PRURITUS

ROLE OF SPINAL CHOLECYSTOKININ SYSTEM IN ITCH

Mitsutoshi Tominaga [1] - Kotaro Honda [1] - Fumiya Kusube [1] - Eriko Komiya [1] - Ryohei Kosaka [2] - Nobuaki Takahashi [1] - Hisashi Naito [3] - Fumiyuki Yamakura [4] - Yasushi Suga [5] - Yasuhiro Tomooka [2] - Kenji Takamori [5]

Juntendo University Graduate School Of Medicine, Institute For Environmental And Gender Specific Medicine, Urayasu, Japan [1] - Tokyo University Of Science, Department Of Biological Science And Technology, Faculty Of Industrial Science And Technology, Katsushika-ku, Japan [2] - Juntendo University, Institute Of Health And Sports Science & Medicine, Inzai, Japan [3] - Juntendo University, Faculty Of International Liberal Arts, Bunkyo-ku, Japan [4] - Juntendo University Urayasu Hospital, Department Of Dermatology, Urayasu, Japan [5]

Introduction: Cholecystokinin (CCK) acts as a neurotransmitter and/or neuromodulator in the central nervous system (CNS) during some states, including anxiety, feeding and allodynia. It is known that sulfated CCK-8 (CCK8S) is distributed widely in the CNS, and two types of CCK receptors CCK1R and CCK2R have been identified. However, the relationship between CCK system and itch remains unclear.

Objectives: We investigated the role of spinal CCK system on itch in mice.

Materials & Methods: In at least 6 male C57BL/6J mice (7–12 week-old) in each group, scratching behavior analyses were performed after intrathecal (i.t.) injection of CCK8S at a specific concentration or in combination with CCKR antagonists. Behavior was recorded with the number of scratching bouts counted. Alloknesis assay was performed by application of innocuous mechanical stimuli using von Frey filaments at 10 sec intervals after i.t. injection of CCK8S or in combination with CCKR antagonists. To examine the effect of CCK2R antagonist in dry skin-induced alloknesis, itch was induced by repeated application to skin of acetone/ether (1:1) mixture followed by water (AEW).

Results: Intrathecal injection of CCK8S did not evoke scratching behavior in C57BL/6J mice unless followed by innocuous mechanical stimuli using von Frey filaments. The CCK8S-induced alloknesis was inhibited by i.t. injection of L-365,260, a CCK2R antagonist, but not by SR27897, a CCK1R antagonist. In addition, CCK8S- or AEW treatment-induced alloknesis was inhibited by oral administration of CCK2R antagonist L-365,260 with no effect of locomotion activity.

Conclusions: These results suggest that spinal CCK8S/CCK2R system is involved in induction of alloknesis in mice and may be a promising candidate for anti-alloknesis treatment.