Nutrient intake, nutritional status, and cognitive function with aging

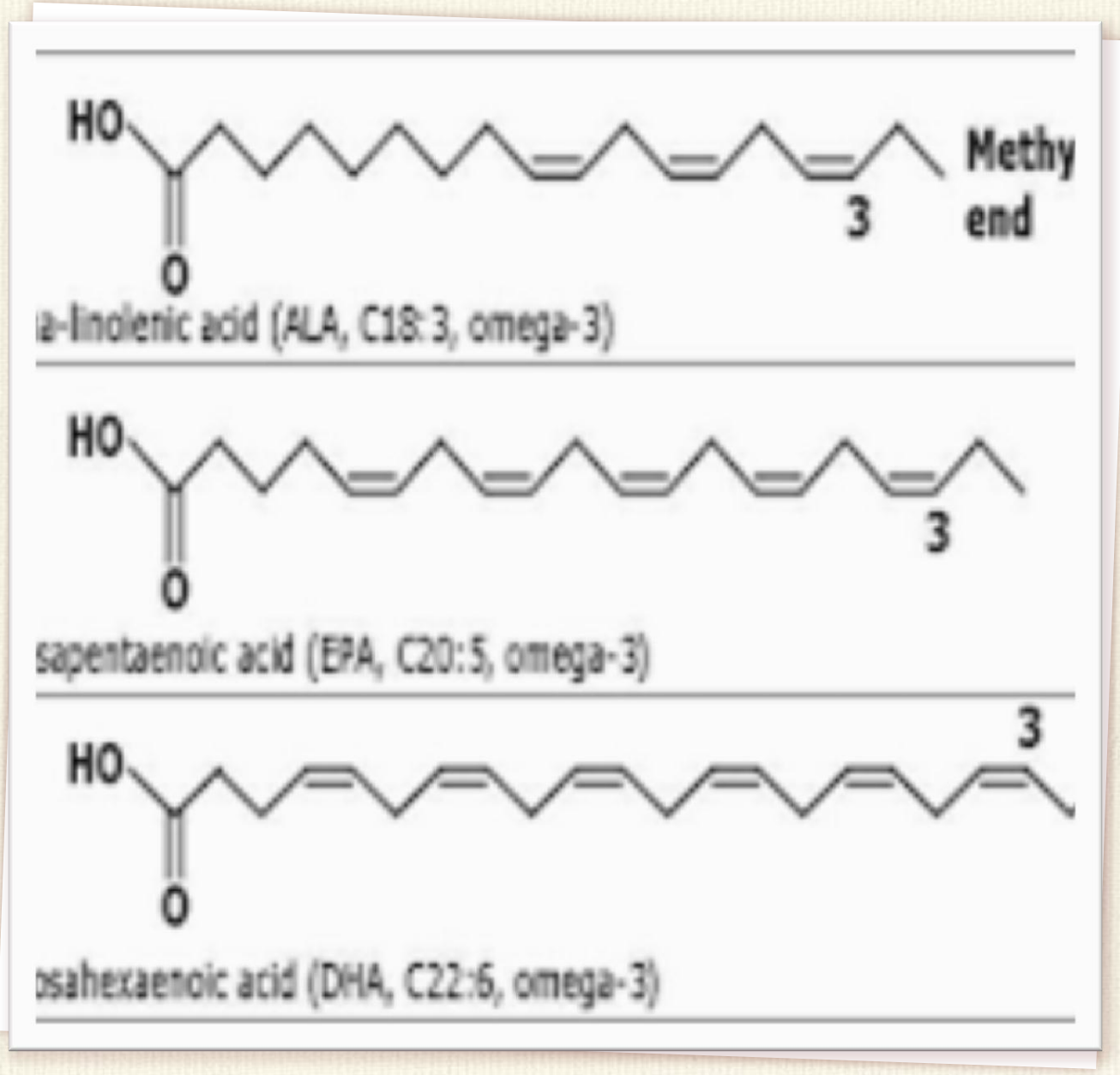
Dr.Reyhane Aminoroaya

Introduction


Ω3

Omega-٣ fatty acids

- long-chain polyunsaturated fatty acids,
- associated with protection against several chronic diseases, including those related to cognitive decline,
- limited in the food supply.
- more than ٨٠% of adults aged ٢٠ years and older had plasma omega-٣ fatty acids below those recommended for cardiovascular health.
- eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) appear to be important for brain and CNS function,
- DHA is preferentially taken up by cell membranes in the brain.

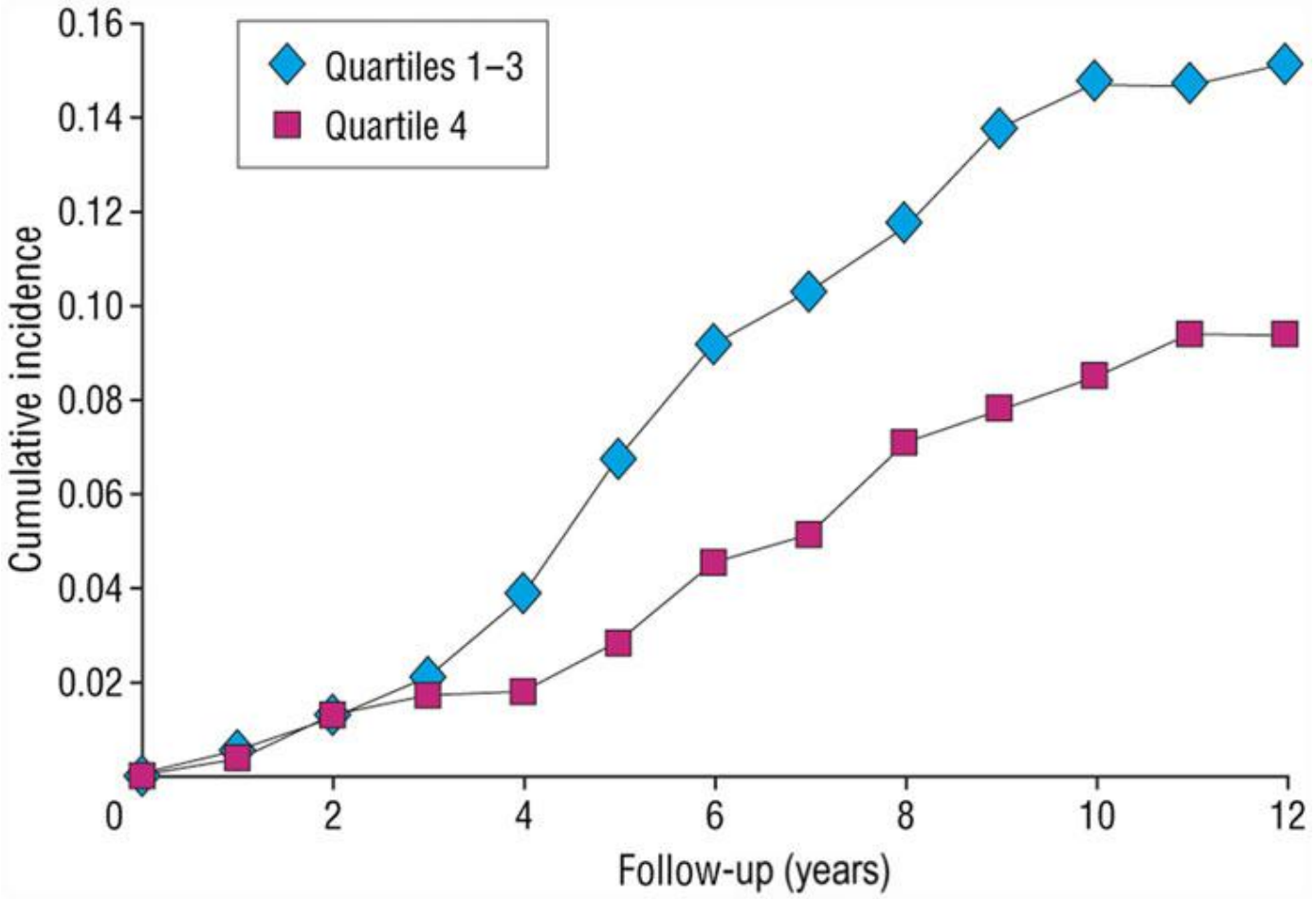


- found mainly in fatty fish, such as salmon, mackerel, tuna, and sardines,
- not widely consumed in the general population.
- In plants, omega-٣ fatty acids are found as a-linolenic acid (ALA), which is a precursor of EPA and DHA.

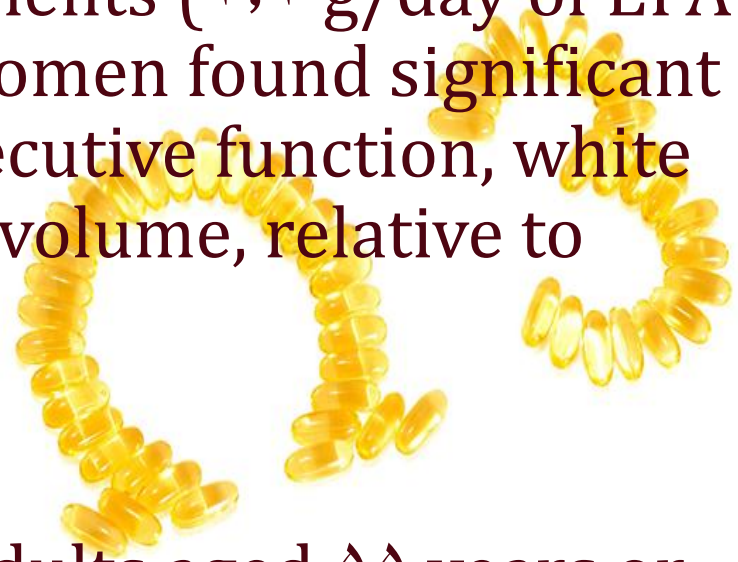
- conversion to these more active forms is relatively inefficient
- Good sources of ALA are also limited and include flax seeds, flax seed oil, walnuts, and canola oil.
- ۰,۶–۱,۲% of total energy intake
- for adults aged ۶۰ years and older, the mean intake of omega-۳ fatty acids was approximately ۱,۴۲ g, providing about ۱۳ kcal/day or ۰,۶۵% of a ۲۰۰۰-kcal diet

- protective associations against cognitive decline and incident Alzheimer’s disease.
- Cross-sectional and case-control studies have demonstrated associations between blood concentration, or brain membrane concentration of DHA and dementia status.
- A meta-analysis of ١٠ studies concluded that blood or tissue omega-٣ fatty acid concentrations were significantly lower in adults with dementia than in same-aged adults without dementia
- In the Framingham Heart Study, cognitive decline over several years was significantly associated with lower baseline concentration of plasma DHA

- DHA status was directly associated with fish intake in the Framingham Heart Study, with a mean intake of three servings per week in the upper quartile.



- A ۲۶-week RCT of fish oil supplements (۲,۲ g/day of EPA and DHA) in ۵۰- to ۷۰-year-old women found significant improvements in measures of executive function, white matter integrity, and gray matter volume, relative to placebo



- another study with ۴۸۵ healthy adults aged ۵۵ years or older showed that ۲۴ weeks of supplementation with ۹۰۰ mg/day DHA improved learning and memory function

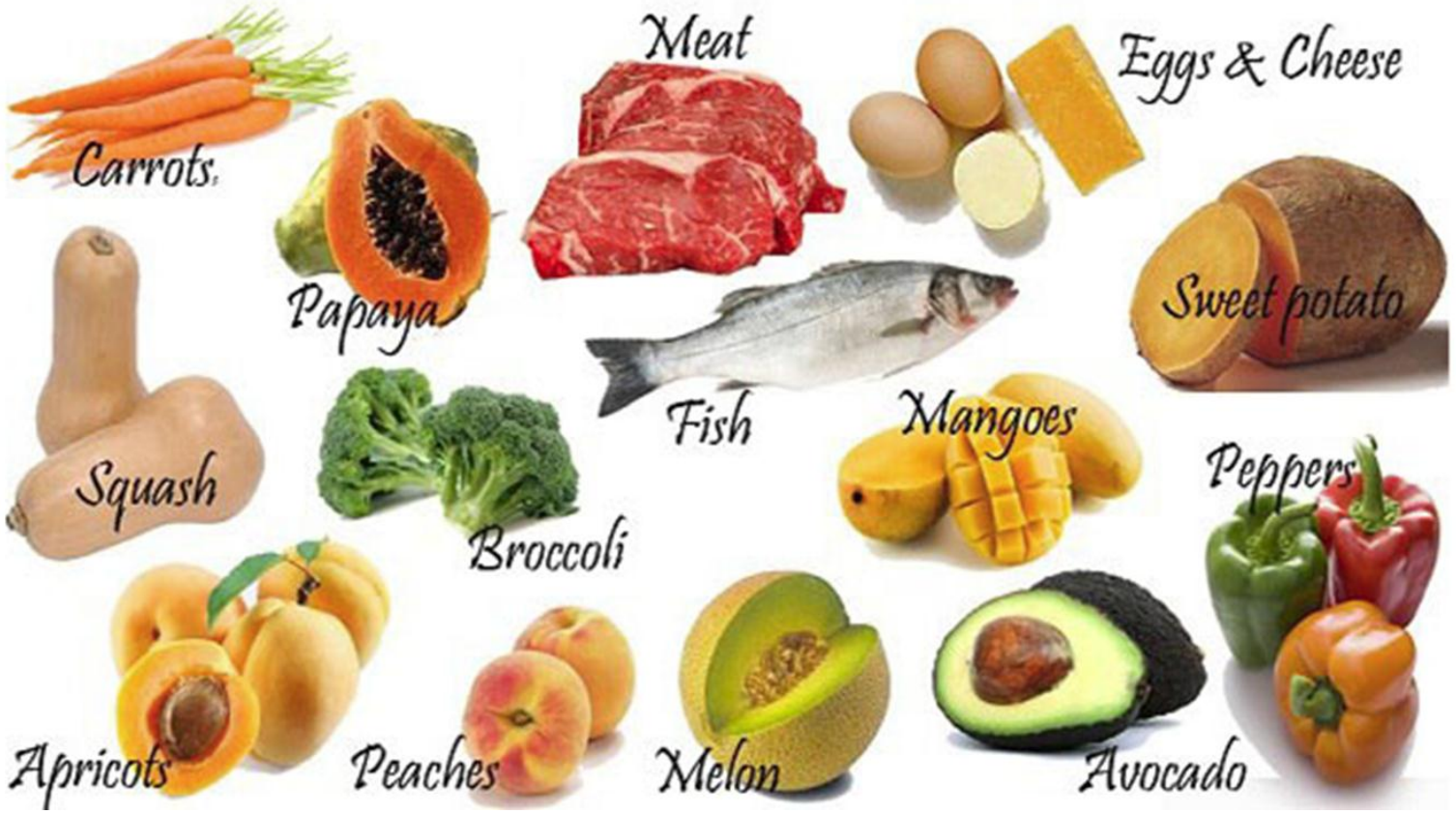
- studies in cell culture have shown protective effects of DHA on inhibition of $A\beta$ fibrillation and reduction of amyloid-induced toxicity, suggesting a mechanism for reduced amyloid plaque buildup in brain tissue

- an RCT of DHA in individuals with mild-to-moderate Alzheimer's disease showed no slowing of cognitive decline over ١٨ months

- It is possible that supplementation may be too late once Alzheimer's disease is in progress and that earlier intervention is needed.

- polyunsaturated fatty acids, either alone or in combination, had no significant effects on cognitive decline over ۳ years in elderly people with memory complaints.
- healthy populations may have preventive benefits from fish and DHA intake, like older adults with memory complaints/mild cognitive impairment, and maybe subgroups of patients with mild/moderate Alzheimer's disease may also show such benefits. Still, more studies are needed.

B VITAMIN FOOD SOURCES



B vitamins

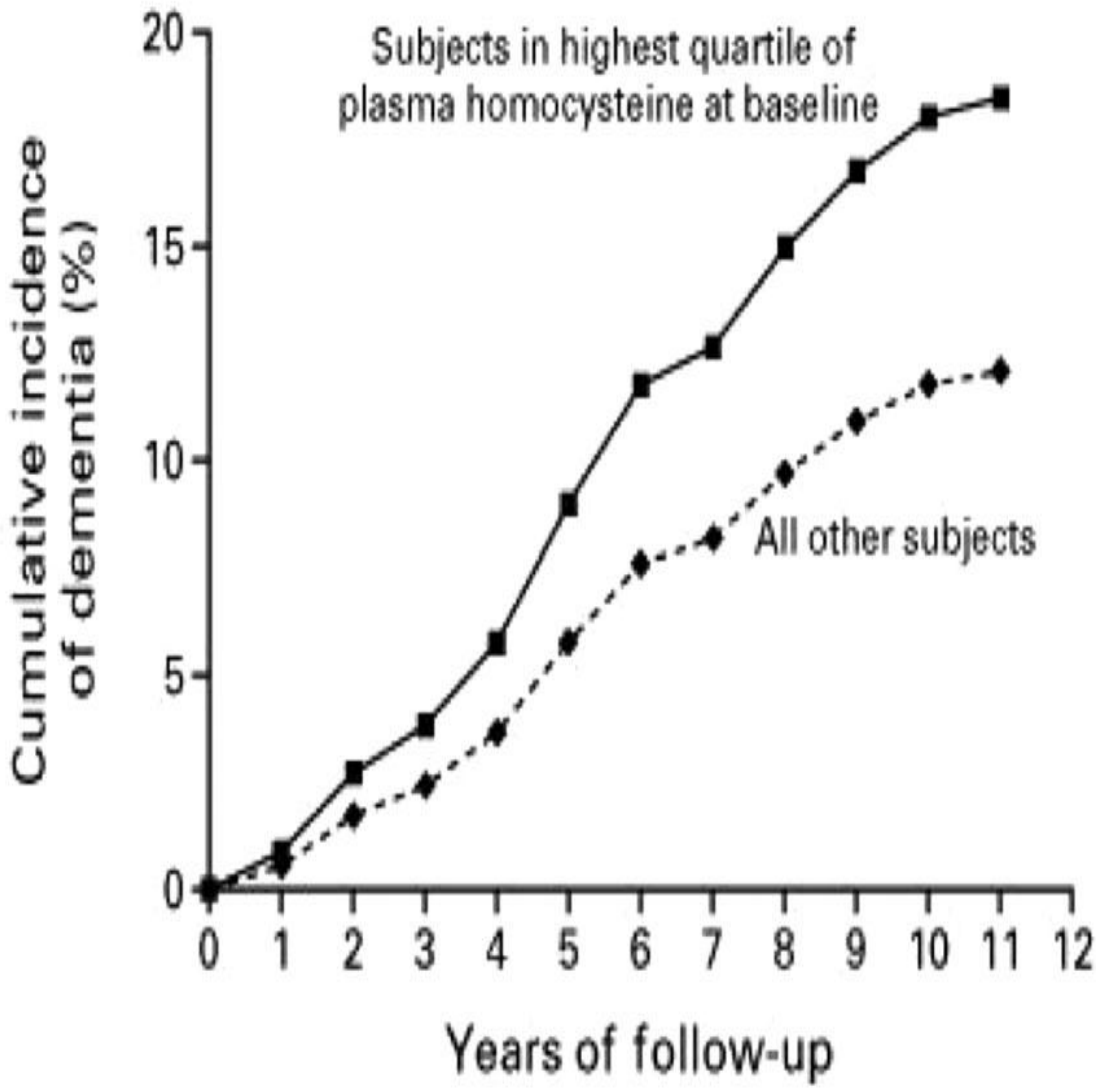
- Several B vitamins are associated with cognitive function in older adults,
- folate, vitamin B_6, and vitamin B_{12}.
- Required for proper DNA methylation
- to prevent the accumulation of homocysteine, an intermediary amino acid that has been associated with cardiovascular disease and stroke, as well as cognitive decline

B vitamins

- Before the U.S. FDA mandated folate fortification in refined grains in the mid-١٩٩٠s, low folate status was common in older adults.
- Since then, vitamins B٦ and B١٢ remain more important as limiting nutrients.
- Recommended dietary allowances (RDAs) for individuals aged ٥١ years and older are ٤٠٠ μg for folate,
- ٢,٤ μg/day for vitamin B١٢,
- and ١,٤ and ١,٧ mg/day for vitamin B٦ for women and men, respectively

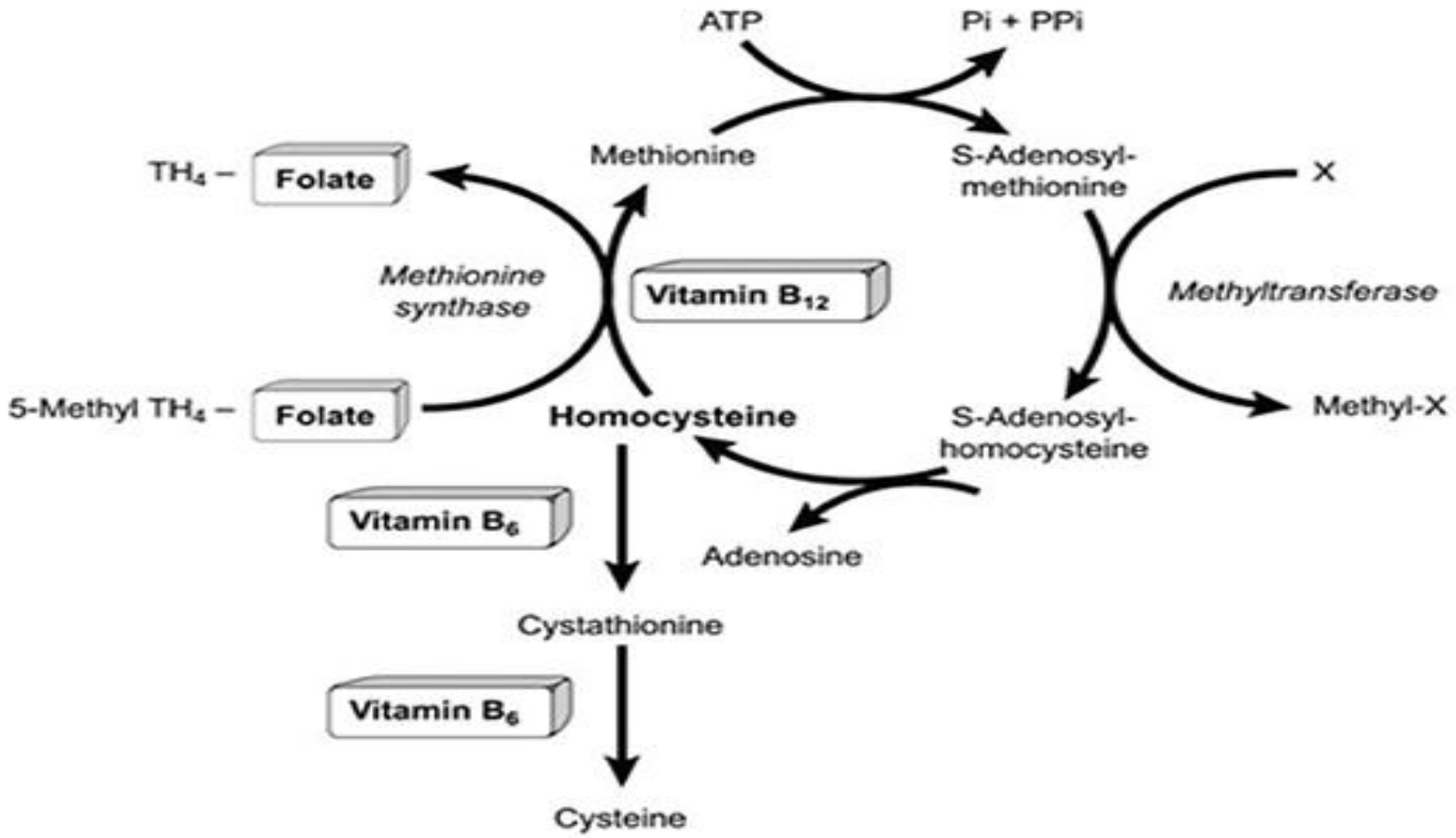
- Major sources of folate include legumes and dark green leafy vegetables;
- major sources of vitamin B_{6} include fish, liver, potatoes, and bananas;
- major sources of vitamin B_{12} include animal-source foods.

- The association between total homocysteine and cognitive decline was clearly illustrated in the Framingham Heart Study, in which, after over ١١ years of follow-up, the incidence of dementia was found to be significantly greater among people in the highest quartile of plasma homocysteine, relative to those with lower concentrations



- Folate is a substrate in the pathway that converts homocysteine to methionine, leading to the synthesis of S-adenosyl methionine, a methyl donor for DNA methylation,
- vitamin B١٢ is a coenzyme in the same pathway.
- Vitamin B١٢ is also centrally important to the maintenance of neurological function, through its protection of the myelin coating of nerves.
- While deficiency of either of these B vitamins leads to high homocysteine, there is concern that exposure of the central nervous system to high folic acid may accelerate the nerve damage from vitamin B١٢ deficiency.

Figure 1. Vitamin B_{12} and Homocysteine Metabolism



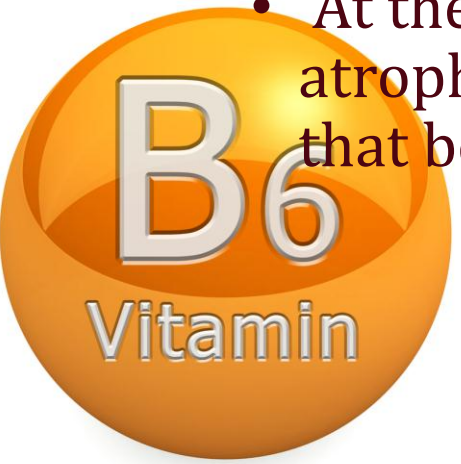
Methionine synthase is a vitamin B_{12}-dependent enzyme that catalyzes the formation of methionine from homocysteine using 5-methyltetrahydrofolate (5-methyl TH_4), a folate derivative, as a methyl donor. Another pathway catalyzed by betaine homocysteine methyltransferase also remethylates homocysteine to methionine using betaine as a methyl donor (not shown here). Methionine, in the form of S-adenosylmethionine, is required for most biological methylation reactions, including DNA methylation.

- **cognitive impairment was significantly more likely in older adults with high plasma folate when in combination with low vitamin B١٢ concentration.**
- **faster decline in cognitive function in individuals with relatively high intake of folic acid from fortified foods and supplements.**

- vitamin B۱۲ deficiency is relatively common in older adults, despite apparently adequate dietary intake.
- In the Framingham Heart Study, more than ۱۶% of older adults had low vitamin B۱۲ concentration.
- difficulty absorbing vitamin B۱۲ because of low stomach acid from atrophic gastritis,
- affect up to ۴۰% of adults above ۶۵ years old.
- **proton-pump inhibitors**
- recommends intake of vitamin B۱۲ in its **non bound crystalline form**, as supplements or in fortified foods (including some breakfast cereals).

- play a role in more than ١٠٠ enzymatic reactions in the body and is required for amino acid and lipid metabolism,
- gluconeogenesis, one-carbon metabolism, and synthesis of nucleic acids and neurotransmitters.
- legumes, nuts and seeds, unprocessed meat, poultry and fish, and selected fruits and vegetables.
- many adults do not consume adequate vitamin B٦, as it tends to be lost with processing in the **modern food supply**.
- The ٢٠٠٣–٢٠٠٦ NHANES showed that deficiency in vitamin B٦ (pyridoxal ٥- phosphate <٢٠ nmol/l) was higher than that of any other micronutrient in ١٠,٥% of U.S. individuals aged ≥١ year.

- Vitamin B^{6} has been associated with **cognitive function** but has received less attention than folate or vitamin B^{12}.
- Several studies have linked vitamin B^{6} **with cardiovascular Disease and depression,** but more research is needed on this important vitamin to understand its possible role in cognitive function.
- another supplementation Trial with vitamin B^{6}, vitamin B^{12}, and folic acid in older adults with mild cognitive impairment found that B vitamins were effective only in those individuals with relatively high baseline n-^{3} fatty acid concentrations.
- At the same time, n-^{3}fatty acid status was protective against brain atrophy only in the presence of B vitamin supplementation, suggesting that both nutrient types are needed for effectiveness.




Eggs
Cheese
Salmon
Vitamin
D
Sunlight
Shiitake
mushroom
Fortified
foods

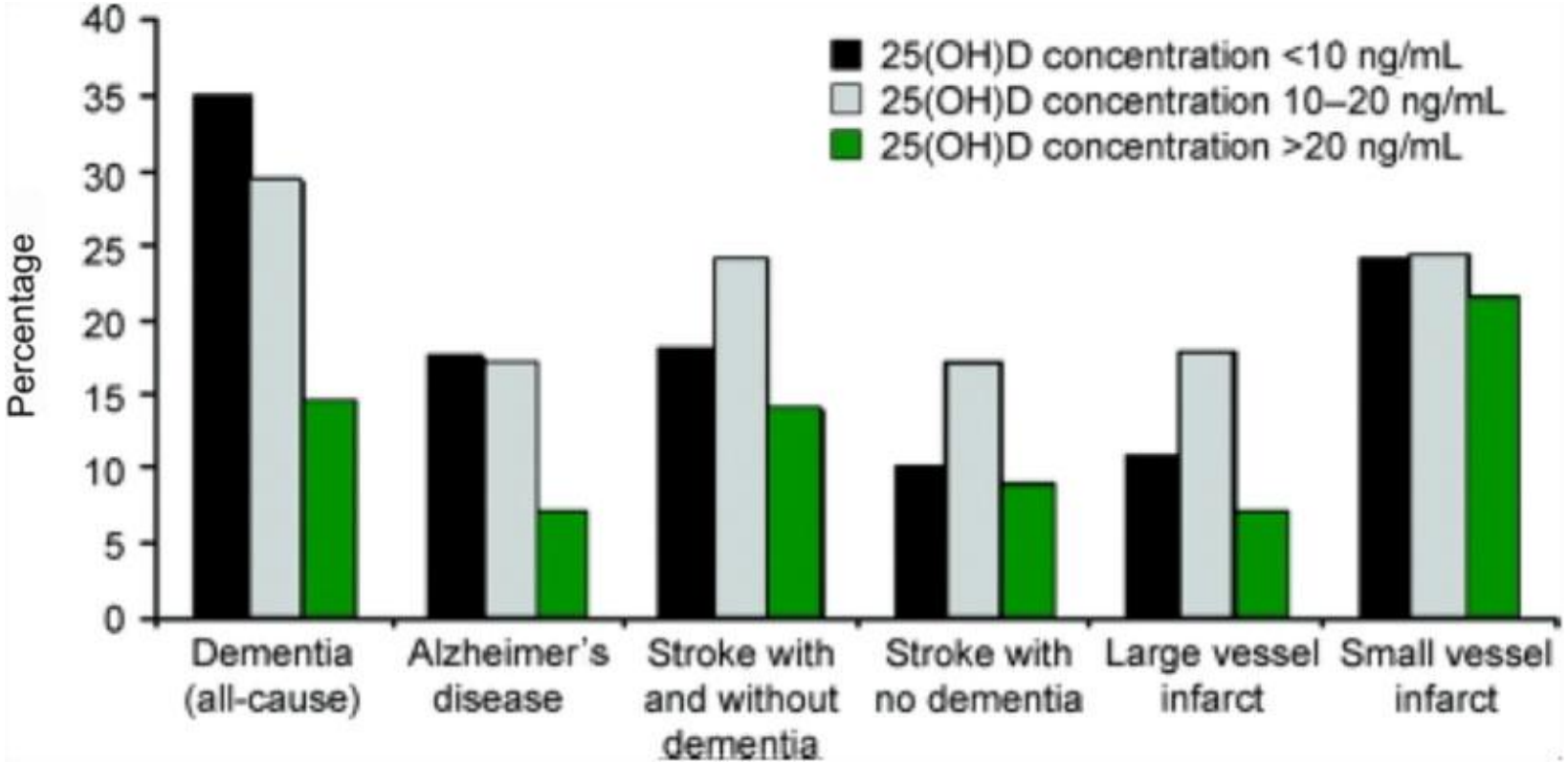
Vitamin D

- Until recently, vitamin D was considered important mainly for bone health, as it aids calcium absorption and metabolism.
- Over the past few decades, a rapidly growing body of research has shown that vitamin D plays many roles in the body, including **prevention of neurological, autoimmune, and psychiatric diseases.**
- **Vitamin D receptors** are now known to be widespread throughout the body, and their presence in the central nervous system of rat embryos supports a mechanistic **role of vitamin D in the development and maintenance of the nervous system**

- metabolic pathways for activation of vitamin D have been found in **neuronal and glial cells**,
- vitamin D has been shown to affect **expression of neurotrophins for brain function.**
- Effects of vitamin D on the cardiovascular system may affect brain health as well.
- protective against **vascular smooth muscle cell proliferation, inflammation, vascular calcification, and blood pressure elevation through the renin–angiotensin system**

- Studies support the importance of vitamin D in protection against cognitive decline.

- **serum vitamin D status** was associated with **cognitive performance on a variety of tests and that those with vitamin D concentration ≤٥٠ nmol/l (٢٠ ng/mL) were significantly more likely to have large vessel infarcts, greater volume of white matter hyper intensities, and twice the odds of dementia**, relative to those with higher vitamin D concentrations.

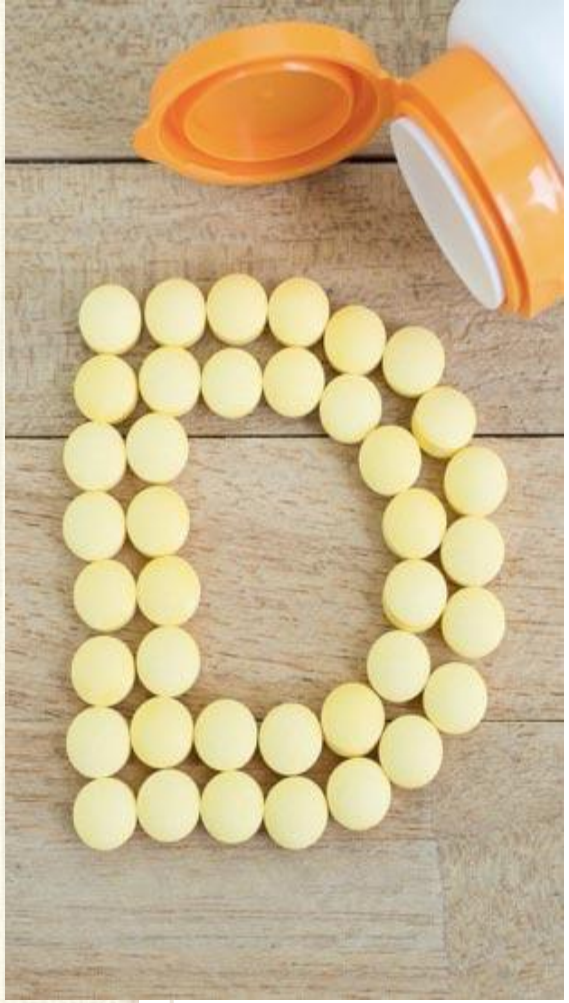


- A longitudinal evaluation in elderly individuals, assessed every ۳ years over ۹ years, showed that vitamin D concentration<۲۵ nmol/L was associated with significant decline in tests of executive function over time, relative to Those with concentration≥۷۵ nmol/L (۳۰ng/mL).

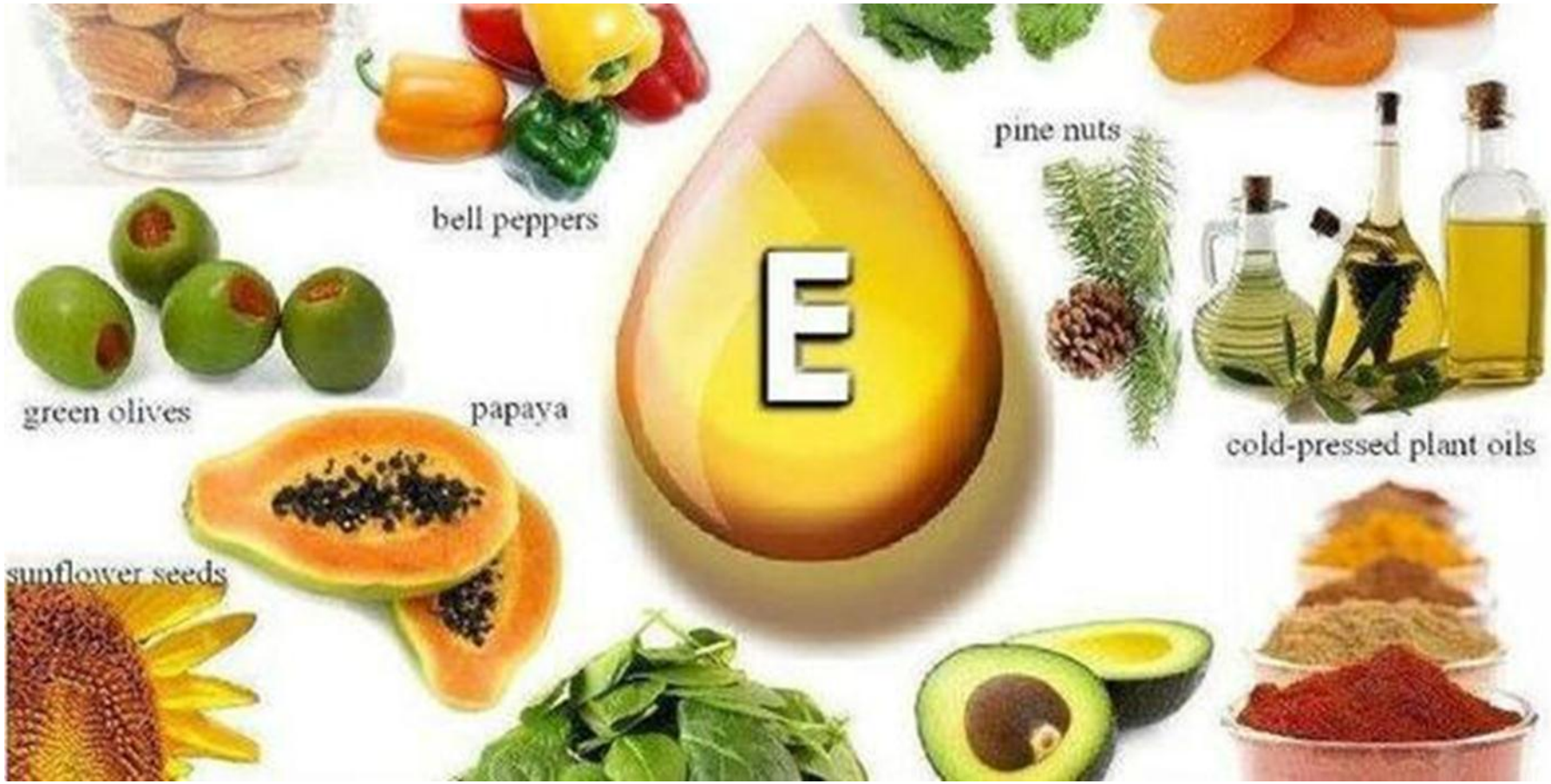
- one systematic review of ٢٨ studies **supported an association between vitamin D status and cognitive decline** in the aging population,
- another showed **significant protective associations between vitamin D and cognitive** measures in ١٨ of ٢٥ cross-sectional studies and in four of six longitudinal studies.
- **the evidence suggests that vitamin D may protect brain health through direct and indirect mechanisms, particularly through prevention of vascular dementia.**

- Inadequacy of vitamin D is prevalent in the entire population but is particularly prevalent among **older adults**, making it an important nutrient of concern **for cognitive decline.**
- This vitamin is unique in that it is synthesized in the skin with exposure to UV radiation from the sun.
- However, the abilities of the skin to synthesize vitamin D, and of the liver and kidney to convert it to the active form**, decline with age.**

- Many older adults, particularly those who are **homebound or institutionalized**, do not spend much time outside and therefore have limited exposure to sunlight.
- In healthy younger adults, **just ١٠ min/day of summer sunlight** can ensure sufficient vitamin D levels, although this is less effective during winter months in northern latitudes.
- The dietary RDA for vitamin D is **١٥ μg/day for adults aged ٥١–٧٠ years and ٢٠ μg/day for those aged >٧٠ years.**



- Food sources of vitamin D are limited, and the major sources —fatty fish and fortified milk— are not widely consumed by older adults.
- Therefore, **supplements are recommended**, particularly for the homebound or institutionalized, and for all older adults during the winter months in northern climates.


bell peppers
pine nuts
E
green olives
papaya
cold-pressed plant oils
sunflower seeds

Vitamin E

- a potent antioxidant and has received considerable attention for its possible role in **slowing the effects of aging**.
- most older adults do not come close to meeting the RDA for vitamin E , which is ١٥mg/day ∝-tocopherol.
- Good sources of vitamin E are limited and found mainly in **nuts, seeds, and oils.**

- A study of vitamin E–deficient mice showed **significant cognitive impairment** relative to control mice, with evidence of **greater lipid peroxidation products** in the brain, suggesting that vitamin E deficiency may accelerate brain oxidation.
- However, human studies of cognitive status and vitamin E remain limited.

- There is some observational evidence of **protective effects of vitamin E intake** or plasma status against **cognitive decline**.
- One recent trial found that ٢٠٠٠ IU/day of ∝-tocopherol led to **slower cognitive decline**, relative to placebo.
- However, another trial of vitamin E supplementation (as ∝-tocopherol) to reduce risk of Alzheimer's disease showed no benefit

- Importantly, vitamin E supplements in the form of ∝-tocopherol have been shown to reduce plasma γ-tocopherol, which may also be important for optimal health.
- A recent study found that, in addition to ∝-tocopherol, γ-tocopherol, and β-tocotrienol, **total tocotrienols were also associated with lower risk of cognitive impairment in older adults.**

- Importantly, a study of tocopherols in brain tissue found that concentrations of **∝-tocopherol were associated with protective effects on Alzheimer's neuropathology only when *γ* -tocopherol was also high.**
- it may be important to obtain vitamin E from **natural sources** (mainly vegetable oils, nuts, and seeds), which include a variety of tocopherols and tocotrienols

Use of supplements versus food as sources of nutrients

- While there is some evidence that supplements with key nutrients may help slow cognitive decline, the strongest evidence in most cases suggests that dietary sources of these nutrients may be safest and most protective.
- multivitamin supplementation**, no benefit to cognitive function** was seen in ۵۹۴۷ men aged ۶۵ years and older after ۱۲ years of supplement use, relative to placebo.
- Exceptions include the need for many older individuals to take vitamin D, particularly if homebound or residing in cold northern latitudes, and vitamin B۱۲, particularly if there is likelihood of atrophic gastritis or if using acid-blocking medication

- With fortification of cereal grains and additions to breakfast cereals and other foods, care must be taken with folic acid, as the upper limit of ١٠٠٠ mg is easily reached, and there is evidence of possible negative effects of excessive intake.
- the evidence for vitamin E suggests that supplements of ∝–tocopherol are **not effective** and may cause **imbalances** relative to food sources.
- On the other hand, for individuals who have inadequate intakes, supplements may make a difference.

Fish

- Strong evidence for the importance of n-٣ fatty acids in cognitive function points to **fish as the major source** in modern diets.
- Fatty fish, such as salmon, mackerel, and sardines, are rich sources of DHA and EPA, which are the active forms of n-٣ fatty acids, with DHA preferentially incorporated into brain tissue.
- Plant sources (e.g., flax seeds, walnuts, and selected plant oils, including canola oil) contain the precursor of these active forms as the essential fatty acid ALA.

- conversion from ALA to DHA and EPA is inefficient, making inclusion of fish an important factor in adequacy of intake.
- Many of the same studies that have linked n-٣ fatty acid intake to cognitive function have noted that fish intake was also associated with cognitive function.
- A recent review of ٢١ cohort studies noted that fish intake is associated with lower risk of cognitive impairment and that intake of DHA from fish was associated with lower risk of dementia and Alzheimer's disease

Nuts and seeds

- Excellent sources of vitamin E include nuts and seeds, particularly almonds and sunflower seeds.
- good sources of vitamin B۶, as well as dietary fiber and other beneficial phytonutrients.
- reducing the risk of heart disease, diabetes, and total mortality, but less evidence is available for cognitive function.
- adults, aged ۲۰–۵۹ years and ۶۰ years and older and who had consumed nuts, had significantly higher scores on story recall and digit–symbol substitution, faster reaction time, faster symbol–digit substitution time, and greater single-digit learning scores compared with non consumers.

- Results from the Nurses' Health Study, including ١٥,٤٦٧women, also showed protective effects of nut intake on cognitive function;
- women consuming at least five servings of nuts/week had significantly higher scores on global cognitive function, although not significantly associated with rates of cognitive decline over time.
- A trial examining intake of Brazil nuts among older adults with **mild cognitive impairment** found that the treatment group showed significant improvement in verbal fluency and constructional praxis, compared to controls.

- A recent review of nut consumption and health noted that nuts have been shown to protect against cognitive disorders and Alzheimer's disease, through not only **their vitamin E content**, but also through possible **effects of polyunsaturated fatty acids and polyphenolic compounds**

Fruits and vegetables

- Fruits and vegetables are a key food group contributing needed nutrients for cognitive function, as well as for protection against most chronic conditions of aging.
- Higher intake of fruits and vegetables is well known to lower risk of cardiovascular disease, stroke, some cancers, and total mortality.
- It is not surprising that higher intakes of fruits and vegetables also show protection against cognitive decline.

- A recent review **reported significant benefit from higher intake of fruits and/or vegetables in older adults in relation to measures of cognitive function.**
- One phytonutrient that has been recently linked with brain health is the carotenoid lutein, which is found mainly in dark green leafy vegetables.
- Berries have also been shown to contain relatively potent polyphenolic compounds, particularly anthocyanins, which protect against cognitive decline.
- Studies in rats have shown that berry diets improved motor performance and working memory, and increased hippocampal neurogenesis.

- greater intakes of blueberries and strawberries were associated with lower rates of cognitive decline;
- the authors concluded that greater intakes of anthocyanidins and total flavonoids were associated with a delay in cognitive aging by up to ٢,٥ years.

Flavonoids

- A recent review notes significant antioxidant and anti-inflammatory effects of flavonoid intake, mainly from fruits and vegetables, but also from tea, against cognitive impairment.
- There is growing evidence for the importance of flavonoids in protection against cognitive decline with aging.
- one study showed that flavanols from cocoa enhanced hippocampal vascular plasticity and cognitive function in older adults.
- Because different fruits and vegetables contribute different nutrients**, they may not all offer the same protection against cognitive decline**, and the combination of different types may be important.

Added sugars

- A counterpoint to consider relates to excess consumption of certain foods, such as added sugars, and negative effects on cognition.
- An analysis of sugar intake showed significantly lower MMSE scores among older Puerto Rican adults with higher intake of total sugars, added sugars, sucrose, glucose, and fructose, as well as with total intake of sugar-sweetened beverages.

Saturated and trans fat

- Saturated and trans fats are well known as risk factors for cardiovascular disease.
- they are likely to also affect brain vessels and contribute to cognitive impairment.
- Several, but not all, longitudinal observational studies have demonstrated an association of both saturated and trans fat with cognitive decline in the Women's Health Initiative and in older men and women in the Chicago Health and Aging Study.

Dietary patterns

- the evidence clearly suggests that a healthy diet can protect against cognitive decline and the development of dementia.
- Several recent studies, have shown interactions between different nutrients, showing that the combination of healthy nutrients is critical.
- This may also explain why clinical trials with single nutrients or limited nutrient combinations show mixed results
- It is also likely that the nutrients work best within the composition of the food matrix and total dietary pattern, which may explain why consistent results may be seen in observational studies for nutrients in the diet, but are not confirmed when isolated in clinical trials.

- many recent studies have moved toward examination of the whole diet rather than considering individual nutrients.
- As with heart disease, key benefits have been shown with the Mediterranean diet, which includes a focus on healthy oils, nuts, fish, and fruits and vegetables. Each of these food groups contributes key nutrients that work together to protect the aging brain.
- A recent review summarizing the benefits of the Mediterranean diet concludes that this diet may be helpful in the **treatment of dementia, while another highlights the diet as a strategy to reduce risk of cognitive decline**, noting that the current Western diet may contribute to dementia risk.

Conclusion

- Accumulating evidence shows the tremendous importance of nutrition to brain health and in preventing cognitive decline with aging.
- While there is convincing evidence of the importance of several nutrients in brain health, particularly n-۳ fatty acids, folate, and vitamins B۶, B۱۲, D, and E, there is also evidence for the importance of **phytonutrients found in plant foods** and for the combination of these nutrients seen in **key foods**, including fish, nuts, and a variety of fruits and vegetables.
- At the same time, the high content of sugars in the modern Western diet may be harmful.

- Evidence of interactions between nutrients supports the role of **the total dietary pattern**, ensuring adequacy of all of these nutrients, as opposed to the use of any individual supplement for preventing cognitive decline.
- The Mediterranean diet includes most of these foods and has been shown to be protective.
- deficiencies in specific nutrients in older individuals may have important negative effects.
- In the case of inadequate sun exposure, poor absorption, negative interaction with medications, or low plasma concentration of specific nutrients, supplements of specific nutrients may also be beneficial, particularly for vitamins D and B_{12}

References

- Cederholm, T. (٢٠١٧). Fish consumption and omega-٣ fatty acid supplementation for prevention or treatment of cognitive decline, dementia or Alzheimer's disease in older adults–any news?. Current Opinion in Clinical Nutrition & Metabolic Care, ٢٠(٢), ١٠٤-١٠٩.
- Baleztena, J., Arana, M., Bes-Rastrollo, M., Castellanos, M. C., Gozalo, M. J., & Ruiz-Canela, M. (٢٠١٧, November). Does Omega-٣ supplementation after the age of ٦٥ influence cognitive function? Results of a systematic review. In Anales del sistema sanitario de Navarra (p. ٥٨٧٤٦).
- Offman, E., Davidson, M., & Nilsson, C. (٢٠١٧). No Effect of Omega-٣ Carboxylic Acids on Pharmacokinetics/Pharmacodynamics of Warfarin or on Platelet Function When Co-administered with Acetylsalicylic Acid: Results of Two Phase I Studies in Healthy Volunteers. American Journal of Cardiovascular Drugs, ١-١٠.
- Andrieu, S., Guyonnet, S., Coley, N., Cantet, C., Bonnefoy, M., Bordes, S., ... & Desclaux, F. (٢٠١٧). Effect of long-term omega ٣ polyunsaturated fatty acid supplementation with or without multidomain intervention on cognitive function in elderly adults with memory complaints (MAPT): a randomised, placebo-controlled trial. The Lancet Neurology, ١٦(٥), ٣٧٧-٣٨٩.

thanx