Nutritional Prevention of Cognitive Decline[1,2]

Regan Bailey* and Lenore Arab

David Geffen School of Medicine, University of California, Los Angeles, CA

By the year 2030, 1 in 5 Americans will be over the age of 65 y (1). The demographic shift will increase the prevalence of age-related chronic diseases and place considerable demands on the healthcare system. Chronic disease, common among older adults, contributes to disability and diminishes quality of life (2). Thus, there is a critical need to understand the preventative role of nutrition in modifying the risk of age-related chronic disease.

Cognitive impairment results from a complex interplay of many factors. The single most important predictor of cognitive decline is age (3). However, demographic, genetic, socio-economic, and environmental factors, including nutrition, play important roles. Thus, nutritional strategies to prevent or slow cognitive decline could have a tremendous public health impact. Previous evidence suggests the preventative role of nutrients and foods, either singly or in combination, through specific patterns of intake on reduction in cognitive decline. Recently, a scientific symposium was held at the 2012 Experimental Biology Meeting to present emerging research in this field, focusing on 4 topic areas: B vitamins; coffee, tea, and caffeine; (n-3) fatty acids; and vitamin D.

The role of B vitamins: Martha Morris

The roles of the B vitamins folate and vitamin B-12 in cognitive function and decline have been extensively studied, stemming from their functions in methylation pathways and reducing homocysteine (both) or methylmalonic acid (vitamin B-12 only) concentrations. Substantial differences among the randomized controlled trials (RCT) in the population groups studied, the doses and duration of supplementation, and the cognitive assessments employed make the interpretation of the available clinical data problematic. However, observational studies have consistently linked hyperhomocysteinemia to slow information processing and low folate status to poor memory. Low vitamin B-12 status may increase the risk of rapid global cognitive decline, but the susceptible population subgroup has yet to be clearly defined. Whether supraphysiologic folate status is harmful or helpful is another area of uncertainty. Clearly, a deficiency in either vitamin is problematic for cognitive function, but the utility of these vitamins in preventing and treating cognitive decline in replete populations remains unclear.

Tea, coffee, and caffeine: Lenore Arab

Observational studies suggest that consumption of tea or coffee may confer a beneficial effect on cognition. It is not known if this effect is mediated by caffeine, one of the active ingredients common to both beverages, or by other bioactive components, or due to characteristics of consumers compared with nonconsumers. Caffeine is related to increases in information processing speed, attention, and reaction time, and consumption has been associated with enhanced acute cognitive performance. In general, cohort studies provide evidence that consumption of coffee and tea may modestly reduce the rate of cognitive decline (data from 6 studies, follow-up time 1–10 y). The cohort literature in general suffers from the lack of attention to item response bias in the measures of cognition, missing data, and loss to follow-up that can bias findings. Data from the few prospective studies on this topic indicate gender-specific differences and a lack of a dose-response association.

(n-3) Fatty acids: Tommy Cederholm

The (n-3) fatty acids DHA and EPA are important constituents in the brain and may affect cognition by a variety of mechanisms related to cell membrane fluidity, receptor affinity, and gene regulation and through inflammation pathways. Experimental studies have demonstrated the potentially ameliorating effects of DHA on amyloid fragment formation, signal transduction, and angiogenesis. Data from animal and in-vitro studies consistently show a positive effect of DHA/EPA on cognitive variables, but the human data are less clear-cut. Epidemiological evidence suggests that diets high in fish [a rich source of (n-3) fatty acids] may reduce the risk of cognitive decline and Alzheimer's disease and that higher plasma or RBC DHA and EPA concentrations are related to higher scores on various measures of cognitive function and a lower risk of dementia. Whereas fish intake clearly

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* To whom correspondence should be addressed. E-mail: baileyr@mail.nih.gov.

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seems beneficial, intervention trials using (n-3) fatty acids as dietary supplements have been less clear-cut because of equivocal findings. This may in part be due to issues in study design. The data from both the epidemiological and clinical data indicate that the beneficial role of (n-3) fatty acids on cognition is stronger among those with mild cognitive impairment rather than for either healthy adults or those with Alzheimer's disease.

Vitamin D: Josh Miller

Vitamin D has several health functions beyond bone health, including roles that are central to cognition such as immune modulation and gene regulation. Vitamin D receptors have been found in many regions of the brain as has the enzyme 1-α-hydroxylase, which converts 25-hydroxyvitamin D to the active form, 1,25-dihydroxyvitamin D. The active form of vitamin D induces gene transcription for several key cognitive processes such a synaptogenesis, neuroplasticity, neurotransmission, and neurotransmitter synthesis, which all ultimately influence cognition and, more specifically, memory and learning. The majority of cross-sectional studies suggest that lower serum 25-hydroxyvitamin D concentrations are related to increased risk of dementia, mild cognitive impairment, and/or lower global cognition scores. Longitudinal data seem to support the role of poor vitamin D status and increased rates of cognitive decline and increased risk of dementia. There is a need for RCT to further investigate the role of vitamin D in cognitive function and the prevention of cognitive decline.

Issues with assessing nutrition and cognition

Although this session focused on very different nutrients, bioactives, and foods, several major themes emerged. It appears that in many cases, the RCT data (if even available) either do not support or contradict the observational evidence, making the totality of available scientific evidence difficult to synthesize. There is a clear lack of uniformity in the way researchers measure cognition and what specific domains are assessed. In cohort studies of elderly populations, the biases associated with loss to follow-up require imputation and modeling strategies that are not uniformly applied. Furthermore, among the available data, there are substantial differences in the population groups studied, the doses and duration of supplementation, and the vehicle for delivery (i.e., the nutrient supplied by a dietary supplement vs. a food or beverage) that makes the interpretation of the available clinical data problematic. There are also strong genetic components to Alzheimer's disease. One gene coding for apoE is known to influence the risk of developing the disease and at what time (i.e., early or late onset). Aside from genetics, there also appears to be responsive subgroups for some of these nutritional factors such as females and caffeine or those with mild cognitive impairment and (n-3) fatty acids.

Conclusion

Given the prevalence of cognitive-related disease in older adults and the tremendous burden these issues cause for individuals, families, caregivers, and the healthcare system, scientific research on the modifiable risk factors related to prevention or treatment are absolutely critical (3). Future studies, both in populations and using RCT, need to focus on the maintenance of cognitive function in healthy adults or prevention of decline in those who are already affected.

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