

Do intrathecal PACAP-evoked aversive behaviors represent itch-like behaviors ? – Possible involvement of PACAP signaling system in spinal itch transmission in mice.

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We have previously reported that a single intrathecal (i.t.) injection of PACAP or a PACAP type 1 (PAC1) receptor selective agonist, maxadilan, in mice induced spontaneous aversive behaviors (licking/biting/scratching directed toward the caudal part of body) for several hours. In this study, we explored possible involvement of itch-like components in the aversive responses and evaluated the importance of PACAP/PAC1 receptor signaling in several mouse models of itch.

The PACAP (i.t.)-evoked aversive behaviors were significantly inhibited by subcutaneous pretreatment with the μ -opioid receptor antagonist naltrexone and i.t. pretreatment of bombesin-saporin. We also found that i.t. pretreatment of PA-8, a novel small-molecule PAC1 receptor antagonist, attenuated 5-HT-induced scratching behaviors. Furthermore, single oral administration of PA-8 suppressed itch-associated behaviors in both dry skin (acetone/ether/water model) and 2,4-dinitrofluorobenzene (DNFB)-induced atopic dermatitis models. In addition, the development of 5-HT and DNFB-induced itch-like behaviors was markedly depressed in PACAP deficient mice. These results suggest that spinal PACAP/PAC1 receptor signaling is involved in an important mechanism underlying the itch-like behaviors, and blocking PAC1 receptor system may be a new strategy to manage itch sensation.