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学位論文の題名	<p>Monosodium glutamate ingestion during the development period reduces aggression mediated by the vagus nerve in a rat model of attention deficit-hyperactivity disorder.</p> <p>（注意欠陥多動性障害モデルラットにおいて発育期のグルタミン酸ナトリウムの摂取は迷走神経を介して攻撃性を減少させる）</p> <p>Brain Research1690: 40-50, 2018.</p>
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## Abstract

We used an umami substance, monosodium glutamate (MSG), as a simple stimulant to clarify the mechanism of the formation of emotional behavior. A 60 mM MSG solution was fed to spontaneously hypertensive rats (SHR) from postnatal day 25 for 5 weeks kept in isolation. SHR are used as models of attention-deficit hyperactivity disorder since they show hyperactivity and impulsiveness when they are young. Emotional behaviors (anxiety and aggression) were then assessed by the open-field test, cylinder test and social interaction test. MSG ingestion during the developmental period resulted in a significant reduction in aggressive behavior but had few effects on anxiety-like behavior. Several experiments were performed to identify the reason for the reduced aggression with MSG intake. Blood pressure in the MSG-treated SHR was comparable to that of the controls during development. Argyrophil III staining to detect the very early phase of neuronal damage revealed no evidence of injury by MSG in aggression-related brain areas. Assessment of plasma amino acids revealed that glutamate levels remained constant ( $\sim 80 \mu\text{M}$ ) with MSG ingestion, except for a transient increase after fasting ( $\sim 700 \mu\text{M}$ ). However, lactate dehydrogenase assay in an in vitro blood-brain barrier model showed that cell toxicity was not induced by indirect MSG application even at  $700 \mu\text{M}$ , confirming that MSG ingestion caused minimal neuronal damage. Finally, vagotomy at the subdiaphragmatic level before MSG ingestion blocked its effect on aggressive behavior in the isolated SHR. The data suggest that MSG ingestion during the developmental period can reduce aggressive behavior in an attention deficit-hyperactivity disorder model rat, mediated by gut-brain interaction.

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