CSF-contacting nucleus

The CSF-contacting nucleus is a special nucleus within the brain that has been recognized in recent years. ... Its neural somas are located in the parenchyma and communicate with other structures, such as non-CSF-contacting neurons, glia cells, and blood vessels in the brain.

Cerebrospinal fluid-contacting nucleus (CSF-CN) has been reported to be involved in the development of neuropathic pain and inflammatory pain. However, whether CSF-CN contributes to cancer-induced bone pain (CIBP) remains unknown. In this study, we aimed to illustrate the role of CSF-CN in the pathogenesis of CIBP and identify its potential mechanism via the MKP-1-mediated MAPK pathway. The Walker 256 cancer cells were injected into the tibia cavity of female Sprague-Dawley rats to induce CIBP models. Intracerebroventricular injection of cholera toxin subunit B- saporin (CB-SAP) was performed to “knockout” the CSF-CN. Morphine and LV-MKP-1 were applied. Mechanical and thermal hyperalgesia behaviors, double immunofluorescence staining and Western blot were conducted after CIBP induction. The results revealed that CIBP significantly reduced the mechanical withdrawal threshold and the thermal threshold. Double immunofluorescence staining revealed that c-Fos-positive neurons in CSF-CN were significantly higher in the CIBP group than that in the sham group. Targeted ablation of CSF-CN dramatically aggravated pain sensitivity. Moreover, MKP-1 was down-regulated in the CSF-CN after CIBP induction. Pharmacological intervention with morphine significantly ameliorated the mechanical and thermal hyperalgesia through reversing the down-expression of MKP-1 in the CSF-CN on day 14 after CIBP induction. Mechanically, overexpression of MKP-1 by LV-MKP-1 injection significantly relieved CIBP via inhibiting the expression of phosphorylated p38, which subsequently decreased the protein levels of Bax, cleaved caspase-3 and Iba-1, and reduced the mRNA levels of IL-1β, TNF-α and IL-6 in CSF-CN. In conclusion, CSF-CN contributed to CIBP via regulating the MKP-1-mediated p38-MAPK pathway. Future therapy targeting the expression of MKP-1 in the CSF-CN may be a promising new choice [1)].

1)
Chen P, Pan M, Lin QS, Lin XZ, Lin Z. CSF-CN contributes to cancer-induced bone pain via the MKP-1-mediated MAPK pathway. Biochem Biophys Res Commun. 2021 Feb 13;547:36-43. doi: 10.1016/j.bbrc.2021.02.010. Epub ahead of print. PMID: 33592377.