Chemosensory receptor genes promoting liking onions lower blood pressure and type 2 diabetes risk

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Background: A major challenge in nutritional epidemiology is distinguishing causal effects from observational associations. While Mendelian randomization (MR) offers an alternative to randomized controlled trials for causal inference, its application to dietary exposures has been criticized due to the frequent use of invalid genetic instruments, which may reflect reverse causality or horizontal pleiotropy. This study aims to identify genetic variants with direct effects, biologically plausible effects on dietary exposures, and to use these in MR to assess the causal effect of food preferences and intake on cardiometabolic outcomes.

Methods: We tested the association between 1,214 nonsynonymous variants within 295 taste and 30 olfactory receptor genes and 140 food liking traits and their corresponding intake traits in UK Biobank (n up to 162,006; age 37 to 73; 54% female). Replication of food liking associations was conducted in the Avon Longitudinal Study of Parents and Children cohort (ALSPAC; n = 2,779; age 25; 64% female). Two-sample MR was used to evaluate the causal effects of food liking and food intake on body mass index, blood pressure, serum glucose and lipid levels, type 2 diabetes, and coronary artery disease using publicly available summary results statistics.

Results: We identified 700 significant associations across 117 receptor genes and 96 food liking traits, 84 of which were also associated with corresponding intake traits. Forty-five associations replicated in ALSPAC. MR analyses showed that a genetic predisposition to liking onions was causally associated with lower blood pressure and reduced risk of type 2 diabetes.

Conclusion: These findings provide novel insight into the direct genetic influences on food preferences and their consequent impacts on eating behaviors and cardiometabolic health. They also demonstrate the potential of chemosensory genetics to strengthen causal inference in nutritional epidemiology, offering a promising path toward more precise public health strategies for preventing and managing conditions such as hypertension and type 2 diabetes.