

Central Amygdala is Related to the Reduction of Aggressive Behavior by *UMAMI* Ingestion during the Period of Development in an ADHD Model Rat

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Introduction: Monosodium glutamate (MSG), an umami substance, stimulates gut-brain axis communication via the gut umami receptors and subsequent vagus nerves. However, the brain mechanism underlying the effect of MSG ingestion during the developmental period on aggression has not yet been clarified. In this study, we investigated the effect of MSG ingestion on aggressive behavior during the developmental stage of ADHD model rat. **Methods:** The resident-intruder test was first assessed using a detailed analysis of aggressive behavior, including the frequency, duration, and latency of anogenital sniffing, aggressive grooming, and attack behavior. Immunohistochemistry of c-Fos expression was then conducted on all strains to predict potential aggression-related brain areas. Finally, the most aggressive strain, SHR/Izm, a known model of attention-deficit hyperactivity disorder (ADHD), was used to investigate the effect of MSG ingestion (60 mM solution) on aggression, followed by c-Fos immunostaining in aggression-related areas. **Results:** We revealed that the resident intruder test conducted during the dark phase reliably induced aggressive behavior. Among the four strains, SHR/Izm rats were the most aggressive in all aggression parameters. SHR/Izm rats also showed the highest number of c-Fos positive cells in aggression-related brain areas, including the pre-frontal cortex (PFC), lateral hypothalamus (LH), and central amygdala (CeA). MSG ingestion significantly decreased the frequency and duration of aggressive grooming and attack behavior and increased the latency of attack behavior compared with the control group. Furthermore, MSG ingestion successfully increased c-Fos expression in the intermediate nucleus of the solitary tract (iNTS), a terminal of the gastrointestinal sensory afferent fiber of the vagus nerve ($p=0.0094$), and decreased c-Fos expression in the CeA ($p=0.0084$). However, c-Fos expression in the PFC and LH was comparable between the MSG-treated and control groups. **Conclusion:** MSG ingestion decreased isolation-induced aggression in the rat model of ADHD, SHR/Izm, which was mediated by the vagus nerve related to c-Fos activation in the iNTS and c-Fos inactivation in the CeA.

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