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Using nonsynonymous mutations in taste and olfactory receptor genes to investigate the influence of eating behaviour on health

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Genome-wide association studies (GWAS) of food preferences⁽¹⁾ and intake⁽²⁾ have identified hundreds of loci, most previously linked to health conditions. This suggests these loci may reflect participants' health status, leaving unclear their direct influences on eating behaviour. Given that taste and olfactory perception play a crucial role in food preferences and choices⁽³⁾, this study aims to: i) investigate the influence of genetic variants within taste and olfactory receptor genes on food preferences and ii) use these variants to investigate the potential causal influence of food preferences on health. We assess the associations across 1214 nonsynonymous variants (minor allele frequency ≥ 0.01) within 425 non-pseudo taste and olfactory receptor genes and 140 food-liking traits in the UK Biobank ($n = 162006$ unrelated Europeans; mean age = 57). Food likings were measured on a 9-point scale, with 1 being 'Extremely dislike' and 9 being 'Extremely like'. We identify 700 associations (FDR-corrected $p < 0.05$), of which 88 are also associated with their corresponding food intake traits in the UK Biobank. We replicate 84 associations in the younger Avalon Longitudinal Study of Parents and Children (ALSPAC; $n = 2802$ unrelated Europeans; mean age = 25), including *OR2T6* rs6587467 for onion liking ($p = 5.4 \times 10^{-41}$ in UK Biobank, $p = 2.9 \times 10^{-4}$ in ALSPAC), whereas others cannot be replicated (e.g., *OR4K17* rs8005245 for garlic liking, p -value = 1.9×10^{-69} in UK Biobank, $p = 0.66$ in ALSPAC). These variants account for greater phenotypic variances in food-liking traits in the ALSPAC than in the UK Biobank (e.g., 0.54% and 0.25% for garlic liking in ALSPAC and UK Biobank, respectively), suggesting genetically determined sensory perception has larger impacts on food preferences in young adulthood. Lastly, we use an epidemiological technique, Mendelian randomisation⁽⁴⁾, to assess the potential causal influence of food preferences on health outcomes using food-liking-associated variants and summary results from large-scale GWAS. Taking likings for onions and bananas as an example, our results show that both are causally associated with lower systolic blood pressure (onions: $\beta = -1.257$, $p = 0.001$; bananas: $\beta = -3.166$, $p = 0.005$; unit = mmHg/liking score). While liking for onions decreases the risk of type 2 diabetes (odds ratio [OR, 95% confidence interval] = 0.856 [0.781, 0.939]), liking for bananas increases it (OR = 1.289 [1.051, 1.579]). We found no evidence for causal associations with coronary artery diseases (onions: OR = 0.995 [0.879, 1.126]; bananas: OR = 0.982 [0.742, 1.299]). This study furthers current knowledge of direct genetic influences on food preferences, which helps understand individual differences in eating behaviour and has implications for personalised nutrition. Results from causal modelling provide complementary evidence for previous observational studies and could be used to guide future trials.

References

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