

“Optimizing Brain Health Through Nutrition: Harnessing The Power of Metabolism and Immunity”

Webinar Questions Answered by Austin Perlmutter, MD, ABIM

- Can mental health conditions, such as depression and anxiety, cause permanent memory loss, or does it often resolve with improvement from various treatment options, including nutrition?
 - Mental health conditions can be associated with both a short-term decline in memory and a risk for longer-term memory problems like dementia. Some cognitive symptoms, including memory, can improve with treatment of an underlying mental health disorder, but I am unaware of research showing percentages breakdown.
- How do we know dementia will increase by 300% in the next 25 years?
 - This projection is primarily a function of the aging and growth of the global population.
- Do saffron supplements have any effect on brain health? Specifically related to ADHD?
 - There are some data suggesting a benefit to ADHD symptoms from *crocus sativus* or saffron but there is need for additional research.
- Do metals like aluminum affect the brain long-term?
 - Metal exposure is a well-known risk factor for brain issues. Mercury, lead, cadmium and arsenic may negatively impact brain health at higher levels of exposure. Higher aluminum levels in the brain and CSF are related to Alzheimer’s disease but conclusive evidence has not been published regarding causality or whether normal exposures pose brain risk.
- What dosage do you recommend for omega 3 (EPA/DHA) supplements if someone doesn’t like fish/seafood since there’s no RDA and some negative research, for example, on doses over 1g/day for afib?
 - For typical/routine omega-3 consumption through food or supplementation, around 500 mg of combined DHA and EPA is typically recommended. This amount was found to increase omega-3 levels over a 16-week trial. Ideally, omega-3 levels are tested and dose is customized to a person’s individual needs.
- Can you talk about how stress can increase A1C?
 - Activation of the HPA axis increases cortisol, which acutely leads to rises in blood sugar and over time can lead to insulin resistance, both supporting a higher A1C. Elevation of epinephrine and norepinephrine during stress also promote higher blood sugar.
- What, if anything, are you most excited about with MAHA and their proposed changes to healthcare?
 - A focus on lifestyle medicine as a core pillar of American preventive health is an exciting concept.
- I have heard that the supplement GABA can be helpful for sleep and brain health. Can you explain why?
 - Gamma-aminobutyric acid (GABA) is the main inhibitory neurotransmitter, and has been linked to anti-stress and sleep-promoting effects. However, there’s limited generalizable data showing GABA’s efficacy in sleep. Interestingly, alcohol acts on GABA receptors, which may explain why people get sleepy after drinking (note, despite this, the quality of sleep after drinking is very impaired)
- Any new information around long COVID and how you can improve brain fog during infections?

- There are a number of groups working to find better solutions to long COVID. Various strategies from prescriptions to pulmonary rehabilitation have been proposed. I am optimistic about brain energy-focused strategies but these are not yet generalizable.
- Are there any long-term effects of the ketogenic diet on the brain?
 - Not too much yet. One recent study suggested that the ketogenic diet may promote cellular aging in several organs. However, in those with impaired brain metabolism, it may prove advantageous.
- When you say UPF, what foods are you specifically talking about? Because many people don't have access to whole foods, many UPFs can be helpful (i.e., protein powders). Is there something more specific in the UPFs that concerns you? i.e., energy density vs nutrient density. I work a lot with ARFID clients, and it's hard to get them to eat fruits and vegetables.
 - Multiple groups are working on better definitions for UPFs, but much research uses the NOVA system. Agreed on your point. Some more processed foods can be healthy while some minimally processed foods are worth minimizing. Generally speaking, I recommend at a first level against added sugar and foods with lots of ingredients you don't recognize, but I think personalizing it to the audience is far more helpful when nuance is possible.
- Can brain health be improved at any stage of life? Is it the case that every little positive change helps?
 - Absolutely and absolutely
- Could increase permeability have a benefit, i.e., more nutrient delivery?
 - Interesting question. It does serve a purpose (see Alessio Fasano's original work on cholera toxin). Gut "leakiness" is generally in the bucket of "bad" but at lower levels may be adaptive.
- Do dried herbs still contain polyphenol?
 - Yes. Dried herbs and spices have among the highest concentrations of polyphenols
- Which third-party tested Omega-3 supplement would you recommend?
 - I work with a company called Big Bold Health and take their omega-3 supplements.
- Recommendation: Is it 1-2 tsp as it says on your slide, or 1-2 Tablespoons as you said in your talk?
 - Tablespoons!
- When you said reduce added sugar, can you give a specific range that you have seen a difference in?
 - The best data here is on reduction of sugar-sweetened beverages. I've seen differences when people stop drinking liter bottles of soda each day be rapid, but generally weaning off of added sugar in foods and beverages and if possible bringing total consumption to around 10 or so grams a day.
- What do we know about the effects of sugar substitutes on gut immunity? If we ask patients to reduce added sugar, they may opt for products with sugar substitutes. Should we condone this?
 - Much more limited data on this at this stage, and mostly preclinical data in terms of risk for sugar sweeteners. I use stevia, allulose and monkfruit, and think they can be helpful in getting people off of sugary beverages. Ideally, I recommend moving away from sweetened products and instead eating natural sugars in real foods (e.g. apples, etc).
- Do you think artificial sugars have a significant impact on brain health in general? I know science usually states that the dose is not harmful against things like cancer or obesity if they are not excessively consumed, but what are your thoughts on this?
 - It's still super early to know if they're a risk. I personally don't consume artificial sweeteners but acknowledge that the data are not as concrete for degree of brain risk at this time.

- Regarding omega-3s, what source or ratio of EPA: DHA do you recommend for brain health maintenance?
 - Mental health benefits seem to favor higher EPA while cognitive benefits may be more tethered to DHA. Generally, getting around 500 mg a day, ideally from food seems most practical.
- What populations with metabolic dysfunction do you recommend low-carb or keto diets?
 - These are ideally done under supervision of a health provider, but there's some emerging quality data on people with type 2 diabetes having major improvements/reversal of diabetes with these diets.
- What are the benefits of coconut oil?
 - Coconut oil has some interesting and potentially healthful fats in medium chain triglycerides and is suggested to therefore increase ketones. However, it's very high in saturated fat content and I would choose other sources of oil for cooking with more established benefit (e.g., olive oil).
- What form of magnesium is best for brain health?
 - Some research suggests Magnesium L-threonate may be best for the brain due to potential to cross the blood brain barrier. However, it's unclear whether the data to date support its higher price tag.
- Can you set the record straight on seed oils and brain health?
 - Seed oils are often a constituent element of ultra-processed foods which are associated with worse brain health. By and large, the concerns about the dangers of seed oils are overblown relative to the actual data on their associations with health outcomes. There are healthier fat options for brain health, including extra-virgin olive oil.
- If olive oil is heated, does it lose its power to influence the brain positively? Is pouring directly from the bottle on salads/foods always the best?
 - There is concern that olive oil may lose health values at a relatively lower heat due to becoming oxidized. However, this has been proven less concrete than once thought. Some data say it's probably fine to cook with it to temperatures up to 375 degrees Fahrenheit. Best bet, if you want to be most cautious, is to eat it cooler.
- As a vegan, what strategies can help maintain optimal brain health, given that specific vitamins and nutrients may be lacking?
 - I would recommend working with a practitioner to test for labs and customize diet/nutrient strategies around B12, omega-3, creatine consumption etc.
- For individuals at higher risk of cognitive decline, what evidence-based dietary strategies show the most substantial impact on both metabolic balance and immune resilience?
 - The best studied diet is the Mediterranean/MIND diet for cognitive health. For those with APOE4 genotypes, reducing saturated fat may be a good bet. Avoiding added sugars in sugary beverages, and limiting highly-processed carbs are also good ideas.

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