The good, bad, and ugly? : How blood nutrient concentrations may reflect cognitive performance

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EDITORIAL

The good, bad, and ugly?

How blood nutrient concentrations may reflect cognitive performance

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A growing body of evidence is supportive of the influence of nutritional factors on cognitive health. There is evidence relating nutrition to cognitive measures to assess cognitive change over time, but such functional changes may not reflect the neuroanatomic or pathologic alterations that have occurred. Brain imaging may complement clinical assessment of dementia and hence, an understanding of how nutrients alter brain structure, specifically volumes, is key. The scarcity of such information is due in part to costs of brain imaging as well as the reluctance of participants to undergo these tests. Further, the complexity of dietary exposures or behaviors, and how best to characterize or quantify their diversity, are not only demanding of the respondent, but also demand a level of expertise in the investigator that is often overlooked. Most efforts have been directed to examining associations between single nutrients and cognitive status. More recently, nutritional epidemiologists have described dietary pattern—disease associations using a variety of approaches. These include a posteriori methods, such as factor or cluster analyses, that reduce nutrient data into investigator-named dietary patterns based on the intercorrelations between food/nutrient items or for cluster analyses on the differences[1]; a comparison of a priori patterns, such as the Mediterranean pattern[2,3]; and reduced rank regression, which is a combination of the 2 methods.[4] All of these approaches are highly dependent on the performance characteristics (validity and reliability) of the dietary instruments used in the intended population. Application of one of these analytical approaches is appealing because extraction of dietary patterns can distill the synergistic and sometimes antagonistic metabolic influences of food groups or nutrients (even anti-nutrients) within foods. Additional advantages of such methods include the ability to summarize dietary behavior when examined in the context of other health behaviors, the avoidance of type I (false-positive) error inflation when many nutrients are examined, and an alternative way to account for redundancy in contribution that several nutrients have on the outcomes (here, cognitive performance, brain volumes).[1–4] Moreover, if a dietary pattern is highly predictive of improved health outcomes, it may be easier to translate that pattern into practice, as has been reported for the Dietary Approaches to Stop Hypertension (DASH) diet plan.[5] People eat foods, not nutrients, and they eat them in combination, not in isolation.

In the current issue of *Neurology*®, Bowman and coworkers[6] describe how several indicator nutrients in blood (30 available in total) are cross-sectionally related to 1) cognitive performance scores of 104 adults from the Oregon Brain and Aging Study cohort (mean age of 87 years) and 2) 2 brain MRI measures in a subsample of 42 participants. These authors use factor analysis to describe patterns for nutrient indicators in blood. They extract 8 different plasma nutrient patterns—3 of which are associated with overall cognitive health (2 with better scores and 1 with poorer scores) and MRI total brain volumes (TBV) and white matter hyperintensity (WMH) volumes.

Nutrient biomarker patterns may afford complementary ways to examine the influence of food mixtures as consumed, independent of limitations described for current food frequency questionnaires and 24-hour dietary recalls. The factor analytic approach allows several important variables to be taken into account simultaneously, such as the bioavailability of nutrients consumed in foods and the genetic variability in bioavailability. Thus, nutrient biomarker patterns may more closely reflect what is available to brain tissues. Moreover, the 2 patterns that are associated with cognitive health and brain volumes are consistent with previous reports of dietary/blood exposures and cognitive outcomes, such as the association of trans fat and cognitive decline in a biracial cohort of elders in Chicago[7] or between serum vitamin B12 markers and cognitive decline.[8] Bowman and coworkers show that a high trans fat

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pattern is related to worse cognitive scores and less TBV. Similarly, a BCDE pattern (reflecting high plasma vitamins B, C, D, and E) is related to better cognitive function and more TBV. Interestingly, the relationship between the BCDE pattern and cognition is not attenuated when TBV is entered into models, suggesting that the contribution to cognitive performance is not entirely explicable by structural changes or cerebral atrophy. The third pattern described associates marine omega 3 with better executive function and lower WMH volume, but these relationships are no longer significant when depression and hypertension are added to models.

If the relationships between cognitive scores and MRI measures with nutrient biomarker patterns are confirmed in a larger, more ethnically diverse sample of older adults, this approach should be exploited to extract nutrient biomarker patterns predictive of cognitive change. Moreover, additional biomarkers for food group and food subgroups might be explored—i.e., reservatrol for wine, hydroxytyrosol for olive oil and nuts, or proline betaine for citrus fruits.

One of the strengths of the work of Bowman et al. was the use of plasma nutrient levels rather than self-reported dietary patterns. Recall errors and biases that occur when individuals report their usual diet, in particular, in those who may be cognitively challenged,[9,10] are major threats to interpretation of dietary patterns. However, limitations are also inherent with a bioassay strategy for estimating diet. First, there are costs underlying analysis of a set of biomarkers to define the pattern. Second, the acquisition of biological specimens to measure nutrient biomarkers is not without burden to the participants, especially if fasting is necessary. Fasting conditions were required for the Oregon cohort participants. Tradeoffs between the challenges of participant burden (convenience and time), costs, and the quality of longitudinal information on dietary exposures and their influence on brain structural changes or clinically relevant function will determine the utility of the approach these authors have spearheaded.

AUTHOR CONTRIBUTIONS

Prof. Tangney: drafting/revising the manuscript, study concept or design, analysis or interpretation of data. Dr. Scarmeas: drafting/revising the manuscript, study concept or design, study supervision.

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