Webinar Will Begin Momentarily

TODAY'S AGENDA:

- Welcome
- Speaker Introduction
- Presentation
- Q&A
- Closing

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The Role of Nutrition in Neuroscience and Psychiatry

WEBINAR HOST:

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About the Webinar

Title	“The Role of Nutrition in Neuroscience and Psychiatry”
The Theme	To enlighten and discuss the importance of nutrition throughout the lifecycle for healthy brain development, healthy neurological systems and supportive of healthy mental health.
The Goals	It is the goal of the speaker to provide and share evidentiary science and discuss the evidence regarding the prominent importance of third-trimester nutrition for healthy eye, brain and mental health development

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About the Speaker

WEBINAR PRESENTER:

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Douglas S. Kalman PhD, RD, FISSN

Co-founder, The ISSN (2003)

Clinical Associate Professor, Nova Southeastern University (Florida, USA).

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Co-editor- Journal of the International Society of Sports Nutrition (JISSN)

Sports Nutritionist – Olympic (6 to date), Collegiate (~ 8 years, 18 teams per), Professional athletes – MMA, boxing, swimming and tennis - ongoing.

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DISCLOSURE

Disclosures

01 Serves on the Scientific Advisory Boards of Iovate Health Sciences, TruSpan, and Creatine for Health

02 Have worked in academia and in contract research for companies from the following industries: pharmaceutical, OTC, foods, beverages, dietary supplements, medical foods and consumer packaged goods (CPG).

03 Substantiation Sciences is a consultancy that works with companies in FDA regulated categories.

04 Orgain is the sponsor of this webinar.

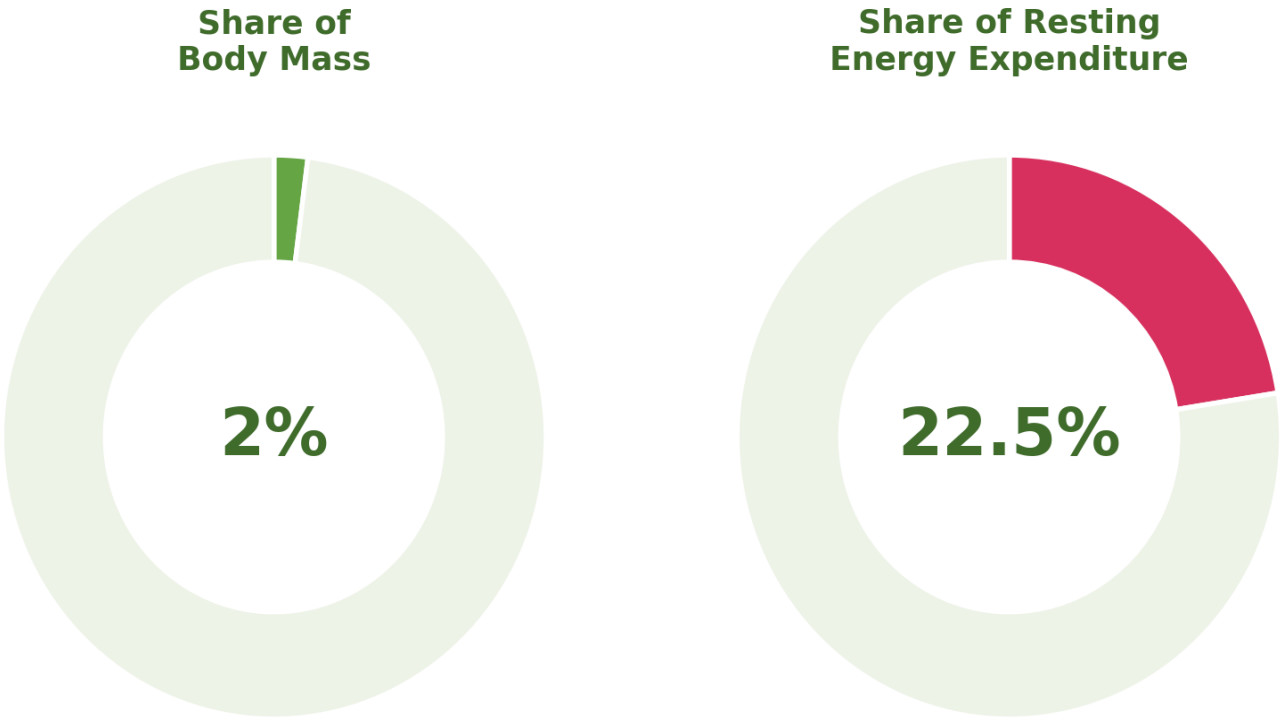
NEUROSCIENCE

Nutritional in the Neurosciences & Psychiatry

- The body is a complex organism.
- The nutritional neurosciences are the scientific discipline centered on the impact of dietary components, such as hydration, vitamins, minerals, essential nutrients, phytonutrients and other dietary compounds have on neurochemistry and neurobiology, and memory, executive function, behavior and cognition.
- This includes feelings of well-being, mood-states and lifecycle health.
- Understanding brain energetics is also important as this too impacts the nutritional neurosciences.
- The human brain is approximately 2% of the human body mass but yet uses 20–25% of the energy expenditure.
- Feeding the brain for optimal support now and later is central for lifetime whole body health.
- Nutrition has an impact on the brain throughout the lifecycle, which can impact on the development of neurodevelopmental conditions and neurodegenerative diseases in later life, while also influencing mental health
- How we eat impacts cognitive and health and disease risks over a lifetime.

Why Brain Nutrition Matters

The Brain: 2% of Body Weight, ~20–25% of Energy Demand



KEY TAKEAWAYS

- The brain draws disproportionate metabolic resources at every age — small size, outsized demand.
- Nutrient effects on brain development follow timing, dose, and duration: a nutrient beneficial at one window can be neutral — or harmful — at another (Georgieff, 2007).
- Brain-relevant nutrition is not a pregnancy-only or elderly-only conversation; it is a continuous thread from conception through aging.

FOUNDATIONS

The Lifecycle Roadmap

In-Utero & Third Trimester	Infancy & Childhood	Adolescence & Adulthood	Aging & Neuroprotection
Neural tube, synaptogenesis, myelination onset; DHA, choline, iron, vitamin D,B12, folate, creatine, others	Rapid myelination continues; iron-dependent dopamine/serotonin systems mature; first 1,000 days Vitamin D B12 Folate	Peak brain metabolic demand; protein & amino acid precursors for neurotransmitters; mood regulation	Oxidative stress accumulates; antioxidant status, B-vitamins, omega-3 and protein adequacy protect against decline

Nutrition acts on the brain continuously — not only during "critical periods" but across a connected lifespan trajectory.

01

PART 1

In-Utero & Third-Trimester Brain, Eye & Mental Health Development

Why the final trimester of pregnancy is a uniquely consequential nutritional window for lifelong brain, visual, and mental health outcomes.

CORE PRINCIPLE

Timing, Dose & Duration Determine Outcome

- Georgieff (2007, Am J Clin Nutr): the developing brain's response to a nutrient depends on when exposure occurs, how much, and for how long — not simply whether the nutrient is “present.”
- Weeks 24–42 of gestation are a period of especially rapid development for the hippocampus (recognition memory), visual and auditory cortex, striatum, and white matter myelination.
- The same nutrient can be protective at physiologic levels and harmful in excess (e.g., iron) — reinforcing that “more is better” is not a safe clinical default.
- This principle underlies why *third-trimester nutrition deserves distinct clinical attention*, rather than being folded into generic “prenatal nutrition” guidance.

Clinical implication: nutrition counseling in pregnancy should be trimester-aware, not one-size-fits-all across the 40 weeks.

Mapping Nutrients to Brain Circuitry

Nutrient	Brain Region / Process Affected	Consequence of Deficiency
LC-PUFAs (DHA)	Eye (retina), cortex — synaptogenesis, membrane structure, myelination	Impaired visual acuity, altered synaptic development
Iron	White matter, striatal-frontal & hippocampal-frontal circuits	Impaired recognition/procedural memory, altered dopamine signaling
Zinc	Autonomic regulation, hippocampus, cerebellum	Altered heart-rate variability, processing speed changes
Copper	Cerebellum	Long-term motor, balance & coordination deficits
Choline / Folate	Global circuitry, hippocampus, white matter (myelin)	Impaired memory, attention, and information-processing speed
B12	Hippocampus, prefrontal cortex, subcortical regions, basal ganglia	Impaired attention, reduced executive function, language difficulties, cognitive decline

Adapted from Georgieff MK. Nutrition and the developing brain: nutrient priorities and measurement. Am J Clin Nutr. 2007;85(suppl):614S–620S.

Weeks 27–40: The Brain's Growth Spurt

- The third trimester is when fetal brain volume, cortical folding, and myelination accelerate most rapidly — a uniquely compressed window of structural development.
- DHA and carotenoids (lutein/zeaxanthin) are preferentially transferred across the placenta and begin accumulating in fetal brain and retina from the third trimester onward.
- Preterm birth truncates this window: infants born before term show measurably lower brain nutrient stores (e.g., white matter creatine, DHA) at the same postmenstrual age as term infants, and correspondingly poorer neurodevelopmental outcomes.
- This is the physiological basis for framing third-trimester nutrition as a distinct priority for eye, brain, and mental health development — not an extension of first/second-trimester guidance.

Choline: The Overlooked Methyl Donor

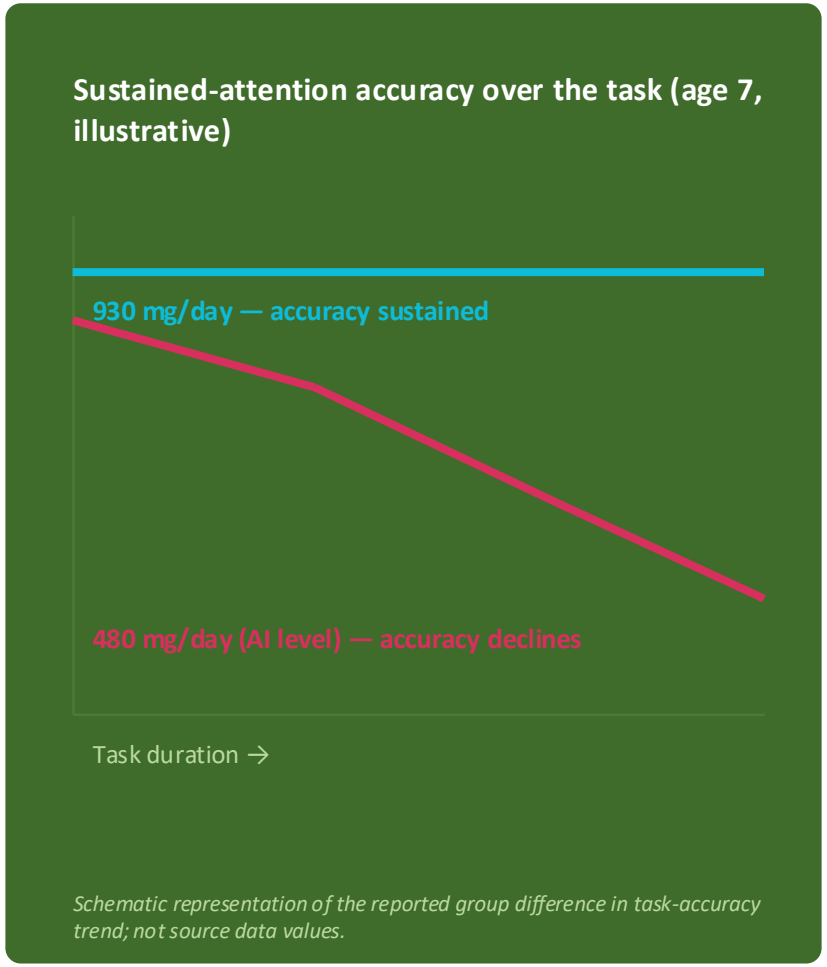
- Choline drives one-carbon metabolism and DNA methylation, and is a precursor for the neurotransmitter acetylcholine — supporting hippocampal development and lifelong memory circuitry.
- Adequate Intake (AI) in pregnancy is 450 mg/day, but research increasingly points to benefit at 550–930+ mg/day in the third trimester for offspring memory, attention, and visuospatial learning.
- 90–95% of U.S. women of reproductive age fail to meet even the 450 mg/day AI — and many standard prenatal vitamins contain little or no choline.
- Food sources: egg yolks, lean meat, fish, poultry, legumes, and cruciferous vegetables.

Counseling opportunity: ask specifically about egg and animal-protein intake in pregnancy — choline is rarely covered by a standard prenatal vitamin.

Prenatal Choline: A Durable Effect on Attention

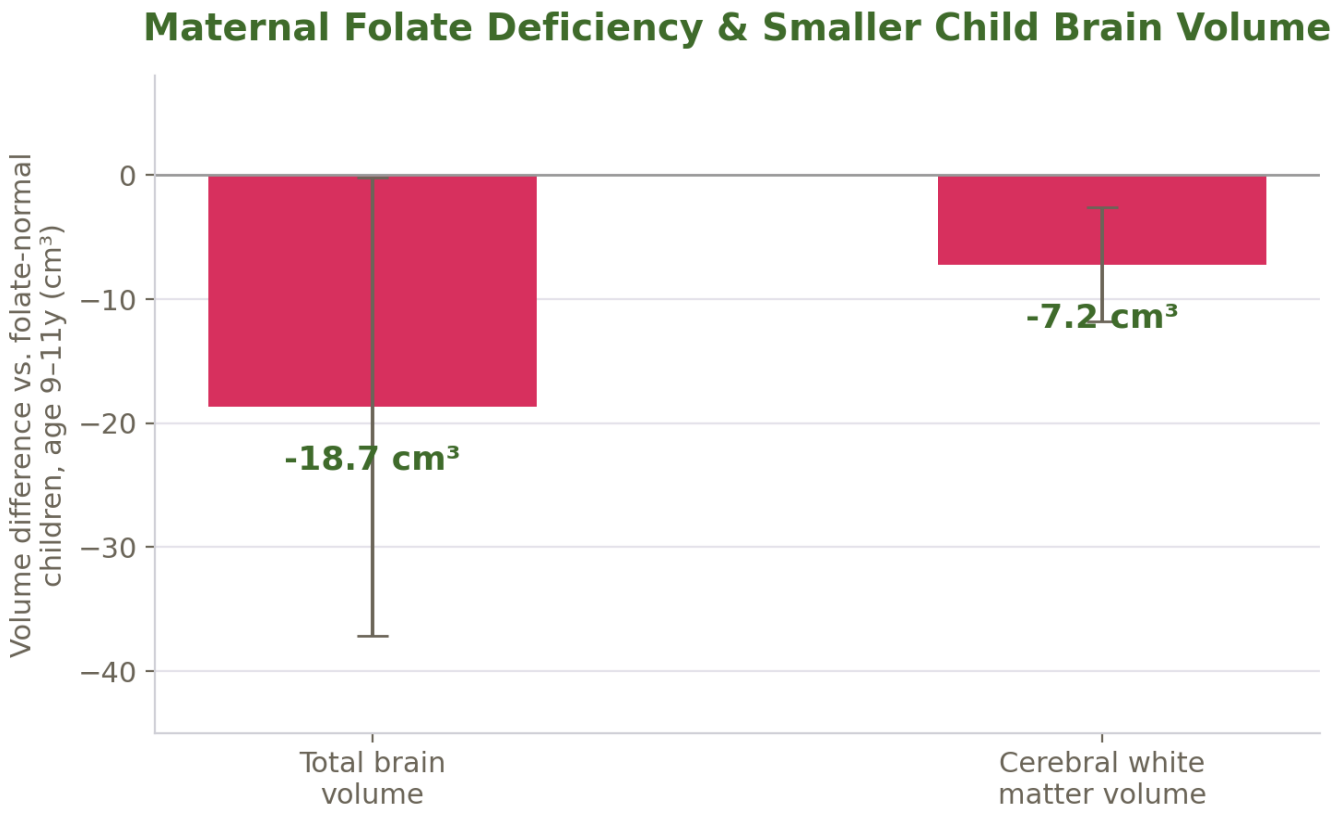
Bahnfleth, Strupp, Caudill & Canfield (2022, FASEB J) — 7-year follow-up of a controlled feeding RCT

- Pregnant participants ate a controlled diet through the third trimester, randomized to 480 mg/day choline (near the AI) or 930 mg/day (~2× AI).
- At age 7, children of mothers in the 930 mg/day group sustained high accuracy throughout an attention task; children in the 480 mg/day group showed accuracy decline as the task went on.
- This built on an earlier finding in the same cohort: higher prenatal choline improved infant information-processing speed in the first year of life.
- First human study to show a prenatal-choline effect on cognition persisting to school age — evidence of durable “nutritional programming.”



Schematic representation of the reported group difference in task-accuracy trend; not source data values.

Maternal Folate & Offspring Brain Volume



Zou et al. 2020, Clin Nutr — Generation R cohort, n=2,095; folate-deficient (<7 nmol/L) vs. folate-normal, fully adjusted model

KEY TAKEAWAYS

- Generation R cohort (n=2,095): children of folate-deficient mothers (<7 nmol/L) had smaller total brain volume (−18.7 cm³) and white matter volume (−7.2 cm³) at age 9–11.
- Repeated scans from the third trimester through age 10 show the gap opens in fetal life and persists throughout childhood — it does not close with age.
- As a continuum, higher maternal folate predicted greater brain volume, plateauing around 10 nmol/L — above the level used only to prevent neural tube defects.
- No differences in cortical thickness or child emotional/behavioral scores remained after adjustment — folate stands alongside choline, DHA, vitamin D, and iron as a distinct third-trimester priority.

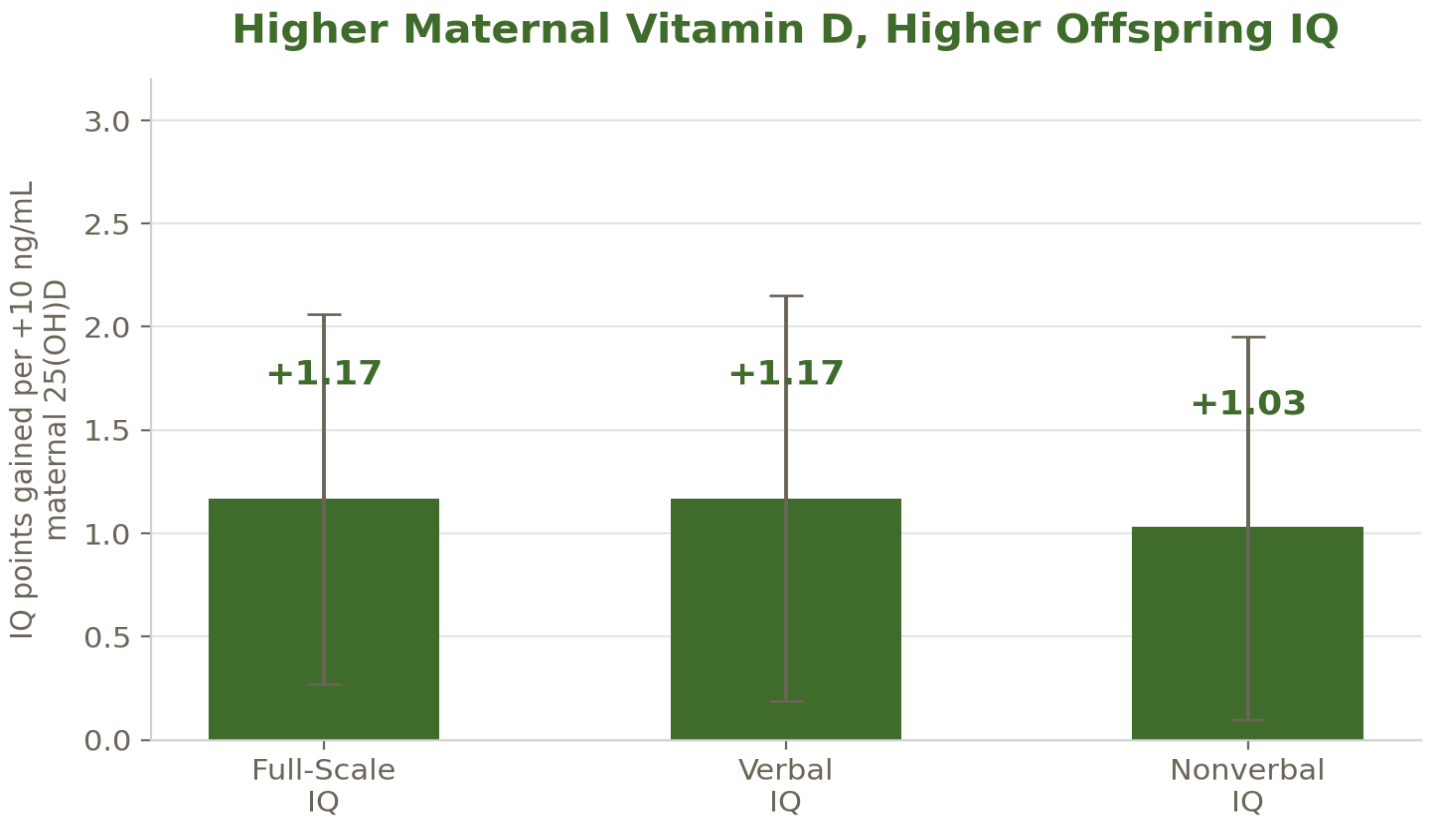
Nutrient Synergy, Not Isolated Nutrients

- Secondary analysis of the PANDA RCT (Christifano et al., 2025, Clin Nutr ESPEN): maternal DHA, choline, and lutein/zeaxanthin status measured at 32 weeks; infant brain function measured via high-density EEG/ERP at 1 and 6 months.
- Maternal DHA status alone predicted stronger auditory brain response at 1 month; maternal choline intake predicted faster visual processing at 6 months.
- Critically, interaction terms — choline × lutein/zeaxanthin × DHA together — predicted brain responses more strongly than any single nutrient alone.
- Egg intake alone (a common food-source proxy) did not predict outcomes — the specific nutrient combination mattered, not just "eating more eggs."

Takeaway for counseling: recommend combined intake of DHA-rich fish/algae oil, choline-rich foods, and colorful produce (lutein/zeaxanthin) together, rather than a single "hero nutrient."

THIRD-TRIMESTER NUTRIENTS

Maternal Vitamin D & Offspring IQ

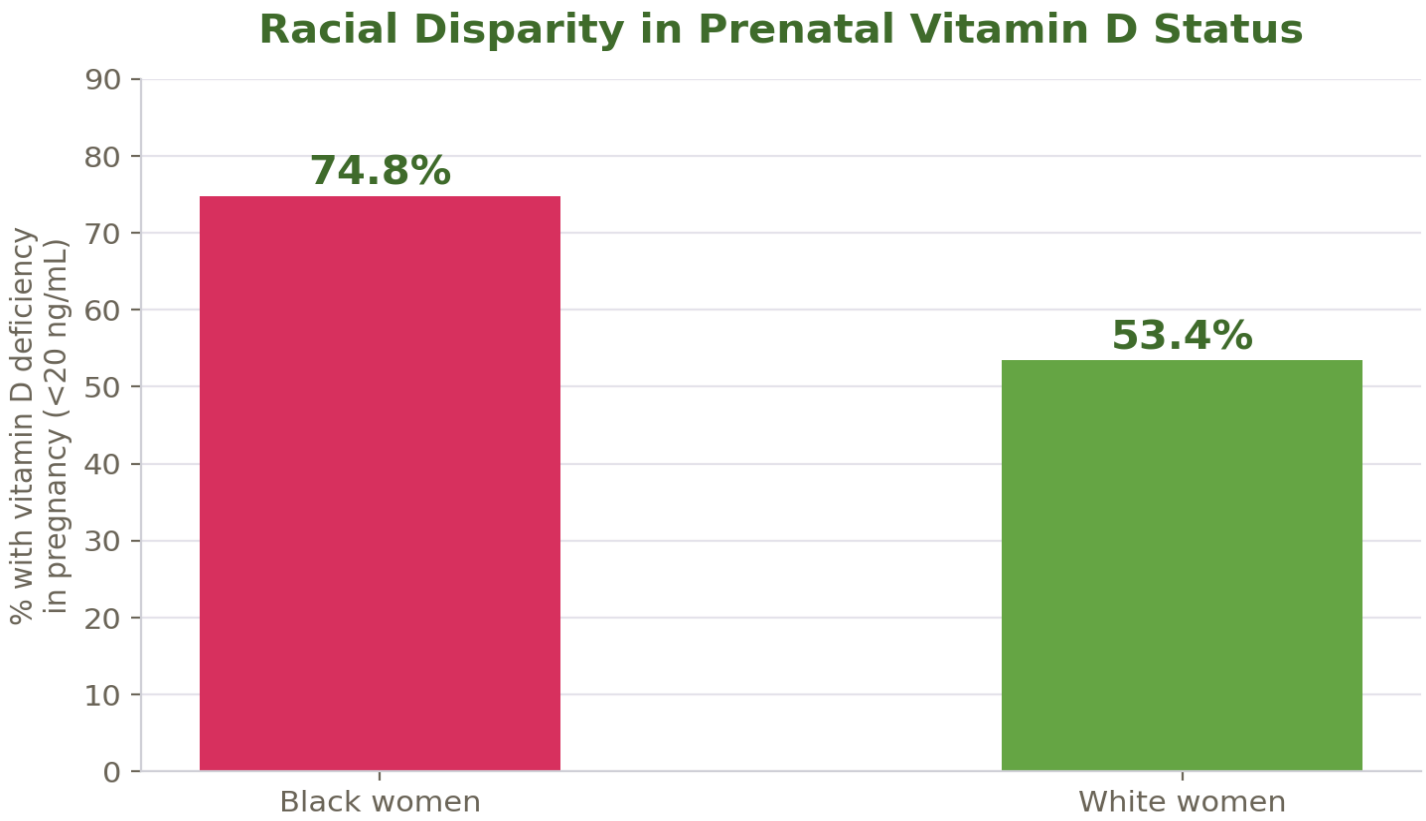


Melough et al. 2021, J Nutr — CANDLE cohort, n=1,019; offspring assessed age 4–6y

KEY TAKEAWAYS

- CANDLE cohort (n=1,019): every 10 ng/mL increase in maternal 25(OH)D was associated with meaningfully higher offspring IQ at age 4–6.
- Relationship was linear up to ~40 ng/mL — no evidence of diminishing returns across the clinically relevant range.
- Mechanism: the vitamin D receptor is expressed in fetal brain from early gestation and regulates genes controlling neuronal differentiation and neurotransmitter balance.
- 45.6% of the study cohort was vitamin D deficient (<20 ng/mL) at a mean of 23 weeks' gestation.

An Equity Gap in Prenatal Vitamin D



Melough et al. 2021, J Nutr (CANDLE cohort); national estimates cited within

KEY TAKEAWAYS

- Darker skin pigmentation reduces cutaneous vitamin D synthesis, contributing to markedly higher deficiency rates in Black pregnant patients.
- Standard prenatal vitamins (400–600 IU vitamin D) are likely insufficient to correct deficiency; repletion often requires 800–1,000+ IU/day, or higher under clinical supervision.
- Screening and correcting vitamin D deficiency in pregnancy is a low-cost intervention with a plausible, dose-dependent cognitive benefit for offspring.
- This gap should be part of any health-equity conversation about prenatal nutrition access.

THIRD-TRIMESTER NUTRIENTS

Iron: A Non-Negotiable Nutrient for the Fetal Brain

- The fetus prioritizes available iron to red blood cell production over brain and other organs — meaning brain iron can be depleted even when the infant is not anemic.
- Iron-dependent enzymes support myelin production (oligodendrocytes), oxidative energy metabolism, and synthesis of dopamine, serotonin, and norepinephrine.
- Maternal diabetes and intrauterine growth restriction are major risk factors, documented to reduce fetal brain iron concentration by 32–40%.
- Deficits from deficiency in the fetal/infant period (6–24 months) can persist 19–23 years after iron is repleted — this is a true critical-window nutrient, not a reversible-any-time one.

30–50% of pregnant women worldwide are iron deficient (WHO). Screening should continue through the third trimester, not stop after first-trimester labs.

Creatine: An Emerging Third-Trimester Nutrient

- The creatine–phosphocreatine–creatine kinase system rapidly buffers ATP for neuronal firing; the placenta both synthesizes and transports creatine to the fetus.
- The third trimester functions as a fetal brain “phosphocreatine loading window” supporting white-matter myelination.
- Preterm infants — who miss part of this window — show significantly lower white-matter creatine at equivalent postmenstrual age than term infants, correlating with poorer neurodevelopmental outcomes.
- Genetic creatine deficiency disorders (AGAT, GAMT, SLC6A8) cause intellectual disability, epilepsy, and autism-like behavior — direct evidence that creatine is non-negotiable for neurodevelopment.
- Average dietary creatine intake is only ~1 g/day (mainly from meat and fish); vegetarian and vegan patients likely have lower baseline intake, with no pregnancy-specific dosing guideline yet established.

Placental Creatine: Synthesis & Transport Machinery

Methionine, Arginine + Glycine
amino acid precursors

→

AGAT ↓
L-arg:Gly amidinotransferase

→

Guanidinoacetate (GAA)
intermediate

→

GAMT ↓
GAA methyltransferase

→

CREATINE
exported to fetus

SLC6A8 (CrT1) transporter: expressed on placental barrier — imports creatine from maternal blood AND exports placental-synthesized creatine to fetal circulation

Placental Expression (Lager et al. 2017)

First characterization of AGAT, GAMT, and SLC6A8 in human term placenta. All three genes localized to villous trophoblast and syncytium—establishing that the placenta is both a creatine synthesis organ **AND** a creatine transporter to the fetus.
The trophoblast is the outer layer of cells in a developing embryo.

Functional Roles in Trophoblasts (Sah et al. 2026)

Placental trophoblasts use both glycolysis and OXPHOS; the Cr–PCr–CK system buffers rapid ATP fluctuations during syncytialization, nutrient transport, and invasion. Loss of this buffer is proposed as a key mechanistic link to placental insufficiency syndromes.

Lager et al. (2017) Placenta; Sah et al. (2026) Biol Reprod; Lefevre et al. (2024) Biol Reprod

INTEGRATIVE SUMMARY

Eye. Brain. Mental Health. One Window.

DHA / Carotenoids

Eye & cortex — synaptogenesis and retinal development

Choline

Attention & memory — sustained to age 7 and beyond

Vitamin D

Neurocognitive development — dose-dependent IQ effect

Iron / Creatine

Myelination & brain energy — largely irreversible if missed

No single nutrient acts alone. Third-trimester nutrition is an integrative, whole-body process — DHA, choline, carotenoids, vitamin D, iron, and creatine interact to build the structural and biochemical foundation for lifelong cognitive and mental health. This does not include the structure/function impacts of vitamin B12 and folate.

02

PART 2

Antioxidants & Antioxidant-Like Compounds Across the Lifespan

How oxidative stress shapes cognitive aging — and which nutrients help the brain defend itself, from the third trimester through late life.

What Counts as “Antioxidant” for the Brain?

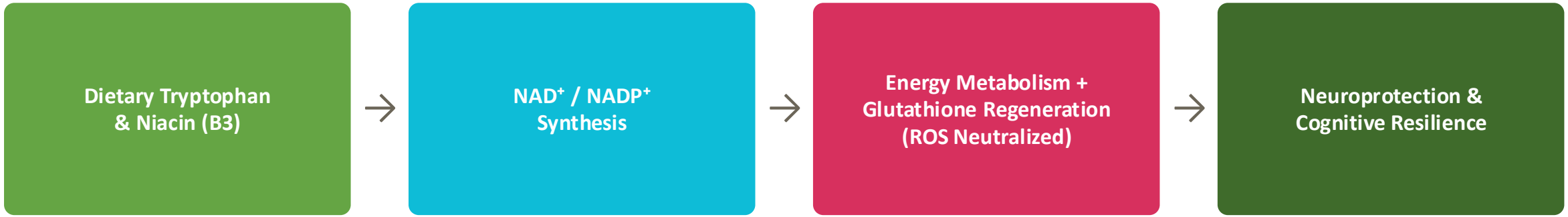
- Classic antioxidant vitamins: vitamin C, vitamin E (especially mixed tocopherols, not alpha-tocopherol alone), and vitamin A.
- Carotenoids: lutein, zeaxanthin, and lycopene — accumulate directly in brain tissue and the retina.
- Polyphenols: resveratrol, flavonoids (e.g., EGCG), anthocyanins — modulate oxidative stress and inflammatory signaling.
- Mitochondrial cofactors with antioxidant-adjacent roles: coenzyme Q10, alpha-lipoic acid, selenium (glutathione peroxidase cofactor), zinc.
- Antioxidant-like redox pathways: niacin/NAD^+ supports glutathione regeneration and reactive-oxygen-species neutralization — a mechanism worth teaching clients even though niacin is not a classic antioxidant vitamin.

Lutein & Zeaxanthin: A Lifecycle Arc

- These carotenoids preferentially accumulate in brain tissue and the macula beginning in the third trimester, continuing across childhood and adulthood.
- Macular pigment density (measurable non-invasively) correlates with brain lutein concentration — offering a proxy window into brain carotenoid status.
- In adults, higher lutein/zeaxanthin status associates with better global cognition, memory, and verbal fluency; supplementation as low as 12 mg/day has shown measurable benefit.
- Patients with mild cognitive impairment show low brain lutein — and, as shown later in this section, Alzheimer's brain tissue shows an even deeper deficit.

Practical tip: lutein/zeaxanthin-rich foods (leafy greens, corn, eggs) are relevant across every decade of the counseling relationship, not just in the eye-health conversation.

Niacin & NAD^+: An Antioxidant-Like Pathway



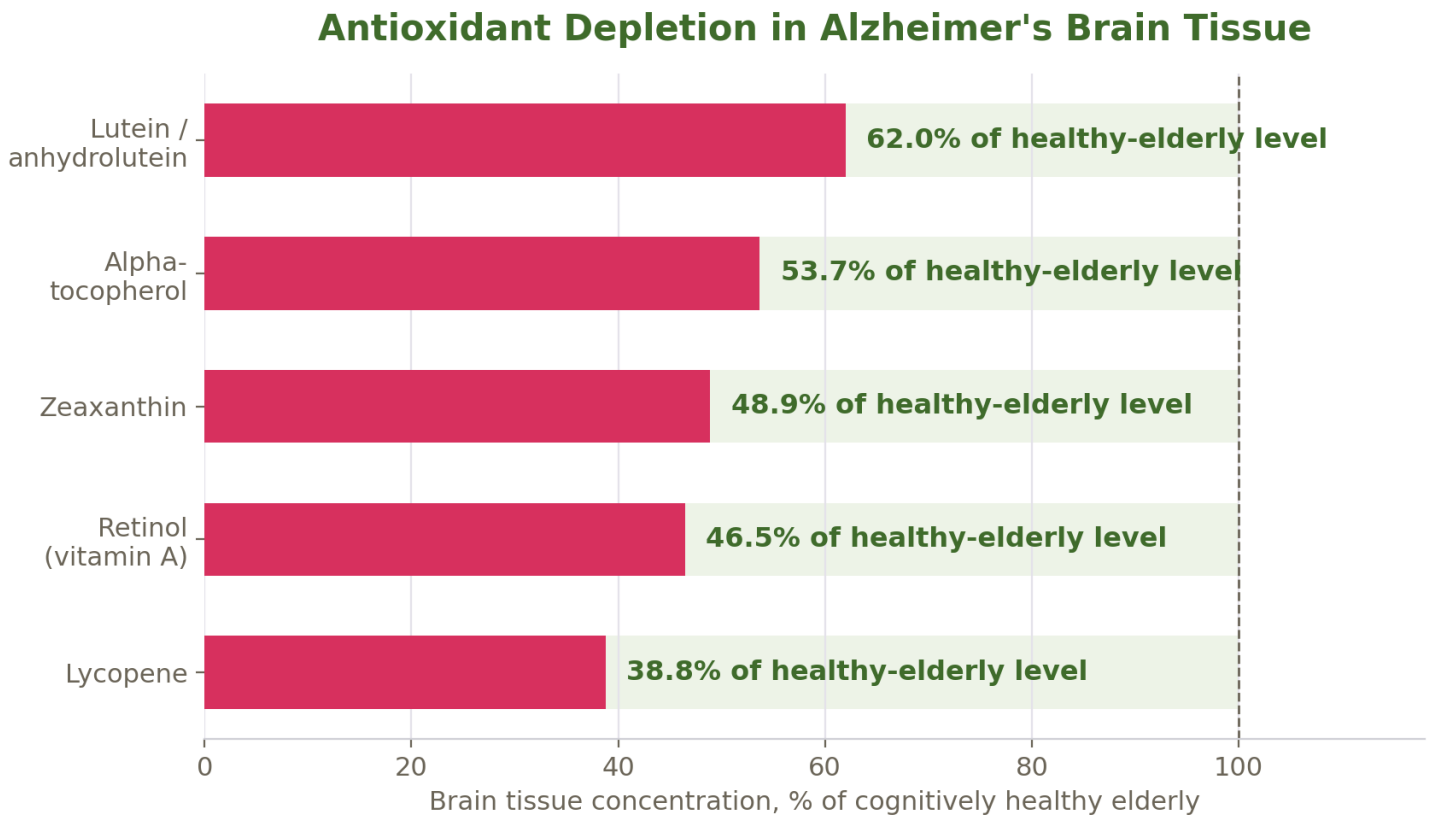
- Niacin (vitamin B3) exists in two active forms — nicotinic acid and nicotinamide — both converted to the coenzymes NAD^+ and $NADP^+$, fundamental for cellular metabolism and signaling in the brain.
- Niacin supports energy production, DNA repair, cell survival, neuronal activity, neurotransmission, and neuroprotection — critical for cognitive function and defense against neurodegenerative processes.
- Deficiency — and likely insufficiency short of overt deficiency — can present with dementia, depression, and cognitive impairment, including pellagra's classic triad of dermatitis, diarrhea, and dementia.

- Energy & mitochondrial function: NAD^+ is the key electron carrier in oxidative metabolism, enabling energy-hungry neurons to generate ATP for signaling and cognitive processing.
- DNA repair & cell survival: NAD^+ fuels PARP enzymes and sirtuins (SIRT family), governing gene expression, stress responses, and aging.
- Neuroprotection: niacin preserves neurons under stress by blocking mitochondrial cytochrome c release and caspase-3/9 activation, while sustaining Akt-dependent survival signaling.
- Oxidative stress defense: NADPH from niacin metabolism regenerates glutathione and neutralizes reactive oxygen species — the "antioxidant-like" pathway shown above.

Only ~2% of dietary tryptophan converts to niacin, so intake is tracked as "niacin equivalents" (RDA 16 mg NE/day men, 14 mg NE/day women); megadosing (grams/day) shows no added benefit — physiologic repletion is the evidence-based target.

ANTIOXIDANTS

Antioxidant Depletion in the Alzheimer's Brain



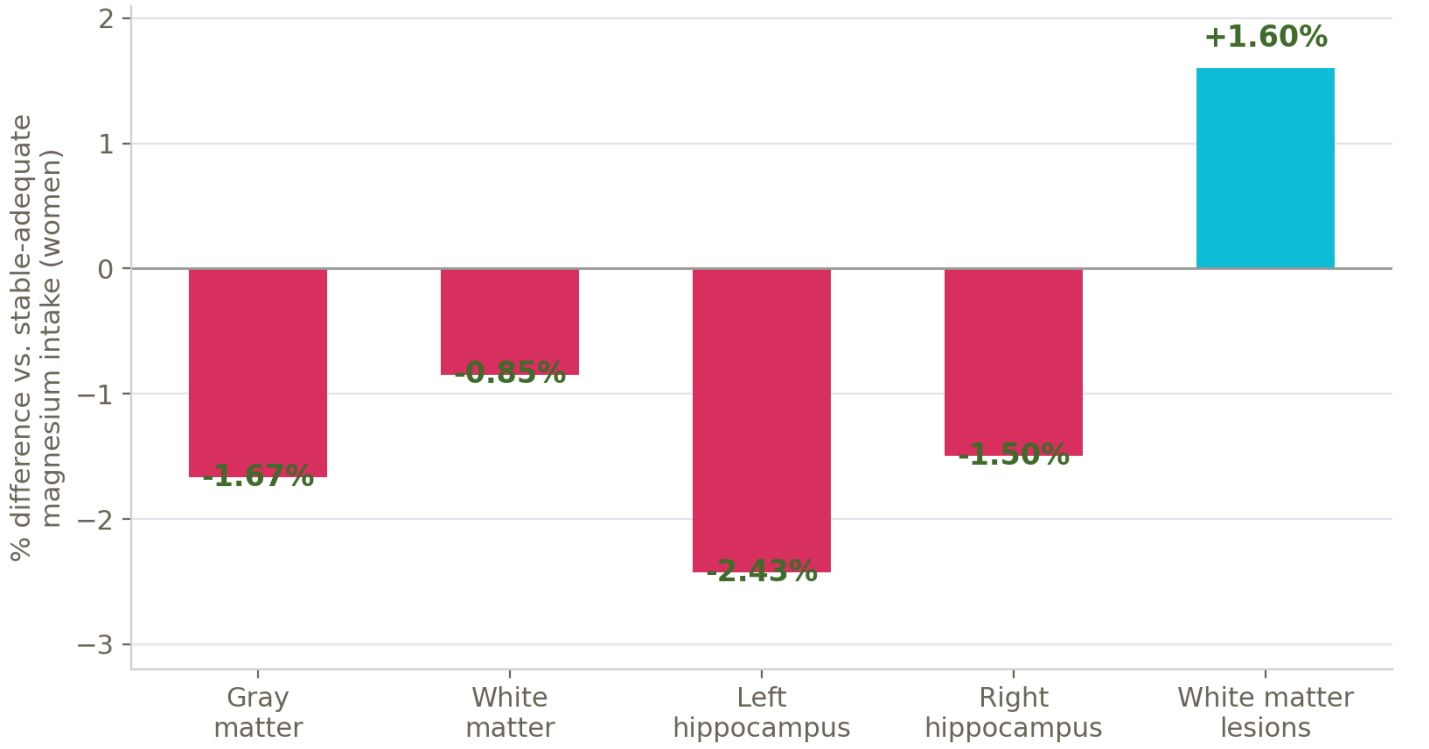
Dorey et al. 2023, J Alzheimers Dis — postmortem brain tissue, 15 AD vs. 10 healthy-elderly brains

KEY TAKEAWAYS

- Direct postmortem comparison: Alzheimer's brains show significantly lower concentrations of every major antioxidant carotenoid and tocopherol measured.
- AD brains had significantly lower levels of lutein, zeaxanthin, anhydrolutein, retinol, lycopene, and alpha-tocopherol, and significantly increased levels of XMiAD, an unidentified xanthophyll metabolite.
- Lycopene showed the largest relative deficit — just 38.8% of the healthy-elderly level.
- Only 6% of Alzheimer's brain samples reached healthy-elderly zeaxanthin/retinol concentrations.
- This is the clearest single piece of tissue-level evidence linking antioxidant status directly to neurodegenerative brain pathology.

Magnesium & Brain Volume Across Midlife

Low, Rising Magnesium Intake Tracks With Smaller Brain Volume



Alateeq, Walsh & Cherbuin 2023, Eur J Nutr — UK Biobank, n=6,001, ages 40–73

KEY TAKEAWAYS

- UK Biobank cohort (n=6,001, ages 40–73): a rising-from-low magnesium intake trajectory tracked with smaller gray matter, white matter, and hippocampal volumes — and more white-matter lesions — mainly in women.
- Effect appeared to begin as early as the 40s, not only in advanced age as previously assumed.
- Mechanism is thought to be anti-inflammatory / anti-oxidative-stress rather than blood-pressure-mediated.
- Practical target: magnesium-rich foods (leafy greens, legumes, nuts, seeds, whole grains) toward the ~350–420 mg/day range, starting well before older adulthood.

03

PART 3

Dietary Patterns at Odds With Optimal Brain Health

Recognizing the dietary exposures — not just individual nutrient gaps — that work against cognitive and mental health across the lifecycle.

The Modern “Western” Dietary Pattern

- High saturated-fat intake is associated with greater Alzheimer's disease risk in multiple cohort studies.
- Typical Western-pattern omega-6:omega-3 intake ratios run far above the ~2:1 ratio associated with favorable cognitive and mood outcomes.
- Midlife obesity is associated with roughly double the risk of later-life dementia.
- The Western dietary pattern has an identifiable metabolomic “signature” distinguishable from Mediterranean/DASH/MIND-style patterns — this is a measurable exposure, not just a label.

Refined Carbohydrates, Glycemic Load & Mood

- Long-term excess intake of simple/refined carbohydrates is linked to greater cognitive decline and Alzheimer's disease risk in the literature.
- Low glycemic-index eating patterns are associated with better attention, memory, and functional capacity than high-glycemic patterns.
- In a head-to-head weight-loss trial, low-carbohydrate and low-fat diets produced comparable weight loss — but the low-carbohydrate group reported significantly worse mood and negative affect.
- The clinical message is about carbohydrate quality, not simply “less carbohydrate” — a nuance worth making explicit with clients who default to carb-restriction for mood or cognitive goals.

PATTERNS OF CONCERN

Restrictive & Unplanned Diets: A Hidden Risk

- Very-low-calorie (<1,000 kcal/day) and low-calorie (1,000–1,200 kcal/day) diets risk inadequate total energy, protein, and micronutrient intake for brain function.
- Unplanned vegan, vegetarian, or macrobiotic patterns (i.e., adopted without dietitian guidance) carry elevated risk for B12, iron, zinc, choline, and omega-3 gaps — all nutrients discussed in this presentation.
- Restrictive athlete diets show the same pattern: cognitive performance is an underappreciated blind spot in sports nutrition counseling, alongside physical performance.
- “Hangry” is a real physiological phenomenon — total caloric adequacy itself is a mood-regulation variable, not just a weight variable.
- Reduced calorie, reduced, insufficient overall protein intake.
- Poor intake of the essential amino acids

Ask every restrictive-diet client how the plan was designed and by whom — self-directed restriction is the highest-risk scenario for silent micronutrient shortfalls.

Protein, Amino Acids: Importance to Neurotransmitters & Health

- The aromatic amino acids (tryptophan, tyrosine, phenylalanine) are the biosynthetic precursors for the neurotransmitters serotonin, dopamine, and norepinephrine.

- Other amino acids active in the CNS and brain include – glutamic acid, aspartic acid, , glutamine, cysteine, methionine, proline, asparagine, GABA, lysine, arginine, glycine, serine, alanine, threonine, beta-alanine.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7503967/

Serotonin

- In serotonergic neurons Trp serves as the precursor for 5-HT.
- Tryptophan is the sole precursor of peripherally and centrally produced serotonin.
- Serotonin plays a role in:

    - Mood states
    - Sleep/wake cycles
    - Appetite
    - Digestion
    - Pain perception
    - Memory
    - Learning
    - Much more!

Ref: https://www.ncbi.nlm.nih.gov/books/NBK545168/#

Phenylalanine and Tyrosine

- Phenylalanine is an essential amino acid that acts as a direct precursor to tyrosine. Phenylalanine can influence dopamine, norepinephrine, and epinephrine
- Tyrosine is an amino acid that is a precursor to several neurotransmitters, including dopamine, norepinephrine, and epinephrine.
  - Dopamine: Helps support a positive mood and mental alertness.
  - Norepinephrine and epinephrine: The main actors in the body's response to acute stress (fight/flight response).
- Tyrosine is also involved in the production of melanin, the pigment that gives color to hair and skin. It also helps the adrenal, thyroid, and pituitary glands function properly

Dopamine

- Dopamine impacts or is impacted by:
    - Reward-seeking/pleasurable experience
    - Plays a role in locomotion
    - Involved in learning and attention
    - Mood states
    - Sleep and arousal
    - Other

Ref: https://my.clevelandclinic.org/health/articles/22581-dopamine

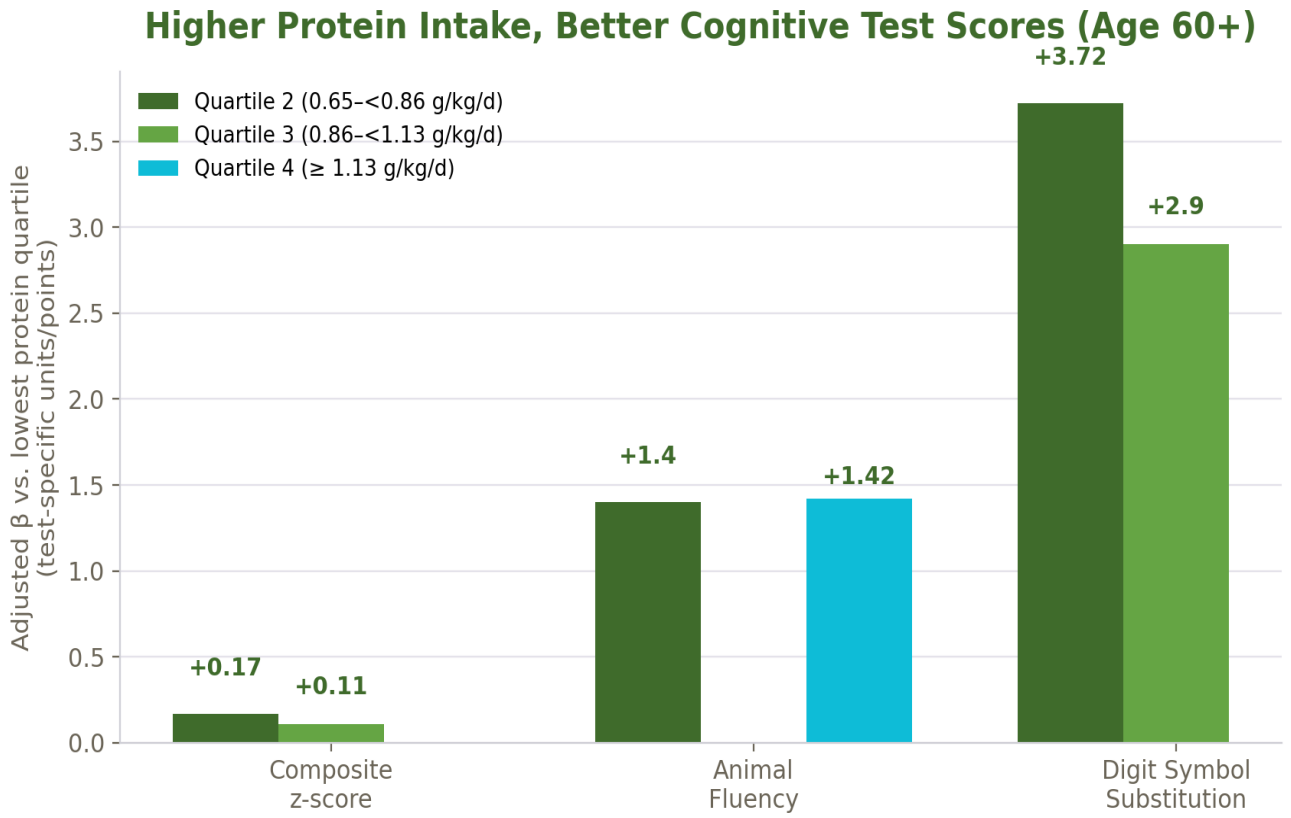
Norepinephrine, Epinephrine

- Low levels associated or contributory to depression, anxiety…

- Functions:
  - Regulate the body's "fight or flight" response
  - Raise HR and BP
  - Stimulate glucose production
  - Dilate pupils and bronchioles
  - Constrict blood vessels
  - Metabolic impacts
  - Memory

Ref: https://www.ncbi.nlm.nih.gov/books/NBK540977/# ;
https://www.medicalnewstoday.com/articles/325485#deficiency

Low Protein Intake & Cognitive Aging



Li, Li, Wang & Zhang 2020, J Nutr Health Aging — NHANES 2011–2014, n=2,460. Each test uses its own scale; bars shown only where statistically significant

KEY TAKEAWAYS

- NHANES data in adults 60+ (n=2,460): higher total protein intake was associated with better performance across memory, verbal fluency, and processing-speed tests.
- The lowest protein quartile (<0.65 g/kg/day) consistently underperformed higher quartiles.
- Protein source mattered: meat, eggs, and legumes tracked with better performance; interestingly, higher dairy protein intake showed an inverse association in this and other cohorts — an area warranting a cautious, “more research needed” framing.
- Practical target for older adults: aim above 0.86–1.0 g/kg/day, emphasizing varied protein sources.

PROTECTIVE PATTERNS

Mediterranean, DASH & MIND Diets

- The Mediterranean pattern (olive oil, fish, fruits/vegetables) supplies MUFA, omega-3, vitamin D, and a wide range of antioxidants and polyphenols in combination — and shows protective associations with cognitive aging in meta-analyses.
- DASH (originally designed for blood pressure) is independently linked to improved psychomotor speed.
- MIND (a Mediterranean–DASH hybrid) specifically targets brain aging: in a middle-aged, obese-adult RCT, the MIND-diet group showed significant improvements in working memory, verbal recognition memory, and attention versus control.
- Higher lutein/zeaxanthin intake sustained over a decade was associated with roughly 50% lower risk of an Alzheimer's diagnosis in the Rush Memory and Aging Project.

The strongest counseling message in this entire deck: recommend whole dietary patterns, not isolated "brain supplements," as the primary intervention.

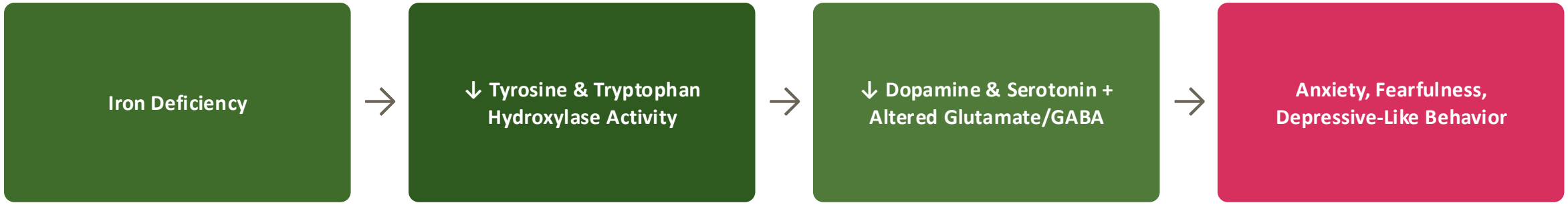
04

PART 4

Nutrient Insufficiency & Mental Health Across the Lifespan

Specific micronutrient gaps have been directly linked to depression, anxiety, psychosis, and other mental health conditions — with clear implications for screening.

Iron Deficiency & Mood: The Mechanism



- Iron is a required cofactor for the enzymes that synthesize dopamine, serotonin, and norepinephrine — and concentrates in dopamine/GABA-rich brain regions.
- Both deficiency AND overload increase anxiety-like behavior via distinct mechanisms (impaired neurotransmission vs. oxidative stress) — a U-shaped relationship.
- Schizophrenia patients show lower serum iron; major depression patients show lower hematocrit and transferrin — supporting a broader “micronutrient-insufficient mood disorder” pattern.

Iron Deficiency: A Lifespan Psychiatric Signal

- In-utero / infant: low maternal iron status has been linked to increased offspring risk of schizophrenia and autism; infant deficiency (6–24 months) predicts anxiety, depression, social problems, and inattention up to 19–23 years later — even after iron is repleted.
- Adults: iron-deficiency anemia is associated with higher rates of anxiety disorders, depression, sleep disorders, and psychotic disorders in population data.
- Clinical pearl: order a ferritin test, not just hemoglobin or serum iron — ferritin reflects total body iron stores, and mental-health-relevant deficits can occur without anemia.
- One clinical review found mental-health symptom improvement in about half of patients with ferritin below 100 ng/mL — a substantially higher functional threshold than the standard 30 ng/mL “deficiency” cutoff.

High-risk groups to screen: pregnant patients, adolescent girls/women with heavy menses, frequent blood donors, and patients with malabsorption or GI surgery history.

B12, Folate & Homocysteine

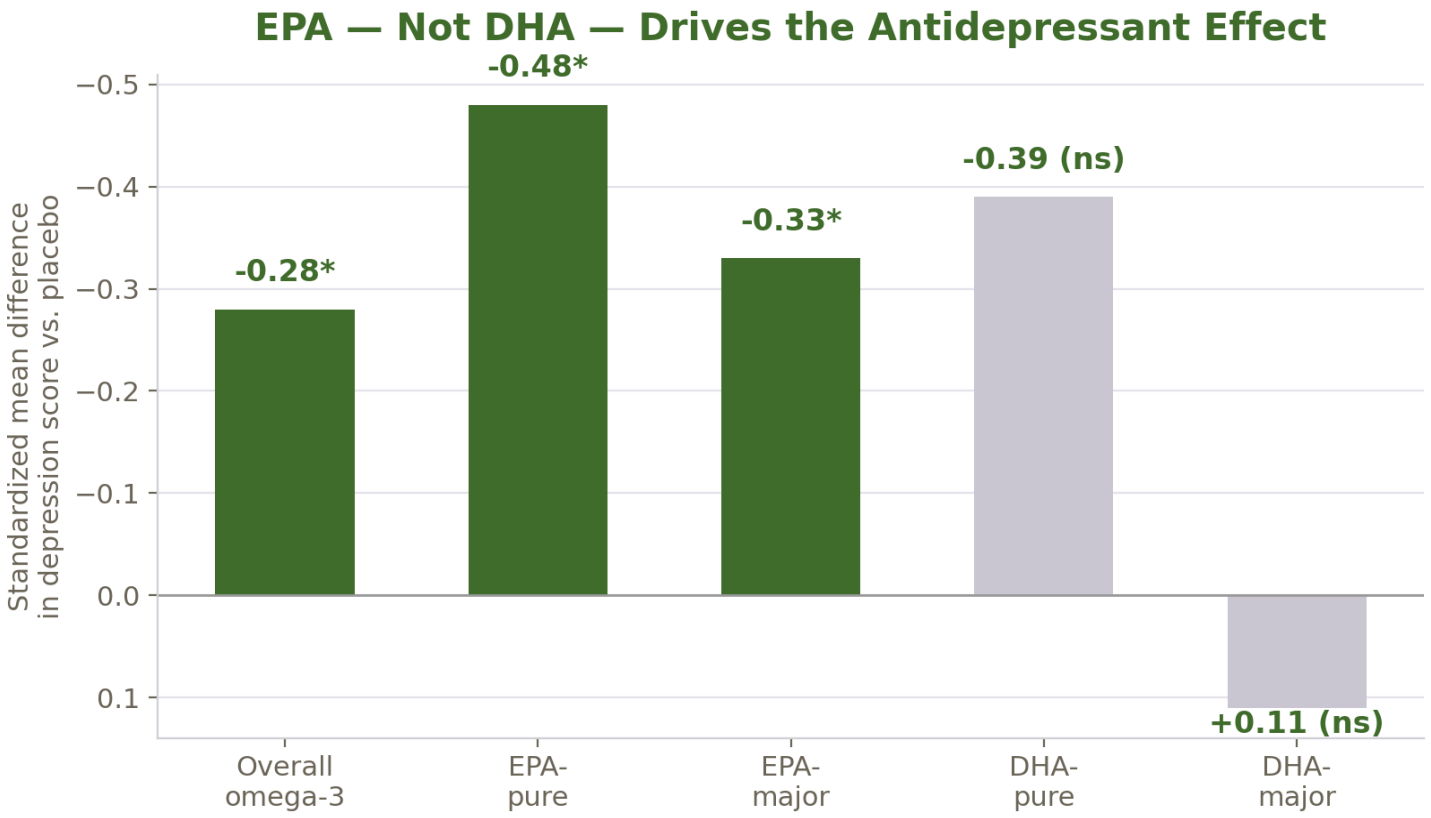
- Folate and B12 drive homocysteine remethylation to methionine, feeding S-adenosylmethionine (SAMe) — the brain's universal methyl donor for neurotransmitter synthesis and myelin maintenance.
- Elevated homocysteine and low folate status are consistently linked to dementia and Alzheimer's disease risk across multiple cohorts.
- “Biochemical” (functional) B12 deficiency — detected via elevated methylmalonic acid — is far more common in older adults (11–50%) than classic pernicious anemia (~0.1–0.2%), and serum B12 alone often misses it.
- Important caution: high-dose folic acid in a patient with marginal, unrecognized B12 status can worsen memory and processing speed — screen B12/MMA before recommending high-dose folate.

Folate & Treatment-Resistant Depression

- Only L-methylfolate — not standard folic acid — crosses the blood-brain barrier to participate directly in neurotransmitter synthesis.
- Standard SSRI/SNRI monotherapy achieves roughly 30% remission in major depressive disorder.
- Deplin® is the Rx folate. In SSRI-resistant MDD, adjunctive L-methylfolate 15 mg/day produced a significantly higher response rate than placebo (32% vs. 15%).
- Benefit was concentrated in patients with markers of inflammation (elevated TNF-α, CRP) or obesity (BMI ≥ 30) — suggesting folate status interacts with inflammatory depression subtypes specifically.
- Learn more here: https://deplin.com/

Clinical distinction worth teaching: folinic acid (not folic acid) is the correct supplement for cerebral folate deficiency — folic acid can worsen that specific condition.

Omega-3 & Depression: What the Evidence Shows



*Liao et al. 2019, Transl Psychiatry — meta-analysis, 26 RCTs, n=2,160. * = significant, p<0.05*

KEY TAKEAWAYS

- Meta-analysis of 26 RCTs (n=2,160): omega-3 PUFAs overall significantly improved depressive symptoms versus placebo.
- The benefit was driven specifically by EPA-dominant formulations (≥ 60% EPA) — DHA-dominant formulations showed no significant effect on depression.
- Lower EPA doses (≤ 1 g/day, roughly 720 mg–1 g/day) outperformed higher doses in this pooled analysis — more was not better.
- Practical takeaway: when omega-3 is recommended specifically for mood, choose an EPA-dominant product rather than a generic fish-oil blend.

Other Nutrient Insufficiencies Linked to Mood

Nutrient	Evidence Base	Clinical Signal
Zinc	Meta-analysis of 23 studies: blood zinc ~1.85 µmol/L lower in depression vs. controls	Low dietary zinc linked to ~80% higher odds of depressive symptoms in women
Magnesium	RCT (n=126): supplementation improved PHQ-9 depression scores by ~4.2 points net vs. control	Consider in patients with anxiety plus depressive symptoms
Vitamin D	Systematic review (15 studies): methodologically strong studies show a positive antidepressant effect	Low-cost, high-yield screening test in mood complaints
L-carnitine	Meta-analysis (12 RCTs): reduced depressive symptoms with efficacy comparable to conventional antidepressants	Fewer adverse events than standard antidepressants in pooled data
CoQ10	Antioxidant/mitochondrial cofactor; low levels linked to treatment-resistant depression	Consider in fatigue-predominant, treatment-resistant presentations

When Genetics Meets Nutrition: Inborn Errors of Metabolism

- Phenylketonuria (PKU): untreated, elevated phenylalanine causes severe intellectual disability, autism-like features, and seizures. Early low-phenylalanine dietary treatment has produced over 50,000 people worldwide living without cognitive deficits — one of medicine's clearest “nutrition-as-treatment” successes.
- Homocystinuria, BCKDK deficiency, and Hartnup disease similarly show that genetic mismanagement of specific amino acids can drive autism-spectrum and psychiatric symptoms — often correctable with targeted dietary and cofactor therapy.
- Cerebral folate deficiency causes irritability, seizures, and developmental regression; folinic acid (not folic acid) is the required treatment.
- These disorders illustrate an important contrast: population-level low protein intake harms cognition, while in these specific genetic conditions, excess intake of one particular amino acid is what causes brain injury — individualized assessment matters.
- Cerebral creatine deficiency syndromes (CCDS): consist of three distinct genetic disorders: Guanidinoacetate methyltransferase (GAMT) deficiency, Arginine:glycine amidinotransferase (AGAT) deficiency, and Creatine transporter (CRTR) deficiency. These conditions prevent the body from making or moving creatine properly, leading to a shortage of creatine in the brain

05

PART 5

Applying the Evidence in Practice

Turning this evidence base into a practical framework for nutrition assessment and client counseling across the lifecycle.

CLINICAL APPLICATION

Counseling Across the Lifecycle: Population Pearls

Population	Priority Focus
Pregnancy (esp. 3rd trimester)	Choline, DHA, vitamin D, iron; assess creatine adequacy in vegetarian/vegan patients; reinforce that standard prenatals often under-supply choline and vitamin D
Children & adolescents	Iron status, especially in menstruating teens; avoid unsupervised restrictive diet patterns during rapid brain development
Adults with mood symptoms	Screen iron/ferritin, B12/MMA, folate/homocysteine, and vitamin D before or alongside pharmacologic treatment
Older adults	Total protein adequacy (≥ 1.0 g/kg/day) from varied sources; B12/MMA; magnesium-rich foods; MIND-style dietary pattern
Restrictive eaters & athletes	Confirm total caloric adequacy and screen for iron, B12, zinc, and omega-3 gaps regardless of outward health appearance

SUMMARY

Key Takeaways

1

Antioxidants and antioxidant-like compounds (carotenoids, tocopherols, niacin/NAD^+) support cognitive function across the entire lifespan, not only in aging.

2

Western-pattern, high-refined-carbohydrate, and unsupervised restrictive diets are consistently linked to worse brain and mood outcomes.

3

Iron, B12/folate, omega-3 (EPA), zinc, magnesium, and niacin insufficiencies each have direct, evidence-based ties to specific mental health conditions.

4

Third-trimester nutrition — carotenoids, DHA, B12, folate, choline, vitamin D, iron, and creatine together — is a uniquely consequential, integrative window for eye, brain, and mental health.

Apply this evidence by assessing dietary patterns and targeted biomarkers (ferritin, B12/MMA, folate/homocysteine, 25(OH)D) at every life stage, and by counseling toward whole dietary patterns rather than single “magic nutrient” fixes.

CLINICAL APPLICATION

The Dietary Pattern Prescription

- Lead with a whole dietary pattern (Mediterranean/MIND-style) rather than isolated “brain supplements” as the primary recommendation.
- Ensure adequate total protein from varied, high-quality sources — meat, fish, eggs, legumes.
- If targeting mood specifically with omega-3, recommend an EPA-dominant formulation around 1 g/day rather than a generic, DHA-heavy blend.
- Tocopherols too!
- Emphasize colorful produce for carotenoids and polyphenols — lutein/zeaxanthin-rich foods belong in every decade of the counseling relationship.
- Avoid recommending or endorsing very-low-calorie or unsupervised restrictive patterns without close nutritional monitoring.
- Individualize by age, sex, life stage, and known risk factors — a supplement or target appropriate for one patient may be inappropriate, or insufficient, for another (Fekete et al., 2023).

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