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Regulatory Mechanisms of Peripheral Salt Sensitivity by Natriuretic Peptides

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Summary

Na^+ is one of the most important minerals for living organisms, and animals need to ingest sufficient amounts of Na^+ to maintain vital activity. Recent studies suggest that an animal's taste sensitivity is dynamically optimized to reflect the nutritional status of the whole body, enabling efficient nutritional intake in response to biological demands. About the salt taste, in mice, angiotensin II (AngII), a hormone that stimulates the secretion of aldosterone, which increases blood pressure and promotes Na^+ absorption in the renal collecting ducts, has been reported to act as a suppressor for the salt taste sensitivity. This regulation mechanism promotes active salt intake when Na^+ is deficient. However, how animals' peripheral salt sensitivity and salt ingestion behavior are regulated when there is an excess of Na^+ in the body. In this study, we focused on natriuretic peptide (NP), a bioactive peptide involved in the regulation of blood pressure and mineral balance. There is an excess of Na^+ in the bloodstream, NP synthesis and secretion are promoted, and inducing increased diuresis and decreased blood pressure. Our experiments revealed the expression of two subtypes of NP receptors (NPRB and NPRC) in mouse taste buds. NPRB is highly coexpressed with epithelial sodium channel (ENaC), a salt taste receptor subunit. Moreover, pharmacological activation of NPRB signaling by vosoritide, a synthesized NPRB ligand, specifically enhanced amiloride-sensitive (ENaC-mediated) NaCl taste responses without affecting other taste qualities (sweet, umami, bitter and sour) in chorda-tympani nerve response recording experiments. Finally, we found that the activation of NPRB signaling significantly suppressed NaCl preference in the physiological concentration range in short-time lick tests. Altogether, NPRB signaling in the peripheral taste system may specifically increase ENaC-mediated salt taste sensitivity, and reduce salt intake when excessive sodium is present in the body. This regulatory mechanism may be one of the important regulatory systems that define salt intake behavior in animals.