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

8 cross-sectional
13 longitudinal studies

Habitual dietary intake of antioxidants and cognition

Mixed findings

large heterogeneity in study design

differential control of confounders

insufficient measures of cognitive performance

dietary assessment

Crichton GE et al. Plant Foods Hum Nutr. 2013

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. Inernist (Berl). 2015

Dietary patterns allows 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)***

The Impact of the Mediterranean Diet on the Cognitive Functioning of Healthy Older Adults: A Systematic Review and Meta-Analysis

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

Loughrev DG et al. Adv Nutr. 2017 jul

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.

important to consider

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

Nutrition and mechanisms in cognitive functioning

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

<u>but also foods</u>

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 therapeutic approach to enhance modification of these mechanisms (i.e. intervention using the MeDi in conjunction with exercise)

Loughrev DG et al. Adv Nutr. 2017 jul

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

Feeney J. J Gerontol A Biol Sci Med Sci 2017

Plasma and erythrocytes' antioxidant parameters levels were associated with APOE rs429358, rs7412 polymorphism.

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

LINHONG YUAN ET AL *NUTRIENTS* **2015**