Clinical Imaging and Case Reports (ISSN 2770-9205)

Distribution of TRPV1 in the Rat Brain Parenchyma's CSF Contacting Nucleus and its Expression in Neuropathic Pain.

Dr. Li-Cai Zhang

Corresponding author

Dr. Li-Cai Zhang, Jiangsu Province Key Laboratory of Anesthesiology, Xuzhou Medical College.

Received Date: May 26 2023
Accepted Date: May 28 2023
Published Date: June 26 2023

Abstract

Background: The ventral periaqueductal central grey (PAG) of the brainstem is home to the cerebrospinal fluid-contacting nucleus (CSF-CN), which may affect the actual composition of the cerebrospinal fluid (CSF) for non-synaptic signal transmission by releasing or absorbing bioactive material. TRPV1 has been identified in areas of the spinal and peripheral nervous systems that are known to play a part in the detection, transmission, and control of pain. Consequently, it is hypothesised that the CSF-CN uses the TRPV1 receptor to engage in pain regulation. The current work aims to examine the expression and distribution of TRPV1 in the rat brain parenchyma's CSF-CN and the role of TRPV1 in neuropathic pain.

Methods: In Spague-Dawley rats, a model of neuropathic pain with chronic sciatic nerve constriction injury (CCI) was created. We measured the mechanical withdrawal threshold (MWT) and thermal withdrawal latency (TWL). In order to investigate CSF-CN, the cholera toxin subunit B conjugated with horseradish peroxidase (CB-HRP) was injected into one of the rats' lateral ventricles (LV). With the help of immunohistochemistry, TRPV1 and CB-HRP were double-labeled in order to better understand its distribution and expression in the CSF-CN. At the peak of allodynia and hyperalgesia (10 days following CCI surgery), SB-366791, a specific TRPV1 antagonist, was administered in 5 g into one of the rat's LVs. Rat behaviour was evaluated at 0, 0.5, 1, 2, 4, and 8 hours before and after injection.

Conclusion: TRPV1 is confined to the mesencephalon's CSF-CN, where CCI surgery has boosted the expression of TRPV1. TRPV1 in CSF-CN has been validated as a viable target for the treatment of neuropathic pain thanks to comparative analgesic effects of a TRPV1 anatagonist in a CCI model of neuropathic pain.

Keywords

dCSF-CNs; CSF-CN; TRPV1; SB366791; Neuropathic pain

Abbreviations

Cerebrospinal Fluid-Contacting Neurons, Distal CSF-CNs, Cerebral Spinal Fluid-Contacting Nucleus, Intracerebroventricular, Lateral Ventricle, Transient Receptor Potential, CB-HRP, Cholera Toxin B conjugated to Horseradish Peroxidase,

Background

The TRPV1 channel, formerly known as the vanilloid receptor VR1, was cloned ten years ago. It is a calcium-permeable nonselective cation channel that responds to a variety of mechanical, thermal, chemical (such as acid and lipid) and other stimuli coming from the extracellular and intracellular milieu [1,2], as well as mechanical and thermal stimuli [3, 7]. It is mostly expressed in nociceptors, which take part in the peripheral nervous system's processing of noxious chemical and heat stimuli (PNS). A fraction of sensory neurons with thin myelinated axons (A fibres), as well as bipolar neurons with unmyelinated axons (C fibres) and somata in dorsal root and trigeminal ganglia, are sensitive to capsaicin [8]. TRPV1 receptors are currently being studied as a novel therapeutic target in the PNS for the treatment of inflammatory and chronic neuropathic conditions pain [9,10,11]. In contrast to the TRPV1 receptors' well-established role in inflammatory pain, the function of these receptors in neuropathic pain is less clear, particularly in the central nervous system.
Additionally, recent research has demonstrated that TRPV1 receptors can be found in the hypothalamus, midbrain PAG, substantia nigra, and locus coeruleus of the CNS [12,13,14]. Despite the fact that there is evidence suggesting that TRPV1 receptors in the CNS are involved in pain transmission or modulation and may be viable therapeutic targets [14–16], there is ongoing debate regarding these receptors' functions

in the CNS.

By increasing glutamate release in the substantia nigra, locus coeruleus, hypothalamus, and PAG, activation of TRPV1 receptors causes hypoalgesia [17–19]. But as compared to peripherally restricted drugs with the same pharmacokinetic and pharmacological profile, centrally penetrating TRPV1 receptor antagonists performed better [20], highlighting the role of central TRPV1 receptor blocking in the analgesic activity. The expression of TRPV1 receptors' functional importance.

Conclusion

Our findings imply that the CSF-CN expresses TRPV1. CCI surgery elevated TRPV1 expression in the CSF-CN. Additionally, SB366791 showed an antiallodynic effect in CCI rats after being administered intravenously. Between the brain parenchyma and CSF, the CSF-CN may play crucial roles in neuromodulation and neuroendocrine regulation.

References

1. Caterina MJ, Schumacher MA, Tominaga M, Rosen TA, Levine JD, et al. (1997)The capsaicin receptor: a heat-activated ion channel in the pain pathway. Nature 389: 816–824
2. Szallasi A, Blumberg PM (1999) Vanilloid (capsaicin) receptors and mechanisms. Pharmacol 51: 159–212.
3. Ramsey IS, Delling M, Clapham DE (2006) An introduction to TRP channels.Annu Pev Physiol 68: 619-647.
4. Nilus B, Voets T (2005) TRP channels: a TR(I)P through a world of multifunctional cation channels. Pflugers Arch 451: 1-10.
5. Pedersen SF, Owsianik G, Nilius B (2005) TRP channels: an overview. Cell Calcium 38: 233-252.
6. Montell C, Birnbaumer L, Flockerzi V (2002) The TRP channels, a remarkably functional family. Cell 108: 595-598.
7. Matta JA, Miyares RL, Ahern GP (2007) TRPV1 is a novel target for omega-3 polyunsaturated fatty acids. Physiol J 578: 397-411
8. Holzer P (1988) Local effect or functions of capsaicin-sensitive sensory nerve endings: involvement of tachykinins, calcitonin gene-related peptid eandother neuropeptides. Neuroscience 24: 739–768.
9. Szallasi A, Cruz F, Geppetti P (2006) TRPV1: a therapeutic target for novel analgesic drugs? Trends Mol Med 12: 545–554.
10. Szallasi A, Appendino G (2004) Vanilloid receptor TRPV1 antagonists as the next generation of pain killers. Are we putting the cart before the horse? Med Chem J 47: 2717–2723.
11. Steenland HW, Ko SW, Wu LJ, Zhuo M (2006) Hot receptors in the brain. MolPain 2: 34.
12. Toth A, Boczan J, Kedei N, Lizanecz E, Bagi Z, et al. (2007) Expression and distribution of vanilloid receptor1 (TRPV1) in the adult rat brain. Mol Brain Res 135: 162–168.
13. Mc Garaughty S, Chu KL, Bitner RS, Martino B, El Kouhen R, et al. (2003)Capsaicin infused into the PAG affects rat tail flick responses tonoxious heat and alters neuronal firing in the RVM. Neuro physiol J 90: 2702–2710.
14. Mezey E, Tóth ZE, Cortright DN, Arzubi MK, Krause JE, et al. (2000) Distribution of mRNA for vanilloid receptor subtype1 (VR1), and VR1-like immunoreactivity, in the central nervous system of the rat and human. Proc Natl Acad Sci USA 97: 3655-3660.
15. Roberts JC, Davis JB, Benham CD (2004) [3H] Resinifera toxin auto radiography in the CNS of wild-type and TRPV1 null mice defines TRPV1 (VR1) protein distribution. Brain Res 995: 176-183.
16. Szabo T, Biro T, Gonzalez AF, Palkovits M, Blumberg PM (2002)Pharmacological characterization of vanilloid receptor located in the brain. Brain Res Mol Brain Res 98: 51-57.
17. Marinelli S, Di Marzo V, Berretta N, Matias I, Maccarrone M, et al. (2003) Pre synaptic facilitation of glutamatergic synapses to dopaminergic neurons of the rats ubstantianigra by endogenous stimulation of vanilloid receptors. Neurosci J 23: 3136–3144.
18. Marinelli S, Vaughan CW, Christie MJ, Connor M (2002) Capsaicin activation of glutamatergic synaptic transmission in the rat locus coeruleus in vitro. Physiol J 534: 531–540.
19. Palazzo E, de Novellis V, Marabese I, Cuomo D, Rossi F, et al. (2002)Interaction between vanilloid and glutamate receptors in the central modulation of nociception. Eur J Pharmacol 439: 69–75.
20. Cui M, Honore P, Zhong C, Gauvin D, Mikusa J, et al. (2006) TRPV1 receptorsin the CNS play a key role in broad-spectrum analgesia of TRPV1 antagonists. Neurosci J 26: 9385-9393.
21. Vígh B, Silva MJM, Frank CL, Vincze C, Czirok SJ, et al. (2004) The system of cerebrospinal fluid-contacting neurons. Its

supposed role in the nonsynaptic signal transmission of the brain. Histol Histopathol 19: 607-628.

22. Zhang LC, Zeng YM, Ting J, Cao JP, Wang MS (2003) The distributions and signaling directions of the cerebrospinal fluid contacting neurons in the parenchyma of a rat brain. Brain Res 989: 1-8.
23. Lu XF, Geng XJ, Zhang LC, Zeng YM (2008) The methodology or labeling the distal cerebrospinal fluid-contacting neurons in rats. Neurosci Methods J 168:98–103.
24. Spaziante R, Merola B, Colao A (1990) Beta-endorphin concentrations both in plasma and in cerebrospinal fluid in response to acute painful stimuli. Neurosurg Sci J 34: 99-106.
25. Wang MS, Zhang LC (1992) Methodological comparison on the tracing CSFCNs with HRP and CB-HRP. Acta Acad Med 12: 286–288.
26. Marinelli S, Di Marzo V, Florenzano F, Fezza F, Viscomi MT, et al. (2007)N-arachidonoyl-dopamine tunes synaptic transmission onto dopaminergic neurons by activating both cannabinoid and vanilloid receptors. Neuro psychopharmacology 32: 298–308.
27. Lipski J, Park TI, Li D, Lee SC, Trevarton AJ, et al. (2006) Involvement of TRPlike channels in the acute is mic response of hippocampal CA1 neurons in brain slices. Brain Res 1077: 187–199.
28. Marsch R, Foeller E, Rammes G, Bunck M, Kossl M, et al. (2007) Reduced anxiety, conditioned fear, and hippocampal long-term potentiation in transient receptor potential vanilloid type1 receptor-deficient mice. Neurosci J 27: 832–839.
29. Shibasaki K, Suzuki M, Mizuno A, Tominaga M (2007) Effects of body temperature on neural activity in the hippocampus: regulation of resting membrane potentials by transient receptor potential vanilloid4. Neurosci J 27:1566–1575.
30. Lu XF, Li YY, Wang CG, Wei JQ, Ye Y, et al. (2011) Substance P in the cerebrospinal fluid-contacting nucleus contributes to morphine physical dependence in rats. Neuroscience Letters 488: 188-192.
31. Du J, Yang XW, Zhang LC (2009) Expression of TRPM8 in the distal cerebrospinal fluid-contacting neurons in the brain mesencephalon of rats. Cerebrospinal Fluid Research 6: 3.
32. Amaya F, Oh-hashi K, Naruse Y, Iijima N, Ueda M, et al. (2003) Local inflammation increases vanilloid receptor 1 expression within distinct subgroups of DRG neurons. Brain Res 963: 190-196.
33. Hudson LJ, Bevan S, Wotherspoon G, Gentry C, Fox A, et al. (2001) VR1 protein expression increases in undamaged DRG neurons after partial nerve injury. Eur J Neurosci 13: 2105-2114.
34. Asai H, Ozaki N, Shinoda M, Nagamine K, Tohnai I, et al. (2005) Heat and mechanical hyperalgesia in mice model of cancer pain. Pain 117: 19-29.
35. Wang P, Yuke T (2009) Research progress in mechanism of spinal cord in neuropathic pain. Chinese Journal of Pain Medicine 15: 1.
36. Gibson HE, Edwards JG, Page RS, Van Hook MJ, Kauer JA (2008) TRPV1 Channels Mediate Long-Term Depression at Synapses on Hippocampal Interneurons. Cell Neuron 57: 746-759.
37. Liapi A, Wood JN (2005) Extensive co-localization and hetero multimer formation of the vanilloid receptor-like protein TRPV2 and the capsaicin receptor TRPV1 in the adult rat cerebral cortex. Eur J Neurosci 22: 825-834.
38. Sasamura T, Sasaki M, Tohda C, Kuraishi Y (1998) Existence of capsaicinsensitive glutamatergic terminals in rat hypothalamus. Neuro report 22: 2045-2048
39. Millan MJ (1999) The induction of pain: an integrative review. Prog Neurobiol 57: 1-164.
40. Millan MJ (2002) Descending control of pain. Prog Neurobiol 66: 355-474.
41. Palazzo E, Luongo L, de Novellis V, Berrino L, Rossi F, et al. (2010) Moving towards supraspinal TRPV1 receptors for chronic pain relief. Molecular Pain 6: 66.
42. Santos AR, Calixto JB (1997) Ruthenium red and capsazepine antinociceptive effect informalin and capsaicin models of pain in mice. Neurosci Lett 235: 73-76.
43. Michael GJ, Priestly JV (1999) Differential expression of the mRNA forthe vanilloid receptor subtype 1 in cells of the adult rat dorsalroot and nodose ganglia and its down reguation by axotomy. Neurosci J 19: 1844 –1854
44. Bodnar RJ, Kirchgessner A, Nilaver G, Mulhern J, Zimmerman EA (1982) Intra ventricular capsaicin: alterations in analgesic responsivity without depletion of substance P. Neuroscience 7: 631-638
45. Bodnar RJ, Simone DA, Kordower JH, Kirchgessner AL, Nilaver G (1983)Capsaicin treatment and stress-induced analgesia. Pharmacol Biochem Behav 18: 65-68.