC PAIN

Injured nerves may become more excitable, causing neuropathic pain. Additionally, sustained spontaneous afferent input causes spinal neurons to become more sensitive, resulting in intensified pain [15]. Both clinical and experimental neuropathic pain can be effectively treated with substances that reduce spontaneous afferent activity. The expression of neuropathic pain is also correlated with spontaneous afferent activity, and the emergence of tactile hypersensitivity coincides with the development of afferent discharge [16]. Discharges are most noticeable one week after the injury, however, they quickly and considerably fade with time. Within 24 hours, nerve damage causes a four- to six-fold rise in spontaneous ectopic discharge, but by post-injury day 5, this increase has mostly subsided. Notably, however, behavioral indicators of neuropathic pain persist for many weeks even after the rate of afferent discharge has decreased. These data raise the notion that, even if the heightened discharge brought on by nerve damage may be crucial at the beginning of neuropathic pain, it may not be enough to keep it going in the absence of additional processes [17].

REFERENCES

- Bardoni R, Takazawa T, Tong CK, et al. Pre and postsynaptic inhibitory control in the spinal cord dorsal horn. Ann N Y Acad Sci. 2013;1279(1):90-6.
- Bardoni R, Tawfik VL, Wang D, et al. Delta opioid receptors presynaptically regulate cutaneous mechanosensory neuron input to the spinal cord dorsal horn. Neuron. 2014;81(6):1312-27.
- 3. Basbaum A.I. Clanton C.H. Fields H.L. Opiate and stimulusproduced analgesia: functional anatomy of a medullospinal pathway. Proc. Natl. Acad. Sci. USA. 1976; 73: 4685-88.
- 4. Basbaum AI, Bautista DM, Scherrer G, et al. Cellular and molecular mechanisms of pain. Cell. 2009;139(2):267-84.

- 5. Beier KT, Steinberg EE, DeLoach KE, et al. Circuit architecture of VTA dopamine neurons revealed by systematic input-output mapping. Cell. 2015;162(3):622-34.
- 6. Breivik H, Collett B, Ventafridda V, et al. Survey of chronic pain in Europe: prevalence, impact on daily life, and treatment. Eur J Pain. 2006;10(4):287-333.
- Finnerup NB, Attal N, Haroutounian S, et al. Pharmacotherapy for neuropathic pain in adults: a systematic review and meta-analysis. Lancet Neurol. 2015;14(2):162-73.
- Reynolds DV. Surgery in the rat during electrical analgesia induced by focal brain stimulation. Science. 1969;164(3878):444-5.
- 9. Eippert F, Bingel U, Schoell ED, et al. Activation of the opioidergic descending pain control system underlies placebo analgesia. Neuron. 2009;63(4):533-43.
- Willer JC, Le Bars D, De Broucker T. Diffuse noxious inhibitory controls in man: involvement of an opioidergic link. Eur J Pharmacol. 1990;182(2):347-55.
- Abraira VE, Ginty DD. The sensory neurons of touch. Neuron. 2013;79(4):618-39.
- 12. Antal M, Petko M, Polgar E, et al. Direct evidence of an extensive GABAergic innervation of the spinal dorsal horn by fibers descending from the rostral ventromedial medulla. Neuroscience. 1996;73(2):509-18.
- 13. Baker KB, Schuster D, Cooperrider J, et al. Deep brain stimulation of the lateral cerebellar nucleus produces frequency-specific alterations in motor evoked potentials in the rat in vivo. Exp Neurol. 2010;226(2):259-64.
- Barbaro NM, Heinricher MM, Fields HL. Putative pain modulating neurons in the rostral ventral medulla: reflexrelated activity predicts effects of morphine. Brain Res. 1986;366(1-2):203-10.
- 15. Kirk EJ. Impulses in dorsal spinal nerve rootlets in cats and rabbits arising from dorsal root ganglia isolated from the periphery. J Comp Neurol.1974;155(2):165-75.
- Devor M. Neuropathic pain and injured nerve: peripheral mechanisms. Br Med Bull.1991;47(3):619-30.
- Han HC, Lee DH, Chung JM. Characteristics of ectopic discharges in a rat neuropathic pain model. PAIN®. 2000;84(2-3):253-61.