Synopsis of Original Research Paper

Elucidation of the molecular neuronal basis of the alloknesis pathway that converts tactile sensation into itch sensation and development of therapeutic method

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Mechanical alloknesis is an itch hypersensitivity phenomenon wherein a minor mechanical stimulus that would not normally cause itch, such as rubbing against clothing, triggers itch. This is a challenging problem in people with dry skin-based diseases such as xerosis and atopic dermatitis, which understandably diminishes their quality of life. However, the precise details of the pathogenic mechanism of mechanical alloknesis remain unclear. Recently, we found that intrathecal administration of sulfated cholecystokinin 8 (CCK8S) induced mechanical alloknesis in mice. Previous studies have identified CCK receptors, CCK1R and CCK2R, but the molecular mechanisms underlying the induction or activation of these receptors are not fully understood. This study was performed to reveal the roles of CCK receptors in induction of mechanical alloknesis. Behavioral analyses using CCK1R- or CCK2R-deficient mice showed that CCK8S-induced mechanical alloknesis was markedly reduced in CCK2R-deficient mice but not in CCK1R-deficient mice. Additionally, CCK2R-deficient mice exhibited a decreased frequency of mechanical alloknesis induced by itch mediators or dry skin. However, their response to heat pain or capsaicin-induced mechanical allodynia was unaffected. Notably, oral administration of a CCK2R antagonist suppressed dry skin-induced mechanical alloknesis. These results suggest that spinal CCK2R is involved in the induction of mechanical alloknesis and could be a potential target for its treatment.