

論 文 要 旨

Malocclusion Impairs Cognitive Behavior via AgRP Signaling in Adolescent Mice

思春期マウスにおける不正咬合は AgRP シグナルを介して
認識行動を低下させる

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Abstract

Introduction: Occlusal disharmony induced by deteriorating oral health conditions, such as tooth loss and decreased masticatory muscle due to sarcopenia, is one of the causes of cognitive impairment. Chewing is an essential oral function for maintaining cognitive function not only in the elderly but also in young people. Malocclusion is an occlusal disharmony that commonly occurs in children. The connection between a decline in cognitive function and malocclusion in children has been shown with chronic mouth breathing, obstructive sleep apnea syndrome, and thumb/digit sucking habits. However, the mechanism of malocclusion-induced cognitive decline is not fully understood. We recently reported an association between feeding-related neuropeptides and cognitive decline in adolescent mice with activity-based anorexia. The aim of the present study was to assess the effects of malocclusion on cognitive behavior and clarify the connection between cognitive decline and hypothalamic feeding-related neuropeptides in adolescent mice with malocclusion.

Methods: Four-week-old mice were randomly assigned to the sham-operated solid diet-fed (Sham/solid), sham-operated powder diet-fed (Sham/powder), or malocclusion-operated powder diet-fed (Malocclusion/powder) group. We applied composite resin to the mandibular anterior teeth to simulate malocclusion. We evaluated cognitive behavior using a novel object recognition (NOR) test, measured hypothalamic feeding-related neuropeptide mRNA expression levels, and enumerated c-Fos-positive cells in the hypothalamus 1 month after surgery. We also evaluated the effects of central antibody administration on cognitive behavior impairment in the NOR test.

Results: The NOR indices were lower and the agouti-related peptide (AgRP) mRNA levels and number of c-Fos-positive cells were higher in the malocclusion/powder group than in the other groups. The c-Fos-positive cells were also AgRP-positive. We observed that the central administration of anti-AgRP antibody significantly increased the NOR indices.

Discussion: The present study suggests that elevated cerebral AgRP signaling contributes to malocclusion-induced cognitive decline in adolescents, and the suppression of AgRP signaling can be a new therapeutic target against cognitive decline in occlusal disharmony.