

## Mechanisms for Sweet Enhancement by Addition of Salt

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### Summary

It is well known that sweet taste is enhanced by addition of NaCl, however physiological/molecular mechanisms for sweet enhancement by addition of NaCl is not elucidated. Sweet receptor forms heterodimeric complex of T1R2 and T1R3. Therefore, sweet enhancement by salt may be caused by modulation of T1R2/T1R3 activity by salt. To test this possibility, the effects of addition of salt to tastants on taste recognition thresholds in humans and human T1R2/T1R3 activity in heterologous expression system were analyzed. In human taste sensitivity tests, sweet recognition thresholds for sucrose, glucose and aspartame were significantly lowered by addition of 3 mM NaCl, which was almost tasteless to participants. In contrast, recognition thresholds for bitter (quinine), sour (HCl) and umami (monosodium glutamate + inosine-5'-monophosphate) were not affected by addition of 3 mM NaCl. Other salts such as N-methyl-D-gluconate chloride (NMDG-Cl), KCl and NaHCO<sub>3</sub> also lowered sweet recognition threshold for sucrose and glucose but not for aspartame. These results suggest that the addition of salt selectively enhances sweet taste sensitivity in humans and that there are multiple sweet receptor systems in humans. In heterologous expression system using human embryonic kidney (HEK) cells, HEK cells were able to respond to their intrinsic receptor agonist isoproterenol even in Na free bath solution, which did not contain Na<sup>+</sup> by substitution of NMDG. However, HEK cell response to isoproterenol was significantly reduced by addition of low concentration of Na<sup>+</sup>, indicating that the effect of Na<sup>+</sup> could not be assessed directly by simple addition of Na<sup>+</sup>. Alternatively, the effect of Na<sup>+</sup> was assessed by adapting HEK cells to Na free and low Na containing bath solution. In such experiments, response of HEK cells expressing human T1R2/T1R3 to sucralose but not to aspartame was significantly larger in low Na containing bath solution. On the other hand, HEK cell response to isoproterenol and response of HEK cells expressing human bitter receptor T2R38 to phenylthiocarbamide were significantly smaller in low Na containing bath solution. In conclusion, Na ion may affect T1R2/T1R3 activity, which would lead to enhanced sweet responses.