Pros/Cons Session

Use of antioxidants in preventive cognitive decline (Y/N)

Antonia Trichopoulou, M.D.

Medical School, University of Athens
and
Hellenic Health Foundation
CONFLICT OF INTEREST DISCLOSURE

I have no potential conflict of interest to report
Antioxidants and improved nutrition have long been considered potential strategies to delay cognitive decline.

Increased production of Reactive Oxygen Species (ROS) may lead to increased oxidation of:

- Lipids
- DNA
- Protein
- Neurons
- apoE4

All of which may contribute to cognitive ageing.
Epidemiological data suggest protective role of

n-3 fatty acids & B-vitamins

on cognitive decline and dementia

in addition to

antioxidant nutrients such as vitamins E and C, carotenoids, and flavonoids

Clinical trials of supplementation with these nutrients have generally failed to uncover a clear benefit

Valls-Pedret C & Ros E. Epidemiology 2013
Dietary antioxidants, cognitive function and dementia —
A Systematic review


Habitual dietary intake of antioxidants and cognition

Mixed findings

13 longitudinal studies

8 cross-sectional studies

Dietary assessment
differential measures of cognitive performance
large heterogeneity in study design
insufficient measures of confounders
Prophylactic supplementation with vitamins is not supported by prospective trials

However

Positive data from observational studies support a Mediterranean diet combined with intake of vitamins, antioxidants and unsaturated fatty acids

Polivka D & von Arnim CA. Internist (Berl). 2015
Dietary patterns allow to combine the synergistic effects of single nutrients

Main biological mechanisms by which diet could potentially protect against dementia risk and cognitive decline:

1. Vascular system (e.g., aortic stiffness or microvascular function)

2. Oxidative stress (e.g., free radicals and brain protection or damage or loss of neuronal homeostasis and neurodegenerative diseases)

3. Attenuation of the inflammatory pathway (e.g., microglial priming)
15 cohort studies with 41,492 participants

Outcome of interest cognitive function
divided into domains of memory and executive function

Meta-analysis of cohort studies revealed a significant association between MeDi and older adults' episodic memory \( (n = 25,369, r = 0.01, P = 0.03) \)
and global cognition \( (n = 41,492, r = 0.05, P \leq 0.001) \)

but not working memory \( (n = 1487, r = 0.007, P = 0.93) \)
or semantic memory \( (n = 1487, r = 0.08, P = 0.28) \).

Meta-analysis of RCTs revealed that compared with controls, the MeDi improved delayed recall \( (n = 429, P = 0.01) \),
working memory \( (n = 566, P = 0.03) \),
global cognition \( (n = 429, P = 0.047) \)

but not episodic memory \( (n = 566, P = 0.15) \), immediate recall \( (n = 566, P = 0.17) \), paired associates \( (n = 429, P = 0.20) \),
attention \( (n = 566, P = 0.69) \), processing speed \( (n = 566, P = 0.35) \), or verbal fluency \( (n = 566, P = 0.12) \).

The strongest evidence suggests a beneficial effect of the MeDi on older adults' global cognition

Commentary: Mediterranean diet and cognitive function: are we approaching clarity in this area?

There is increasing clarity that Med diet may confer protection against cognitive decline

BUT

It is unclear

it is the overall dietary pattern that is important or

select aspects of the diet or

other lifestyle factors that may “travel” with Mediterranean diets or

perhaps the whole package is most important

Whitmer RA & Kushi LH Epidemiology 2013
Intervention trials are needed to elucidate the effects of a high intake of dietary antioxidants on cognitive functioning and to explore effects within a whole dietary pattern.
Antioxidants have well known biological effects besides antioxidant activity including

- reduced inflammation
- improved endothelial vasodilatation
- increased production of vasodilatory compounds, such as nitric oxide

All of these mechanisms could be related to changes in cognitive function
Numerous studies have been conducted demonstrating a possible link between the intake of specific nutrients and foods on cognitive functioning.

Examples include:
- omega-3 fatty acids
- vitamin D, vitamin B6
- vitamin B12
- folate
- flavonoids
- and vitamin E

But also foods

such as fish, nuts and seeds, and fruits and vegetables.
Due to pathological differences between dementia types,
different mechanisms by which dietary antioxidants exert their effects may exist
depending on the dementia subtype
Careful consideration should also be given to potential confounding factors such as Genetics, Smoking, physical activity, supplemental and total energy intakes.
The pathology underlying cognitive impairment may begin decades prior to onset of detectable symptoms.

Thus, long-term antioxidant intake could be most relevant for cognitive outcomes in later life.

Launer LJ. Neurobiol Aging. 2005
Thank you for your attention
Future observational studies and trials should examine the influence of individual components of the MeDi with cognitive outcomes.

Studies examining the impact of the MeDi on biomarkers that reflect inflammation would give further insight into any potential mechanisms underpinning the effects of the MeDi on cognition.

Future trials taking a multi therapeutical approach to enhance modification of these mechanisms (i.e. intervention using the MeDi in conjunction with exercise).

Micronutrient supplementation improved serum micronutrient status, with improved metabolic markers for B vitamins but not for intracellular antioxidant status

.........there is a necessity of determining micronutrient status
........................in nutritional supplementation trials

Von Arnim CA et al. Nutr J 2013
Plasma Lutein and Zeaxanthin Are Associated With Better Cognitive Function Across Multiple Domains in a Large Population-Based Sample of Older Adults: Findings from The Irish Longitudinal Study on Aging

Methods:

association between plasma lutein and zeaxanthin and domain-specific cognitive performance

4,076 community-dwelling adults aged 50 years or older

Results:

Higher plasma lutein and zeaxanthin were independently associated with better composite scores across the domains of global cognition, memory, and executive function.

We also found evidence that higher plasma zeaxanthin, but not lutein, was associated with better processing speed. These associations were consistent across domains.

Conclusions:

Further investigation of the prognostic value of carotenoid concentrations, and their changes, on cognition in similar population-based samples longitudinally is warranted.

The influences of APOE rs429358 polymorphism on plasma and erythrocytes’ antioxidant parameters could be modified by GSTT1 genotype; the influences of APOE rs7412 could be modified by GSTM1 genotype.