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How Allelic Variation in the *Tas1r3* Taste Receptor Gene Affects Short-Term Licking Responses to Sweeteners

Individual variation in sweetener consumption is important to understand as health problems related to the over-consumption of foods, such as obesity, increase. To examine the genetic basis of this problem, we focused on mice, which are genetically and behaviorally similar to humans. Two groups of inbred mouse strains, tasters and nontasters, possess different alleles of the *Tas1r3* taste receptor gene. The gene encodes for a TIR3 receptor protein, which when combined with another receptor protein, TIR2, forms a sweet taste receptor. This is a heteromeric G-protein coupled receptor complex, which acts through a second messenger system to send signals to the brain via specific nerves. The taster mouse strains encode for a functional TIR3 receptor protein, while the nontaster form of TIR3 displays impaired binding when combined with TIR2, seemingly leading to a lower taste sensitivity to sweeteners. Previous long-term tests have shown that taster strains have a greater preference for sucrose at low concentrations, and an overall greater intake of sucrose than nontasters. This has led to the current hypothesis that the taster allele of *Tas1r3* leads to a greater functionality of the TIR3 receptor protein, which leads to a higher sensitivity to sweeteners, which in effect leads to a greater intake of sweeteners. However since this hypothesis was derived from long-term tests, there is the potential contribution of non-taste factors such as postingestive effects. Also, a clear explanation is not provided of how taste sensitivity leads to motivation for consumption of sweeteners. From a clinical standpoint, we feel that motivation for intake is more directly related to obesity and other health problems than taste sensitivity.

My project asked whether strains of mice that are more sensitive to sweeteners are also motivated to consume sweeteners, both at low and high concentrations. To this end, we used a short-term (1-minute) licking test so as to minimize the potential contribution of postingestive and experiential effects of the sweeteners on the patterns of intake. We tested 4 taster strains (FVB, SWR, B6, SM/J) and 4 nontaster strains (D2, 129, C3H, Balb). During each test session the mouse was given a choice between water and a sweetener solution. An apparatus called the lickometer recorded the number of licks the mouse took from each bottle. Our results showed sensitivity for sucrose (as indicated by preference thresholds), assorted with taster/nontaster status. However, the motivation to consume intermediate and high concentrations of sweeteners (as indicated by Standardized Lick Ratio, SLR) did not assort by taster/nontaster status. For example, the SLR's for the B6, a taster strain, was lower than those for the D2, a nontaster strain. Furthermore, the SLR's of the SWR's (tasters) and 129's (nontaster) seemed to be generally the same. We repeated these tests with a noncaloric sweetener, SC45647, and found similar results, thus indicating that the sucrose results were not confounded by post-ingestive effects. According to our findings in the 1-minute short-term assay, we conclude that allelic variation in the *Tas1r3* gene alone does not explain strain differences in the motivation to consume sweeteners.