Diet could play a role in cognitive function across diverse races and ethnicities

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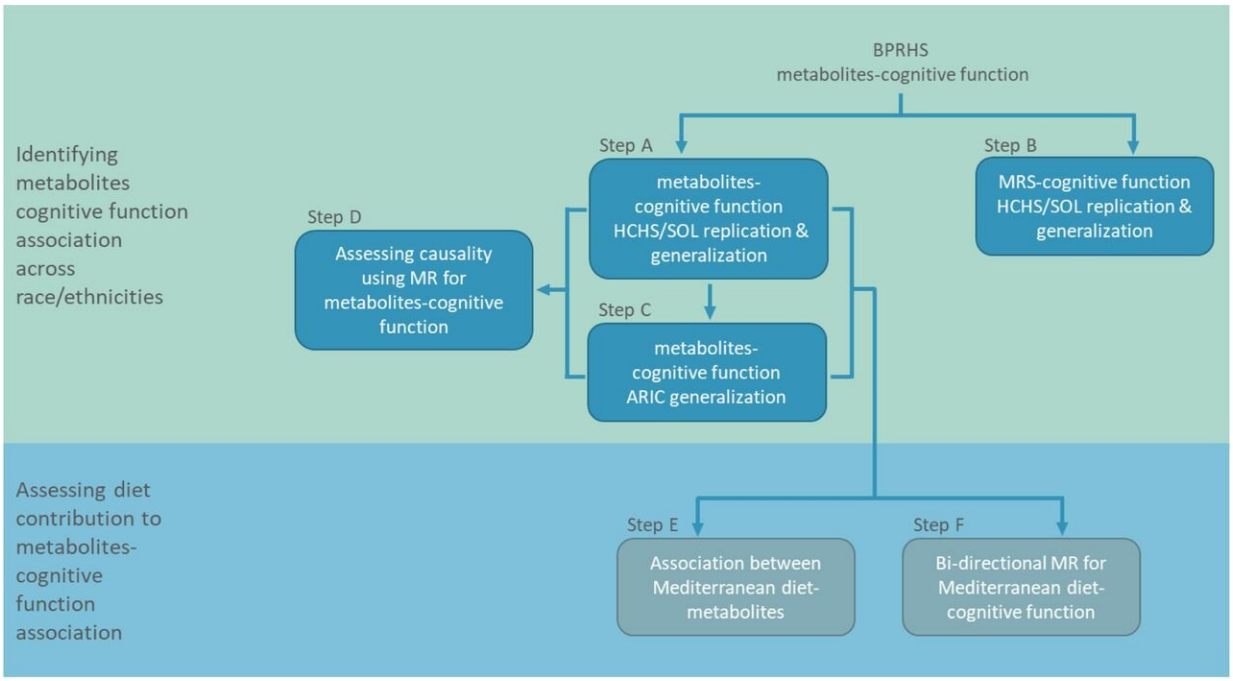

Metabolite—global cognitive function analyses flowchart. Step A: Replication and generalization analysis in HCHS/SOL of previously reported single metabolites associated with global cognitive function in BPRHS (Step A). Step B: Replication and generalization testing in HCHS/SOL of association of the metabolite risk score (MRS) constructed in BPRHS with extremes of global cognition. Step C: Generalization of single metabolite associations with global cognitive function in the Atherosclerosis Risk In Communities (ARIC) dataset. Step D: Two-sample Mendelian randomization (MR) analysis to evaluate causal relationships between the single metabolites and global cognitive function. Step E: Associations between the Mediterranean diet and single metabolites. Step F: Bidirectional MR to understand the cause-and-effect relationships between the

single-food intake scores and global cognitive function. Credit: *Alzheimer's & Dementia* (2022). DOI: 10.1002/alz.12786

Dietary choices and their consequences may certainly influence cognitive function. A new study led by investigators at Brigham and Women's Hospital, a founding member of the Mass General Brigham health care system, along with outside collaborators expands on previously published work (focused on Puerto Rican individuals in the U.S.) by including additional races and ethnicities.

The team found that certain plasma metabolites—substances created when the body breaks down food—were associated with global cognitive function scores across the diverse set of races and ethnicities. Their results are published in *Alzheimer's & Dementia*.

"Our study has huge strengths in expanding the sample size and in adding demographics compared to what previous research has done," said Tamar Sofer, Ph.D., and director of the Biostatistics Core Program in Sleep Medicine Epidemiology and a member of the Division of Sleep and Circadian Disorders at the Brigham.

"It also illustrates that studies that begin by focusing on minorities can give rise to insights that may be beneficial to other populations. We hope our findings will help people in making specific nutritional choices and in improving their cognitive health."

Nowadays, researchers can discover biomarkers associated with health changes and diseases by utilizing approaches like metabolomic profiling, which can survey thousands of metabolites within blood samples. An initial study in Boston looking at older adults of Puerto Rican descent found a series of metabolites that were associated with measured

cognitive functions.

Building off that work, Brigham researchers tested metabolite-cognitive function associations in 2,222 U.S. Hispanic/Latinx adults from the Hispanic Community Health Study/Study of Latinos (HCHS/SOL), and in 1,365 Europeans and 478 African Americans from the Atherosclerosis Risk In Communities (ARIC) Study. They then applied Mendelian Randomization (MR) analyses to determine causal associations between the metabolites and cognitive function, as well as between a Mediterranean diet and cognitive function.

The team discovered that six metabolites were consistently associated with a lower global cognitive function across all of the studies. Four of them were sugars or derivatives of sugars. Another metabolite, beta-cryptoxanthin, was associated with a higher global cognitive function in the HCHS/SOL and is also strongly correlated with fruit consumption.

"It is possible that these metabolites are biomarkers of a more direct relationship between diet and cognitive function," said lead author Einat Granot-Hershkovitz, Ph.D., who worked on this study as a postdoctoral fellow in Sofer's lab at the Brigham.

Diet itself can be an important source of many metabolites, including some with positive or negative associations with cognitive function. In this study, the Mediterranean diet score was associated with higher levels of beta-cryptoxanthin, which was positively associate with cognitive function. The Mediterranean diet was also negatively associated with the levels of other metabolites, which were associated with lower cognitive function. Previous research has also shown that adherence to the Mediterranean diet is associated with cognitive benefits.

While the study did have limitations like its cross-sectional, observational design which limited conclusions about the potential

influence of modifying metabolite levels on cognitive function (causal inference), the researchers attempted to use MR analyses to account for unmeasured confounding and establish some level of causal inference.

Their results showed weak causal effects between specific metabolites and global cognitive function. The researchers recommend that future studies assess metabolite associations with cognitive function and work to evaluate whether observed associations indeed indicate that changes in diet—manifesting in changing metabolite levels—can improve cognitive health.

"While the causal effect seen in our study may be weak, repeated research has shown that the Mediterranean diet is associated with better health outcomes, including cognitive health," said Sofer. "Our study further supports the importance of a healthy diet towards safeguarding cognitive function, consistent across races and ethnicities."

More information: Einat Granot-Hershkovitz et al, Plasma metabolites associated with cognitive function across race/ethnicities affirming the importance of healthy nutrition, *Alzheimer's & Dementia* (2022). DOI: 10.1002/alz.12786

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