Cureus

Serotonergic modulation by 5-HT7 receptors in mouse spinal cord dorsal horn

Antonella Comitato [1] , Enza Lacivita [2] , Marcello Leopoldo [2] , Rita Bardoni [1]

1. Dipartimento Scienze Biomediche, Metaboliche e Neuroscienze, Università di Modena e Reggio Emilia, Modena, ITA
2. Dipartimento di Farmacia - Scienze del Farmaco, Università di Bari, Bari, ITA

Corresponding author: Antonella Comitato, antonella.comitato@unimore.it

Categories: Anesthesiology, Pain Management
Keywords: spinal pain, serotonergic receptors 5-ht7

How to cite this abstract
Comitato A, Lacivita E, Leopoldo M, et al. (September 09, 2021) Serotonergic modulation by 5-HT7 receptors in mouse spinal cord dorsal horn. Cureus 13(9): a667

Abstract

Background

Serotonergic receptors of the 5-HT_7type (5-HT_7Rs) are widely expressed in the central nervous system, where they modulate several functions, such as sleep induction, learning, mood, and vegetative behaviours. Along the pain axis, 5-HT_7Rs are expressed on nociceptive primary afferent fibers and in the dorsal horn, both on neurons and astrocytes. [1]. Behavioural experiments have produced controversial results about anti- and pro-nociceptive actions of 5-HT_7Rs. The low agonist selectivity and the different pain animal models used have likely contributed to the heterogeneity of the results [2].

To investigate the effects of 5-HT_7Rs on spinal pain, we have performed an electrophysiological study on mouse spinal cord slices, using the selective agonist LP-211 [3]. The recorded neurons have been functionally characterized, in order to identify the neural circuits involved in the serotonergic modulation.

Methods

Patch-clamp recording was performed on lamina II neurons in spinal cord slices obtained from postnatal CD1 mice (P15-P25) [4]. Excitatory postsynaptic currents (EPSCs) were recorded in voltage clamp; evoked EPSCs were elicited by stimulating the dorsal root with a suction electrode in the Adand C fibers range.

Results.

Application of 1 mM LP-211 to the spinal cord slice induced a facilitation of glutamatergic transmission: the frequency of spontaneous EPSCs was significantly increased in a subpopulation of neurons (control: 0.9±0.2 Hz; LP-211: 1.8±0.6 Hz; 5 responsive neurons out of 8). The recorded neurons were characterized from their firing pattern: significant effects of LP-211 were observed in both tonic and delayed firing neurons, corresponding to inhibitory and excitatory interneurons, respectively.

Application of 1 mM LP-211 in the presence of 10 mM SB269970 (a 5-HT_7R antagonist) did not alter spontaneous EPSC frequency in 11 lamina II neurons, confirming the involvement of 5-HT_7Rs in glutamate release facilitation.

EPSCs evoked by dorsal root stimulation were also tested with LP-211. The currents, evoked by paired pulse protocol, were significantly potentiated by the compound (mean potentiation: 19±4.2%; 4 responsive neurons out 7). The second EPSC was less potentiated than the first and the paired pulse ratio decreased in 3 neurons.

Conclusion

The compound LP-211 is able to selectively activate 5-HT_7Rs in the dorsal horn, causing a facilitatory effect of both spontaneous and evoked EPSCs. The decrease of paired-pulse ratio suggests that LP-211 activates presynaptic 5-HT_7Rs, increasing glutamate release. The study of specific effects of these receptors on the different neuron populations will be critical to determine whether 5-HT_7Rs exert anti- or pro-nociceptive effects at the spinal level.

Open Access
Abstract
Published 09/09/2021

References

1. Cortes-Altamirano JL et al., Curr. Neuropharm, 2018, 16:210-221

2. Bardoni R, Curr. Neuropharm, 2019, 17:1133-1145

3. Hedlund PB et al, Neurosci Lett. 2010 481:12-6.

4. Betelli C et al., Mol. Pain, 2015, 11:6