This webinar is hosted by Kathie Madonna Swift, MS, RDN, LDN, Food As Medicine Education Director for the Center for Mind-Body Medicine, present by Mark Pettus, MD and made possible by a grant from the Scheidel Foundation.
Disclosures

- Chief Medical Officer of Functional Formularies
- Chief of Clinical Innovation at Novolux Lighting Technologies
Learning Objectives

- Review the prevalence and importance of micronutrient deficiencies essential to brain health, mind and mood.
- Review the contributing factors to the growing prevalence of important micronutrient deficiencies.
- Examine the importance of the MTHFR SNP and its clinical implications for personalized micronutrient-nutritional intervention.
- Review recent studies supporting nutritional intervention and supplementation for addressing common nutrient deficient states in individuals with “brain disruption”.

The Center for Mind-Body Medicine
Epigenetics, nutrition and mental health. Is there a relationship?

Stevens AJ¹, Rucklidge JJ², Kennedy MA¹.
“There is now a wealth of research that has demonstrated the importance of inflammation, gut dysbiosis, oxidative stress, and mitochondrial dysfunction for mental health. The nutritional research reviewed herein justifies treating patients through either improved diet or supplementation (or both), given that such treatments could well have beneficial effects on all of these variables.”
Growing recognition of nutrition as central determinants of both physical and mental health.
Essential Micronutrients

- Biotin
- Folic acid
- Niacin
- Pantothenate
- Riboflavin
- Thiamine
- Vit A
- Vit B6
- Vit B12
- Vit C
- Vit D
- Vit E
- Vit K
- Calcium
- Chloride
- Chromium
- Cobalt
- Copper
- Iodide
- Iron
- Magnesium
- Manganese
- Molybdenum
- Phosphorous
- Potassium
- Selenium
- Sodium
- Zinc
- Linolenic Acid (EPA/DHA)
- Linoleic acid
- Choline
- Isoleucine
- Leucine
- Lysine
- Methionine
- Phenylalanine
- Threonine
- Tryptophan
- Valine
- Histidine
What Americans Eat: Top 10 sources of calories in the U.S. diet

1. Grain-based desserts (cakes, cookies, donuts, pies, crisps, cobblers, and granola bars)
2. Yeast breads
3. Chicken and chicken-mixed dishes
4. Soda, energy drinks, and sports drinks
5. Pizza
6. Alcoholic beverages
7. Pasta and pasta dishes
8. Mexican mixed dishes
9. Beef and beef-mixed dishes
10. Dairy desserts

Source: Report of the 2010 Dietary Guidelines Advisory Committee

Carbohydrate-dense and high GI
- Loss of nutrient density
- Glucose-insulin
- Dysbiosis
- Fermentable Fiber deficient
- Pro-inflammatory
- Increased oxidative stress
## Optimal Lifestyle Metrics

<table>
<thead>
<tr>
<th>Habit</th>
<th>Definition and criteria</th>
<th>Do you comply with it?</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Smoking</strong></td>
<td>Absence of regular tobacco consumption</td>
<td>0</td>
</tr>
<tr>
<td><strong>Physical activity</strong></td>
<td>Amount of moderate and vigorous physical activity (more than 10 minutes/activity) that spans more than 150 minutes per week (the amount of time dedicated to vigorous physical activity accounts for double)</td>
<td>0</td>
</tr>
<tr>
<td><strong>Healthy diet</strong></td>
<td>Daily consumption of at least 5 pieces of fruit and vegetables</td>
<td>0</td>
</tr>
<tr>
<td><strong>Alcohol consumption</strong></td>
<td>Consumption of less than 2 alcoholic beverages a day for men and 1 in the case of women</td>
<td>0</td>
</tr>
</tbody>
</table>
Make an educated guess:

Of the 2 million people managed by HealthPartners, what **percentage** follows all four (4) conditions of the OLM?

*What do you think?*
### The “OLM” Universe

<table>
<thead>
<tr>
<th>Diet OLM Flag</th>
<th>Tobacco OLM Flag</th>
<th>Alcohol OLM Flag</th>
<th>Physical Activity OLM Flag</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1288 (0.26%)</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>2363 (0.47%)</td>
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<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>20667 (4.13%)</td>
</tr>
<tr>
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<td>0</td>
<td>1</td>
<td>1</td>
<td>39918 (7.98%)</td>
</tr>
<tr>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>2073 (0.41%)</td>
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<td>0</td>
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<td>5783 (1.16%)</td>
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<td>1</td>
<td>1</td>
<td>0</td>
<td>90656 (18.1%)</td>
</tr>
<tr>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>255344 (51.0%)</td>
</tr>
<tr>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>40 (0.01%)</td>
</tr>
<tr>
<td>1</td>
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<td>0</td>
<td>1</td>
<td>205 (0.04%)</td>
</tr>
<tr>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>661 (0.13%)</td>
</tr>
<tr>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>4071 (0.81%)</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>189 (0.04%)</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1386 (0.28%)</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>10674 (2.13%)</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>65026 (13.0%)</td>
</tr>
</tbody>
</table>

- <0.5% meet **zero** OLM component
- 5% meets **one** OLM component
- 27.5% meets **two** OLM components
- 54% meets **three** OLM components
- **13% meets four** OLM components

- 83.6% does **not** meet the diet OLM component (5 F&V daily)

N = 500,344
Data based on self-reported health assessment questions

Adherence to OLM and New Disease

Difference in 2-year incidence of new disease between people who adhere to OLM 0 or 1 and OLM 3 or 4 (%)

- High Blood Pressure: -15
- Cholesterol: -17
- Cancer: -24
- Back Pain: -43
- Heart Disease: -45
- Diabetes: -66

Dirt Poor: Have Fruits and Vegetables Become Less Nutritious?

Because of soil depletion, crops grown decades ago were much richer in vitamins and minerals than the varieties most of us get today.
Short-Term Effects
- Micronutrient intake almost non-existent
  - Ex. Scurvy

Long-Term Effects
- Micronutrient intake below RDA
  - Ex. Cancer and aging-associated diseases

Healthy
- Micronutrient intake adequate
  - Ex. Super-agers
We need a broad spectrum of micronutrients for optimal function

- Biochemical individualization
- Compressed morbidity
- Goal to assist optimal biologic function e.g. identify “relative deficiencies”.
- Our needs change over time... a very dynamic metabolic landscape e.g. triage theory and conditionally essential nutrients
- Moving beyond vitamins and minerals e.g. sufficient fermentable fiber and phytonutrients

Agarwal S¹, Reider C, Brooks JR, Fulgoni VL 3rd.

Figure 1: Percentage of the adult population (aged 19 years) with vitamin and mineral intakes below the EAR for individuals (data from NHANES 2001–2008). Usual intakes from foods were estimated by using the National Cancer Institute (NCI) method (Agarwal, 2014).


No RDA for choline, fiber and potassium. It is estimated that 93% Americans are deficient in choline, 95% fiber, and 97% Potassium!

estimated by using the National Cancer Institute method.

a, b, cBars with different letters are significantly different at \( p < 0.05 \) (Agarwal. 2014).
Center for Disease Control (testing blood and urine)

- **90 million** Americans deficient in vitamin D
- **30 million** Americans deficient in vitamin B6
- **18 million** Americans deficient in vitamin B12 (using MMA)
- **16 million** Americans deficient in vitamin C
- **8 million** Americans deficient in iron; *Latinos 12%; blacks 16%; children ages <5 years of age 7-10%*
- Many women ages 25-39 with “borderline” low iodine levels
Common Signs of Nutrient Deficiency

- Poor night vision - Vit A
- Chelitis – B2, B12, Fe, Zn
- Glossitis – B2, B3, Folic acid
- Spooning, spotted or ridged nails – Zn, Fe
- Easy bruising – Vit K
- Muscle weakness – Vit D
- Muscle cramps - Potassium, Magnesium, Riboflavin B2, B6-Pyridoxine
- RLS/Neuropathy – Fe, B12, Folate
- Loss of smell/taste - zinc
- Skin- Vitamin A (bumps on back of arms); Dermatitis- B2, B3, Biotin
- Hair loss- B2, B5, Biotin, D, zinc
Drug-Nutrient Interactions

- Alcohol - zinc, magnesium, phosphorous, B1, B2, B6 and Folate
- Antibiotics – Vitamin K
- Diuretics – potassium, magnesium, zinc, B6
- Metformin – B12
- Trimethoprim - Folate
Drug-Nutrient Interactions

- Proton pump inhibitors not only block the release of stomach acid but also something else called “intrinsic factor,” making it impossible to absorb vitamin B12.
- It’s well known that calcium is best absorbed in the presence of acid.
- Proton pump inhibitors are thought to inhibit active transport of magnesium in the intestine, leading to deficiencies and potentially serious health outcomes.
• Your absorption of folic acid is inhibited, disrupting the production of new cells, which helps your body grow and repair itself.
• The absorption of zinc is impaired, which is needed for many enzyme reactions in the body.
• The inhibition of dietary iron can contribute to anemia over a long period of time.
Seasonal Affirmations

• May you be safe
• May you be happy
• May you be at peace
# Special Dietary-Nutrient Considerations

<table>
<thead>
<tr>
<th>TYPE OF DIET</th>
<th>RESTRICTED FOODS</th>
<th>NUTRIENTS OF CONCERN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vegetarian (lacto-ovo)</td>
<td>Meat, poultry, fish/seafood</td>
<td>Iron, Zinc, Omega 3 fatty acids, Protein</td>
</tr>
<tr>
<td>Lacto-vegetarian</td>
<td>Meat, poultry, fish/seafood, eggs</td>
<td>Iron, Zinc, Omega 3 fatty acids, Protein</td>
</tr>
<tr>
<td>Ovo-vegetarian</td>
<td>Meat, poultry, fish/seafood, dairy products</td>
<td>Calcium, Iron, Zinc, Vitamin B12, Vitamin D, Omega 3 fatty acids, Protein</td>
</tr>
<tr>
<td>Vegan</td>
<td>All animal products including meat, poultry, fish/seafood, eggs, and dairy products</td>
<td>Calcium, Iron, Zinc, Vitamin B12, Vitamin D, Omega 3 fatty acids, Protein</td>
</tr>
<tr>
<td>Gluten-free</td>
<td>Wheat, rye, barley and their derivatives. Oats unless certified gluten-free.</td>
<td>B vitamins, Iron, Fiber</td>
</tr>
</tbody>
</table>
Labs for consideration

- 25 hydroxy-vitamin D
- B12 and Methylmalonic acid
- Folate
- Iron, TIBC, Ferritin
- Homocysteine
- MTHFR
- RBC magnesium and zinc
- RBC Omega 3/6 Index (want 8+ %)
- Urinary Organic Acids-Metabolic Profile
Vitamin D and the omega-3 fatty acids control serotonin synthesis and action, part 2: relevance for ADHD, bipolar disorder, schizophrenia, and impulsive behavior

Rhonda P. Patrick¹ and Bruce N. Ames¹
Nutrition and Metabolism Center, Children’s Hospital Oakland Research Institute, Oakland, California, USA

ABSTRACT Serotonin regulates a wide variety of brain functions and behaviors. Here, we synthesize previous findings that serotonin regulates executive function, sensory gating, and social behavior and that attention deficit hyperactivity disorder, bipolar disorder, schizophrenia, and impulsive behavior all share in common defects in these functions. It has remained unclear why supplementation with omega-3 fatty acids and vitamin D improve cognitive function and behavior in these brain disorders. Here, we propose mechanisms by which serotonin synthesis, release, and function in the brain are modulated by vitamin D and the 2 marine omega-3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Brain serotonin is synthesized from tryptophan by tryptophan hydroxylase 2, which is transcriptionally activated by vitamin D hormone. Inadequate levels of vitamin D (<70%)

“The rapid progress true science now makes, occasions my regretting sometimes that I was born too soon. It is impossible to imagine the height to which may be carried, in a thousand years, the power of man over matter. We may, perhaps, deprive large masses of their gravity, and give them absolute levity, for the sake of easy transport. Agriculture may diminish its labor and double its produce: all diseases may by sure means be prevented or cured, (not excepting even that of old age,) and our lives lengthened at pleasure, even beyond the antediluvian standard. Oh that moral science were in as fair a way of improvement, that men would cease to be wolves to one another, and that human beings would at length learn what they now improperly call humanity.”

– Benjamin Franklin, letter to Joseph Priestley, 1780
Figure 2. Micronutrient regulation of the serotonin pathway. A) Tryptophan is transported across the blood-brain barrier, and vitamin D sufficiency allows normal tryptophan metabolism by increasing expression of tryptophan hydroxylase 2 (TPH2) to produce serotonin (5HT). Sufficient levels of eicosapentaenoic acid (EPA) allow 5HT to be released by the presynaptic neuron. Sufficient levels of docosahexaenoic acid (DHA) allow for the binding of 5HT to the serotonin receptor (5HTR) in the postsynaptic neuron. This allows for normal serotonin neurotransmission and executive function, sensory gating, and prosocial behavior. B) When vitamin D status is insufficient, TPH2 is not expressed well and little serotonin is produced. Insufficient EPA status results in inhibition of 5HT release from the presynaptic neuron. Insufficient DHA status changes the serotonin receptor accessibility resulting in less 5HT binding to the serotonin receptor on the postsynaptic neuron. This leads to abnormal serotonin neurotransmission and poor executive function, poor sensory gating, and impulsive behavior.
The main evidence for the effectiveness of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) has been obtained in mood disorders, in particular in the treatment of depressive symptoms in unipolar and bipolar depression. There is some evidence to support the use of omega-3 fatty acids in the treatment of conditions characterized by a high level of impulsivity and aggression and borderline personality disorders. In patients with attention deficit hyperactivity disorder, small-to-modest effects of omega-3 HUFAs have been found.
Observational evidence demonstrates low vitamin D is related to poorer cognition; however, interventional studies are yet to show a clear benefit from vitamin D supplementation. From the evidence to date, there is likely a therapeutic age window relevant to the development of disease and therefore vitamin D therapy.
Well powered clinical studies have shown beneficial effects of supplemental zinc in depression and it important to pursue research using zinc as a potential therapeutic option for psychosis as well. Meta-analyses support the adjunctive use of zinc in major depression and a single study now supports zinc for psychotic symptoms.
Dietary zinc and iron intake and risk of depression: A meta-analysis.

Li Z¹, Li B¹, Song X¹, Zhang D².

Author information

Abstract

A total of 9 studies for dietary zinc intake and 3 studies for dietary iron intake were finally included in present meta-analysis. The pooled RRs with 95% CIs of depression for the highest versus lowest dietary zinc and iron intake were 0.67 (95% CI: 0.58-0.76) and 0.57 (95% CI: 0.34-0.95), respectively. In subgroup analysis by study design, the inverse association between dietary zinc intake and risk of depression remained significant in the cohort studies and cross-sectional studies.

...
The study included 198 healthy postmenopausal women at the average age of 56.26 ± 5.55 years. The lowest Mg levels were observed in women with depressive symptoms (14.28 ± 2.13 mg/l), and the highest in women without depressive symptoms (16.30 ± 3.51 mg/l), (p ≤ 0.05).
The current review suggests that EFAs may be effective in reducing prenatal stress and salivary cortisol and may reduce anxiety during premenstrual syndrome and during menopause in the absence of depression. Magnesium and vitamin B6 may be effective in combination in reducing premenstrual stress, and vitamin B6 alone may reduce anxiety effectively in older women. High-dose sustained-release vitamin C may reduce anxiety and mitigate increased blood pressure in response to stress.

**TYPES OF INTERVENTION(S):** Dietary supplementation with EFAs, B vitamins, vitamin C, magnesium and/or zinc.
CONCLUSIONS: Depression is associated with a lower concentration of zinc in peripheral blood. The pathophysiological relationships between zinc status and depression, and the potential benefits of zinc supplementation in depressed patients, warrant further investigation.
18 studies were included in the review. All reviewed studies recruited samples based upon an existing vulnerability to anxiety: mildly anxious, premenstrual syndrome (PMS), postpartum status, and hypertension. Four/eight studies in anxious samples, four/seven studies in PMS samples, and one/two studies in hypertensive samples reported positive effects of Mg on subjective anxiety outcomes.
Evidence from human studies clearly shows a significant proportion of people suffer from deficiencies or insufficiencies in one or more of B-vitamins. Supplementing, in the absence of an optimal diet at doses greatly in excess of current recommendations would be a rational approach for preserving brain health.
MTFHR SNP

- Folate and MTHFR: Thymine synthesis and methylation
- 40% population heterozygous which results in a 40% reduction in functional MTHFR
- 10% homozygous with 80-90% reduction in the functional efficiency of MTHFR
- Treatment resistant depression
Nutritional Considerations - Supplementation

• Choline: 500 mg/day (4-5 egg yolk equivalents; 4 oz liver/week, cruciferous veggies, nuts). Strongly consider supplementation.
• Folate: 2-3 servings, liver, leafy greens, legumes; Supplementation methyl-folate 1200 mcg/day
• Glycine: non-hydrolyzed whey protein, bone broth,
• Creatine (spares methyl-folate): 3-5 gms/day
Effectiveness of add-on L-methylfolate therapy in a complex psychiatric illness with MTHFR C677 T genetic polymorphism.

Jha S¹, Kumar P², Kumar R², Das A³.

Author information

Abstract
The 5,10-methylenetetrahydrofolate reductase (MTHFR) gene plays a central role in folate metabolism. Many studies have demonstrated an association between MTHFR C677 T variant

Adjunctive L-methylfolate 15 mg/d may be an early option in patients who fail to adequately respond to antidepressant monotherapy, with preliminary evidence demonstrating sustained remission and sustained recovery.

such complex psychiatric phenomenon and comorbid diagnosis with genetic polymorphism of MTHFR C677 T mutation.

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Supplement considerations

- Magnesium threonate, citrate, glycinate: 300-400 mg at bedtime
- Zinc: 15-30 mg/day
- EPA-DHA: 2,000-3,000 mg/day
- Vitamin D to achieve levels 40-60 ng/dl (sun is our friend)
- B6 (pyridoxal-5-phosphate): 25-50 mg/day
- Methylated cobalamin (1,000 mcg) and folate 800-1200 mcg (higher doses in resistant depression with MTHFR)
- Choline 500 mg/day (MTHFR)
- Probiotics: 20 + billion CFUs, broad-spectrum e.g. lactobacillus, bifidobacter, saccharomyces
Summary

- Micronutrient deficiencies will be present in many individuals with disrupted brain function, mind and mood.
- 3-day food diary review
- Personalized testing for micronutrient deficiencies
- Nutritional interventions to include nutrient-dense whole foods; elimination trial; incremental prebiotic rich foods
- Personalized supplementation
- Integrative lifestyle management
Additional References


A Systematic Review and Meta-Analysis of The Effect of Low Vitamin D on Cognition.
Goodwill AM1, Szoeke C1,2.

*Eur J Nutr.* 2017 Sep 4. doi: 10.1007/s00394-017-1514-z. [Epub ahead of print]
Micronutrient intake adequacy and depression risk in the SUN cohort study.
Sánchez-Villegas A1,2, Pérez-Cornago A3, Zazpe I4,5, Santiago S5, Lahortiga F6, Martínez-González MA4,7,8.

Adjunctive Treatment of Psychotic Disorders with Micronutrients.

Vitamin D Deficiency Associated With Cognitive Functioning in Psychotic Disorders.
Nerhus M1,2, Berg AO2,3, Simonsen C2,3, Haram M2, Haatveit B2, Dahl SR4, Gurholt TP2, Bjella TD2,
Ueland T2, Andreassen OA2, Melle I2.
Stevens AJ1, Rucklidge JJ2, Kennedy MA1.
Epigenetics, nutrition and mental health. Is there a relationship?

Dietary zinc and iron intake and risk of depression: A meta-analysis.
Li Z1, Li B1, Song X1, Zhang D2.


Analysis of Relations Between the Level of Mg, Zn, Ca, Cu, and Fe and Depressiveness in Postmenopausal Women.
Szkup M1, Jurczak A2
USING WHOLE FOODS AS MEDICINE
A Primer on Treating Chronic Inflammation with Food

Presented by Tanmeet Sethi, MD
January 17, 2018, 12 PM ET

BONUS WEBINAR
Join us on January 31, 2018 for “Beyond Burnout” with James S. Gordon, MD, Founder and Executive Director of the Center for Mind-Body Medicine
This webinar has been recorded. The presentation and the slides will be available within 24 hours at CMBM.org/webinar.

Also available online:

Nourish & Nurture  
Presented by Deb Phillips

Leaky Gut  
Presented by Dr Sheila Dean
Mind, Mood & Food
Optimal Nutrition for Body & Brain

April 15-20, 2018
Esalen Institute
Big Sur, CA

James S. Gordon, MD
Kathie Madonna Swift, MS, RDN, LDN
Amy Shinal, MSW, LCSW

Mark Hyman, MD
Catherine McConkie, Executive Chef
Cindy Geyer, MD

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