

# Brain-Wide Neural Circuit Controlling Synergistic Effect between Salt and Umami in Mice

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## Summary

Salt is not only an essential ingredient for maintaining our health, but its “salty” effect on food is one of the most basic and important elements in the human diet. Interestingly, umami, another taste component, has the effect of enhancing the salty taste of food, and this effect has been attracting attention as a means of achieving “salt reduction without sacrificing tastiness. However, this synergistic effect of salty and umami tastes is mainly based on sensory evaluation in humans, and lacks neurophysiological evidence. We have previously demonstrated the existence of a salty-umami synergy in animal models, similar to that in humans, and the association of dopamine release to this synergy. On the other hand, the specific mechanism of how taste information, which is fundamentally separated on the tongue (taste cells) as the receptive organ of taste substances, is integrated in the brain remains unclear. In this study, we attempted to identify brain regions that play active roles in the synergism of salt and umami by analyzing the separation and overlap between “salt-responsive neurons” and “umami-responsive neurons” across multiple brain regions involved in taste by using neural activity labeling technology

By combining (1) a neural activity-dependent gene expression method using the promoter sequence of the neural activity marker gene *cfos* and (2) a gene expression manipulation method using the Tet-OFF system, we labeled “salt-responsive neurons” and “umami-responsive neurons” in the whole brain with fluorescent proteins with different colors. The number of each taste-responsive neuron in the nucleus tractus solitarius, parabrachial nucleus, posterior and anterior insular cortex, and orbitofrontal cortex, which are known as taste-related brain regions, was then quantified. The results showed that the proportion of neurons responding to both salty and umami tastes was approximately 10-20% in all brain areas. These results suggest that the integration of salty and umami information may be mediated by a distributed neural mechanism across multiple taste areas rather than by a specific brain region.