December 2019 - Mid-Month Bonus Newsletter

Thank you for subscribing to this newsletter from the Personalized Lifestyle Medicine Institute. Enjoy and share this information, which is for educational purposes only and is not intended to be a substitute for professional medical advice, diagnosis, or treatment. Always consult with a qualified healthcare professional when you are in need of advice regarding a medical condition.

In this issue: Nutrient of the Month: Zinc; Resource: Nothing is Not Connected to the Brain: Talks with The First Functional Neurologist; How Much Do Lifestyle and Genetics EACH Contribute to Dementia Risk?

Nutrient of the Month: Zinc

Zinc is one of the greats: essential for protein synthesis and the growth, integrity, repair, and maintenance of intestinal, connective, nervous, epithelial, and other tissues, it is also crucial in immune cell function and balance, creation of red blood cell heme, taste, smell, and vision, the function and structure of myriad enzymes, blood clotting, and thyroid hormone production and regulation. It is the most abundant metal within cells (found mainly in muscle and bone) and the second most abundant trace metal in the body. In the brain, it concentrates in the hippocampus, amygdala, cerebral cortex, thalamus, and olfactory cortex—areas central to higher brain function, alertness, and the stress response. Foods that provide relatively generous amounts of zinc include oysters and other shellfish, wheat germ, meat, sesame seeds and tahini, watermelon seed, pumpkin seed, hemp seed, flaxseed, poppy seed, dandelion greens, wheat bran, cocoa powder, peanuts, pine nuts, other nuts and seeds, whey, rice bran, wild rice, spinach, collards, cucumbers, asparagus, tomatoes, and spices like chervil, cardamom, basil, celery seed, thyme, parsley, and mustard seed.

Populations at risk for zinc insufficiency include children, teenagers, pregnant and lactating women, older people (due to reduced intake and absorption), vegetarians, smokers, post-bariatric surgery patients, and those taking opioids. Those with inflammatory bowel disease and other conditions of increased gut permeability, skin problems, sickle cell disease, atopy and/or allergy, kidney disorders, cancer, tuberculosis, and rheumatoid arthritis may also have a higher zinc requirement. Some of the more common manifestations of zinc insufficiency include reduced sensory sensitivity, hair loss, weight loss, glucose intolerance, diarrhea, skin problems, poor wound healing, and reduced sperm production. Acids (e.g., gastric or vinegar) tend to aid zinc absorption while other minerals (especially iron and excess copper), fiber, and
excess alcohol consumption can interfere with zinc metabolism. Zinc may have interactions with diabetes drugs, penicillamine, quinolone and tetracycline antibiotics, chelating agents, gastric acid suppressors, diuretics, and other medications, sometimes depending upon genetic variation. Zinc toxicity is relatively rare, but as minerals influence each other's absorption and metabolism, it is important to receive sufficient amounts of each and avoid excessive amounts of any single one unless recommended by a health care practitioner.

Functional Neurologist Dale Bredesen, MD, has emphasized zinc's importance in cognitive function, and how its deficiency induces insulin resistance, affects hormone signaling, and facilitates inflammation and autoimmunity. He mentions the zinc metalloproteinase ADAM10, which may cleave amyloid precursor protein without producing toxic amyloid, and has identified a distinctive subtype of Alzheimer's disease showing very low serum zinc levels (while pointing out that red blood cell zinc is a more accurate clinical test). A 2013 study found that zinc supplementation protected cognitive function in older individuals; this article suggests that it may achieve this in part by protecting brain neurons from glutamate-induced excitotoxicity (which has been associated with stress and cognitive dysfunction), and also notes that amyloid plaques may bind zinc and render it unavailable. Maintaining sensory sensitivity is crucial to successful cognitive aging, and zinc supplementation may help retain the sense of taste in older people. The level of zinc in the visual retina decreases with age, and as zinc level in the exquisitely delicate yet protective retinal pigment epithelium affects risk for age-related macular degeneration (AMD), it is included in the AREDS formulations studied in AMD.

Here are some other research findings regarding zinc:

- As in IBD and AMD (above), zinc plays a central role in building epithelial barriers and their intercellular tight junctions, and zinc insufficiency also relates to atopic dermatitis (eczema), healing pressure ulcers of the skin, and chronic obstructive pulmonary disease (COPD); early research also suggests it may aid the mouth's epithelial barrier.
- Recent work in human stem cells suggests that zinc (as sulfate) may improve genetic expression of telomerase and telomere lengthening; interestingly, treated stem cell populations also showed a lower percentage of senescent (aged) cells, which was associated with different methylation patterning.
- Breaking research has found that obese persons have lower serum levels of zinc as well as a zinc-containing adipokine known to regulate fat distribution and lipid mobilization, which may reflect altered zinc metabolism in obesity.
- Zinc is an important factor in bone formation and mineralization.
- Zinc status affects the activity of antioxidant enzymes like the Nrf2 master regulator of antioxidant enzymes, metallothionein, glutathione enzymes, and hemeoxygenase, and while its deficiency increases oxidative stress, it can also have pro-oxidant properties in excess.
- Lack of available zinc can limit mitochondrial biogenesis, and insufficient as well as excessive zinc can hamper mitochondrial energy production.
- Dysregulated zinc signaling may influence development of inflammation, autoimmunity, and allergy, and in immune cells taken from atopic individuals, zinc exposure moderated the immune response by altering cytokine balance and increasing the number of immune regulatory T cells—actions that would tend to reduce the atopic response without negatively affecting immunity.
- In one study, older adults with the highest zinc intakes were 30-50% less likely to become depressed compared to those at the lowest intakes, which may relate to the effects of zinc signaling on synaptic plasticity and neurotransmitter receptor function.
- Zinc supplementation was associated with notable drops in C-reactive protein (CRP) levels in healthy persons and kidney patients, and in subjects with chronic liver disease (who typically experience elevated oxidative stress and inflammation), circulating zinc levels correlated negatively with CRP levels as well as markers of oxidative stress.
- Zinc status is generally though not conclusively related to male fertility.
- Zinc plays multiple roles in insulin production, secretion, and sensitivity, and zinc supplementation has improved insulin sensitivity in obese adults; in prediabetic persons, higher serum zinc was associated with greater insulin sensitivity.
- A 2018 meta-analysis cautiously concluded that blood levels of zinc may relate to measures of intelligence in children, though confirmation may be needed.
- In meta-analysis, hypertensive adults showed significantly lower serum zinc levels, though the significance of this is not certain.
Somewhat like iron within hemoglobin or magnesium within chlorophyll, zinc nests in the center of zinc finger proteins, which aid gene expression and silencing. Over 3000 human zinc finger proteins have been identified, and they are estimated to be found at 3% of human genes. Other zinc proteins facilitate DNA repair, production of enzymes and structural proteins, and molecular transport and storage, and zinc is also a component in some sirtuins and related histone deacetylase (HDAC) enzymes whose activity helps regulate cellular aging processes.

Particular genetic polymorphisms may affect zinc transporter function as well as metabolic requirements for zinc, and through them, the potential for deficiency and dysfunction.

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**Resource: Nothing is Not Connected to the Brain: Talks with The First Functional Neurologist**

As a neurologist applying the concepts of Functional Medicine to help each patient re-establish healthy communications between his/her brain, gut, and immune system, David Perlmutter, MD has long worked to disprove the notion that the brain lacks regenerative capacity. In his podcast *The Empowering Neurologist*, he takes a specialized look at how lifestyle can add to or subtract from health over time, and the difference made by better-informed choices. His guests include well-known clinicians like Terry Wahls, MD, Mark Hyman, MD, and his colleague Dale Bredesen, MD, and with an enduring interest in groundbreaking science, he has also interviewed researchers like metabolic detoxification expert Deanna Minich, PhD and his own mentor, the Father of Functional Medicine Dr. Jeffrey Bland.

Here are links to a few of Dr. Perlmutter's recent interviews:

- How can ‘nourishing’ and ‘starving’ be very strategically combined to activate rejuvenating stem cells while clearing out dysfunctional cells and restoring healthier immune balance? What is the magic amount of exercise for triggering some of the same biochemical benefits as fasting? What does cellular aging have to teach us about getting rid of belly fat? In this talk, Valter Longo, PhD explains how the Fasting-Mimicking Diet came into being and how profoundly it contrasts to modern lifestyles of ‘starving in the face of overnutrition.’

- Why should we try to reconnect to the prefrontal cortex (with its relationship to more feminine behaviors) and away from fear, the cortisol response, and the amygdala, as modern life often seems to encourage? With gynecologist and biohacker Sara Gottfried, MD, Dr. Perlmutter discusses how male and female brains specialize and are activated in different ways, how this maps into different health conditions—especially during aging—and how we can take advantage of that to produce health in an individualized way.

- What do ketones do to the brain, especially during stress and biological aging? In this deep dive, fellow ketogenic diet proponent Dominic D’Agostino, PhD describes how ketones carry epigenetic, anti-inflammatory, and anti-excitotoxic messages that go beyond their benefits as clean and even antioxidant energy sources for mitochondria, particularly in the brain. Ketones are a normal body metabolite during fasting, yet have been discovered to be extremely efficient at addressing certain types of brain dysfunction, with implications in health issues ranging from cancer and Lou Gehrig’s disease to stress endurance and physical performance.

- How was a computer scientist able to confirm that the rapid growth in autistic disorders is related to environmental factors, gut issues, and micronutrient deficiencies—and not primarily a genetic problem? What essential nutrients does glyphosate chelate? MIT’s Stephanie Seneff, PhD talks with Dr. Perlmutter about food contamination with glyphosate and the impacts of widely-used toxics on human (not to mention soil!) microbiomes, metabolic detoxification, methylation function, and other issues linked to autism. It turns out that humans (and our folate production) are not, after all, immune from these substances’ effects on
microbes. Don’t miss the graph mapping glyphosate application to corn and soy with numbers of children being treated for autism.
- Find out what kindness has to do with clean arteries, the curious relationship between the microbiome and breast health, the seasonal message of glucose in ripe fruits, and how andropause and menopause are more like beginnings than endings in this talk with board-certified ob/gyn Christiane Northrup, MD, whom Dr. Perlmutter has known and learned from for decades and is the author of one of the most important books he has ever read: Goddesses Never Age.
- “In holistic medicine, there are no specialties.” From this eye-opening discussion with board-certified holistic psychiatrist Kelly Brogan, MD (author of A Mind of Your Own), we learn the web view of what depression really is, question the “serotonin theory” and perceived necessity of medication, hear evidence from unpublished negative studies, relearn how to listen to the body’s urgent and insistent messaging, and consider the central importance of the gut in brain, mood, blood sugar level, and immune balance as well as the disconnect among human evolution, modern chemical usage, and unremitting inflammatory response. Bringing Functional Medicine to psychiatry, Drs. Perlmutter and Brogan agree on dietary adjustment as the single most powerful intervention, able to address more aspects of pathology simultaneously than any other treatment.

The main page (above) for Dr. Perlmutter’s podcast includes links to previous interviews, which is accessible page by page, expanding over time:
https://www.drperlmutter.com/learn/empowering-neurologist/page/2/
https://www.drperlmutter.com/learn/empowering-neurologist/page/3/
https://www.drperlmutter.com/learn/empowering-neurologist/page/4/
https://www.drperlmutter.com/learn/empowering-neurologist/page/5/
https://www.drperlmutter.com/learn/empowering-neurologist/page/6/
https://www.drperlmutter.com/learn/empowering-neurologist/page/7/
https://www.drperlmutter.com/learn/empowering-neurologist/page/8/
https://www.drperlmutter.com/learn/empowering-neurologist/page/9/

Dr. Perlmutter’s website also includes his informative blog, descriptions of his Grain Brain book series, and other valuable resources, like this article he recently wrote about a typical day’s worth of functional brain food in the Perlmutter household.

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**How Much Do Lifestyle and Genetics EACH Contribute to Dementia Risk?**

Nutrient-dense eating patterns during a limited daily “eating window” can encourage more effective immunometabolic, cardiovascular, neurocognitive, and autophagic function over time, with considerable scope on what these eating patterns may look like in a given person’s life. These effects are bolstered by regular and sometimes intense physical activity, mind-body practices, avoiding toxic exposures, limiting alcohol intake, and solid sleep. But genetics and epigenetics also impact these aspects of health, in equally individualized fashion. Is it possible to tease out the overlapping effects of genes and lifestyle on overall risk for dementia? Recent research highlighted in the July 2019 issue of JAMA aimed to find out.

This retrospective study included almost 200,000 older individuals of European origin without cognitive impairment who had been evaluated for ancestry and genetic point mutations associated with these conditions, and tracked them for an average of about 8 years. Genetic risk was determined as low, intermediate, or high according to polygenic evaluation for the presence of single-nucleotide polymorphisms (SNPs) identified by previous genome-wide association study (GWAS) as both common among those with European ancestry and related to dementia risk in this population. With available lifestyle information on study participants, researchers scored contributions according to a simple 0- or 1-point scale for four variables (resulting in an overall 0-4 score):
- current smoking
- moderate alcohol consumption (0-1 drink daily for women and 0-2 drinks daily for men)
- healthy diet (eating at least 4 of 7 food groups linked to better cardiometabolic health)
- sufficiency of physical activity (75 weekly minutes’ vigorous, 150 weekly minutes’
moderate, 5 days per week moderate, 1 day per week intense, or any equivalent combination)

The researchers found that individuals with combined increased risk from both lifestyle and genetics showed almost tripled the risk for dementia, compared to those with low lifestyle as well as genetic risk. High genetic risk alone resulted in almost doubling of dementia risk, yet persons with high lifestyle risk alone showed about 1.5 times the dementia risk of those with high genetic risk alone. Persons with intermediate genetic risk but a favorable lifestyle showed a lower dementia risk than persons with low genetic risk but high lifestyle risk.

The final conclusion? A healthier lifestyle significantly reduces dementia risk regardless of whether genetic risk is high, intermediate, or low.