



## Food & Mood

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## Disclosures

• Dr. Deanna Minich is the Chief Science Officer of Symphony Natural Health (independent contractor), speaker for Genova Diagnostics and Metagenics, Inc.

- She is a health educator and author of several books on wellness topics.
- She is CEO of her company, Food & Spirit, LLC.



## Disclaimer

This presentation contains educational material only and is not intended to take the place of advice from your own physician(s) or to be a means of diagnosing or treating an illness.



## Objectives:

- To understand scientific mechanisms for why mood disorders exist
- To learn at least three eating strategies to help with mental health
- To become familiar with **clinical tools** to help patients with their foods and moods

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• To learn about **key nutrients** and a list of foods that contain these nutrients to help with moods



## Select "root causes" related to mental health

- Inflammation ("brain on fire")
- Gut microbiome
- Nutrient imbalances



## Brain, Inflammation, and Cortisol

The triangle of mood dysregulation



Functional Medicine Deep Dive

## Inflammation and Mood States: **"Brain on Fire"**



Figure from: Jiang S, Postovit L, Cattaneo A, Binder EB, Aitchison KJ. Epigenetic Modifications in Stress Response Genes Associated With Childhood Trauma. *Front Psychiatry*. 2019;10:808. Published 2019 Nov 8. doi:10.3389/fpsyt.2019.00808; No changes have been made. Copyright © 2019 Jiang, Postovit, Cattaneo, Binder and Aitchison. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0).



#### **Functional Medicine Deep Dive**

## Less healthy food & lifestyle choices during stress

- High-calorie food with unhealthy sugars and fats are preferred foods for stressed individuals, especially women.
- For men, stress-coping behaviors include smoking and alcohol intake more than eating.
- High cortisol reactors tend to consume more than low cortisol reactors.

Ans AH, Anjum I, Satija V, et al. Neurohormonal Regulation of Appetite and its Relationship with Stress: A Mini Literature Review. *Cureus*. 2018;10(7):e3032. Published 2018 Jul 23. doi:10.7759/cureus.3032; Newman E, O'Connor DB, Conner M. Daily hassles and eating behaviour: The role of cortisol reactivity status. Psychoneuroendocrinology. 2007 Feb;32(2):125-32. Epub 2007 Jan 2.

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### Desire for food changes with stress levels



Hyldelund NB, Frederiksen C, Byrne DV, Andersen BV. Is Stress Taking the Pleasure Out of Food?-A Characterization of the Food Pleasure Profiles, Appetite, and Eating Behaviors of People with Chronic Stress. Foods. 2022 Jul 4;11(13):1980. doi: 10.3390/foods11131980. PMID: 35804795; PMCID: PMC9265269. CC-BY 4.0.



#### **Functional Medicine Deep Dive**

## Food product preference changes with different levels of stress





Hyldelund NB, Frederiksen C, Byrne DV, Andersen BV. Is Stress Taking the Pleasure Out of Food?-A Characterization of the Food Pleasure Profiles, Appetite, and Eating Behaviors of People with Chronic Stress. Foods. 2022 Jul 4;11(13):1980. doi: 10.3390/foods11131980. PMID: 35804795; PMCID: PMC9265269. CC-BY 4.0.



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# Emotional eating leads to eating high-energy, low-nutrient foods

- Emotions as immediate; mood as prolonged.
- Emotional eating can present as eating high-calorie, intensely-tasting foods rich in sugar and fats in response to emotion (positive & negative).
  - Sweet-tasting foods: cake, ice cream, soda
  - Salty foods: chips, breads, pastas, snack foods

 Fuente González CE, et al. Relationship between Emotional Eating, Consumption of Hyperpalatable Energy-Dense Foods, and Indicators of Nutritional Status: A Systematic Review. J Obes. 2022 May 18;2022:4243868. doi: 10.1155/2022/4243868. PMID: 35634585; PMCID: PMC9132695.

Nguyen-Michel ST, et al. Dietary correlates of emotional eating in adolescence. Appetite. 2007 Sep;49(2):494-9. doi: 10.1016/j.appet.2007.03.005.
Epub 2007 Mar 19. PMID: 17466408; PMCID: PMC2020451.

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## **Emotions affect taste**

- N=550 hockey game attendees
- 4 wins, 3 losses, 1 tie
- Positive emotions were associated with more sweet and less sour taste intensity.
- Negative emotions were associated with more sour and less sweet taste.

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Noel C, Dando R. The effect of emotional state on taste perception. Appetite. 2015 Dec;95:89-95. doi: 10.1016/j.appet.2015.06.003. Epub 2015 Jun 27. PMID: 26122754.



## Taste can be affected by mental or physical stress

- Bitter, sour, and sweet tastes were tested after either mental tasks on a computer or physical tasks on an ergometer for 10-40 min.
- After mental tasks:
  - Duration of bitter, sour, and sweet taste was shortened compared with control.

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- The amount of each of these flavors was also decreased.
- After physical stress:
  - Sourness shortened

Nakagawa M, Mizuma K, Inui T. Changes in taste perception following mental or physical stress. Chem Senses. 1996 Apr;21(2):195-200. doi: 10.1093/chemse/21.2.195. PMID: 8670698.



### Psychoneuroendocrine Interface with Inflammation

Body and mind are one.



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Gassen J, Prokosch ML, Eimerbrink MJ, et al. Inflammation Predicts Decision-Making Characterized by Impulsivity, Present Focus, and an Inability to Delay Gratification. *Sci Rep.* 2019;9(1):4928. Published 2019 Mar 20. doi:10.1038/s41598-019-41437-1; This article is licensed under a Creative Commons Attribution 4.0 International License



#### **Functional Medicine Deep Dive**

Physiology & Psychology Related to Chronic Stress States

#### PHYSIOLOGY

- <sup>†</sup>Stress hormones (CRH, ACTH, cortisol)
- ↑Glucose and insulin
- ↑ **Free fatty acids**
- Insulin resistance
- <sup>†</sup>Heart rate
- **†Blood pressure**
- **†**Heart rhythm

#### PSYCHOLOGY

- "Type A"
- Difficult to relax
- Reactive
- Anxious, agitated, angry
- Nervous energy
- Impatient/Irritable



### HPATG DOWNREGULATED – Stress non-responsive

### PHYSIOLOGY

- ↑CRH hyper-secretion leading to down-regulation of pituitary CRH receptors
- Increased negative HPA axis feedback
- Morphological changes (i.e. adrenal atrophy)
- Reduced synthesis or depletion of stimulating factors and hormones (i.e. CRH, ACTH, cortisol)

#### PSYCHOLOGY

- Lack of interest (anhedonia)
- Fatigue (debilitating)
- Low self esteem and self-blame or guilt
- Difficulty concentrating
- Thoughts of death or suicidal behavior
- Sleepiness
- Poor appetite
- Weight loss, catabolism
- Lack of interest in sex



#### **Functional Medicine Deep Dive**



• Nakagawa M, Mizuma K, Inui T. Changes in taste perception following mental or physical stress. Chem Senses. 1996 Apr;21(2):195-200. doi: 10.1093/chemse/21.2.195. PMID: 8670698.

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• Newman E, O'Connor DB, Conner M. Daily hassles and eating behaviour: the role of cortisol reactivity status. Psychoneuroendocrinology. 2007 Feb;32(2):125-32. Epub 2007 Jan 2.



## Eating can initiate inflammation

The physiology and psychology of one meal







#### **Functional Medicine Deep Dive**

#### DIGESTION

#### FRUITION



Riccio P, Rossano R. Undigested Food and Gut Microbiota May Cooperate in the Pathogenesis of Neuroinflammatory Diseases: A Matter of Barriers and a Proposal on the Origin of Organ Specificity. *Nutrients*. 2019;11(11):2714. Published 2019 Nov 9. doi:10.3390/nu11112714. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<u>http://creativecommons.org/licenses/by/4.0/</u>). Full-article link: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6893834/



#### **Functional Medicine Deep Dive**

One meal can result in postprandial inflammation

**Image Credit**: Meessen ECE, Warmbrunn MV, Nieuwdorp M, Soeters MR. Human Postprandial Nutrient Metabolism and Low-Grade Inflammation: A Narrative Review. *Nutrients*. 2019 Dec 7;11(12):3000. doi: 10.3390/nu11123000. PMID: 31817857; PMCID: PMC6950246. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution license CC BY 4.0

SP	- LF3 - TLR4 - Nf-κB - ROS - Complemer - Interleukin 1 - TNF-α - sCD14

1	breakfast 0730	lunch 1300	dinner 1900	24
	5	Time of	day	
Postpra	andial me	diated i	nflammato	ory effects
Macron	nutrients		Inflam	matory effect
- Gluco:	se			1
- Lipids	154			1
- N-3 P	JFAS			↓ it
- Amino	acids			ΨI
Entero	kines/hor	mones		
- Insulin				1Ť
- Bile ad	ids			Ĩ
- FGF19	)			Ĩ
- GLP-1				Ĩ
Ghreli	ר			i
- Leptin				Ť
Inflamr	natory me	diators		
- LPS				1
- TLR4				1
- Nf-κB				Ť
- ROS				Ť
- Comp	lement C3			Ţ
- Interle	ukin 1β & (	6		Ť
- TNF-o				Ţ
SCD14	+			L.

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## One meal can create hours of inflammation

A single fast food-style meal can increase serum IL-6 by 100%, peaking about 6 hours after a meal.

Sample meals included in the review:

- White bread, butter, cheese, milkshake
- Eggs, muffin, butter, sugary drink
- Sugar, heavy cream, chocolate syrup, powdered milk
- Bagel, cream cheese, potato, milk, apple juice

Emerson SR, Kurti SP, Harms CA, et al. Magnitude and Timing of the Postprandial Inflammatory Response to a High-Fat Meal in Healthy Adults: A Systematic Review. *Adv Nutr.* 2017 Mar 15;8(2):213-225. doi: 10.3945/an.116.014431. Print 2017 Mar.



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## The format of food is essential to consider with inflammation.



**Image Credit:** Dreher ML. Whole Fruits and Fruit Fiber Emerging Health Effects. *Nutrients*. 2018;10(12):1833. Published 2018 Nov 28. doi:10.3390/nu10121833. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution license (<u>http://creativecommons.org/licenses/by/4.0/</u>). No changes made.

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## Inflammatory foods

- 1. Sugar
- 2. Cooking oils (corn, cottonseed, safflower, soy, sunflower)

- 3. Trans fats
- 4. White flour/refined grains
- 5. Excessive alcohol
- 6. Browned, fried foods



# Reducing advanced glycation endproducts (AGEs) to reduce inflammation

- Endogenous & dietary compounds resulting from nonenzymatic reactions between the aldehydes of reducing sugars with proteins, lipids, or nucleic acids
- Formation/accumulation of AGEs related to accelerated aging and diabetes perhaps through gut inflammation and permeability
- Marker of oxidative stress and inflammation
- Binding to rAGE and upregulating cellular inflammation
- Reduce high heat cooking like grilling or broiling
- Use of phytonutrients to buffer effects (e.g., resveratrol, spices)

Del Turco S, Basta G. An update on advanced glycation endproducts and atherosclerosis. *Biofactors.* 2012 Apr 10. doi: 10.1002/biof.1018. [Epub ahead of print]; Snelson M, Lucut E, Coughlan MT. The Role of AGE-RAGE Signalling as a Modulator of Gut Permeability in Diabetes. *Int J Mol Sci.* 2022 Feb 3;23(3):1766. doi: 10.3390/ijms23031766. PMID: 35163688; PMCID: PMC8836043.

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### Herbs and spices help to reduce glycation with cooking: Apply to foods before heat

- Spice more effective than herb extracts; inhibition of glycation was associated with phenolic acid content
- Most potent were extracts of cloves, ground Jamaican allspice, and cinnamon, followed by sage, marjoram, tarragon, and rosemary.
- Consider quality, expiration dates, storage and rancidity

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Dearlove RP, Greenspan P, Hartle DK, Swanson RB, Hargrove JL. Inhibition of protein glycation by extracts of culinary herbs and spices. *J Med Food*. 2008 Jun;11(2):275-81. doi: 10.1089/jmf.2007.536.

# Address inflammation with general principles of an anti-inflammatory diet

- Less high-heat cooking and frying
- Balanced omega-3/omega-6 index
- Higher dietary antioxidants
- Low to moderate glycemic index/load
- Reduce or avoid ultraprocessed foods
- Eat the rainbow of whole plant foods
- Avoid allergenic foods

Calle MC, Andersen CJ. Assessment of Dietary Patterns Represents a Potential, Yet Variable, Measure of Inflammatory Status: A Review and Update, Disease Markers, vol. 2019, Article ID 3102870, 13 pages, 2019. https://doi.org/10.1155/2019/3102870.



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## Consider total amount and balance of omega-3 fatty acids

- For many people eating a processed food diet, dietary omega-6 fats exceeds that of omega-3 fats.
- The current n-6/n-3 ratio is 20-50/1.
- Higher ratios of n-6/n-3 in modern diets translate into greater allergic, inflammatory, proliferative, and cardiovascular symptoms.
- Recommendation would be to keep n-6/n-3 ratio at 4-5/1.

Mariamenatu AH, Abdu EM. Overconsumption of Omega-6 Polyunsaturated Fatty Acids (PUFAs) versus Deficiency of Omega-3 PUFAs in Modern-Day Diets: The Disturbing Factor for Their "Balanced Antagonistic Metabolic Functions" in the Human Body. *J Lipids*. 2021 Mar 17;2021:8848161. doi: 10.1155/2021/8848161. PMID: 33815845; PMCID: PMC7990530.



## The Omega-3 Index: Aim for 8% or higher

- 'ω-3 index' is the % eicosapentaenoic acid (EPA, 20:5 n-3) and docosahexaenoic acid (DHA, 22:6 n-3) in red blood cells relative to other fatty acids
- Used as an index of coronary heart disease mortality.
- Average omega-3 Index in the U.S. is about 4%
- Ideal is 8% for cardiovascular health
- Risk for fatal CHD could be reduced by ~ 30% with shifting from 4% to 8%.
- **Personal clinical experience** has indicated that even those who are relatively healthy, and supplement with omega-3s may have lower levels (5-6%).

Harris WS, Del Gobbo L, Tintle NL. The Omega-3 Index and relative risk for coronary heart disease mortality: Estimation from 10 cohort studies. *Atherosclerosis*. 2017 Jul;262:51-54. doi: 10.1016/j.atherosclerosis.2017.05.007. Epub 2017 May 6.

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### Barriers in the gut and brain: A connection to mental health



Image Credit: Riccio P, Rossano R. Undigested Food and Gut Microbiota May Cooperate in the Pathogenesis of Neuroinflammatory Diseases: A Matter of Barriers and a Proposal on the Origin of Organ Specificity. *Nutrients*. 2019;11(11):2714. Published 2019 Nov 9. doi:10.3390/nu11112714. Licensee MDPI. Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (http://creativecommons.org/licenses/bv/4.0/). Full-article link: https://www.ncbi.nlm.nih.gov/pmc/articles/PM C6893834/



#### Functional Medicine Deep Dive

## Pathways to depression through the gut



2019;13:1196. Published 2019 Nov 5. doi:10.3389/fnins.2019.01196. Copyright © 2019 Westfall and Pasinetti. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0).



#### **Functional Medicine Deep Dive**

## Anxiety and the GI tract

- Anxiety may be caused by a disturbance in the gut microbiome or even by gut inflammation.
- Mood disorders like anxiety can lead to changes in the gut microbiome and result in dysfunction



**Image Credit:** Kelly JR, Kennedy PJ, Cryan JF, Dinan TG, Clarke G, Hyland NP. Breaking down the barriers: The gut microbiome, intestinal permeability and stress-related psychiatric disorders. *Front Cell Neurosci*. 2015;9:392. Published 2015 Oct 14. doi:10.3389/fncel.2015.00392. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0).

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## Multiple potential "root causes" in Irritable Bowel Syndrome (IBS)



**Image Credit:** Brown, B.I. Does Irritable Bowel Syndrome Exist? Identifiable and Treatable Causes of Associated Symptoms Suggest It May Not. *Gastrointest. Disord.* **2019**, *1*, 314-340. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY 4.0).

#### **Functional Medicine Deep Dive**

### Anxiety and/or depression and active gut dysfunction



Image Credit: Byrne G, Rosenfeld G, Leung Y, et al. Prevalence of Anxiety and Depression in Patients with Inflammatory Bowel Disease. Can J Gastroenterol Hepatol. 2017;2017:6496727. doi:10.1155/2017/6496727; CC-BY 4.0.



#### Functional Medicine Deep Dive

## Metabolic endotoxemia: The inflammatory potential of high-fat meals

Metabolically-triggered inflammation, metabolic endotoxemia effects (1)

An acute high-fat meal (42 g vs. 1 g) can impair vascular function (SBP, DBP, total peripheral resistance) in healthy, normotensive people (2)

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Polyphenol-rich oils may help to reduce inflammatory effects (3)

Arya F, Egger S, Colquhoun D, Sullivan D, Pal S, Egger G. Differences in postprandial inflammatory responses to a 'modern' v. traditional meat meal: a preliminary study. *Br J Nutr.* 2010 Sep;104(5):724-8. doi: 10.1017/S0007114510001042. Epub 2010 Apr 9.
Jakulj F, Zernicke K, Bacon SL, et al. A high-fat meal increases cardiovascular reactivity to psychological stress in healthy young adults. *J Nutr.* 2007 Apr;137(4):935-9. doi: 10.1093/jn/137.4.935

3. Widmer RJ, Freund MA, Flammer AJ, et al. Beneficial effects of polyphenol-rich olive oil in patients with early atherosclerosis. *Eur J Nutr.* 2013 Apr;52(3):1223-31. doi: 10.1007/s00394-012-0433-2. Epub 2012 Aug 8.


# Fiber restores the gut

Beukema M, Faas MM, de Vos P. The effects of different dietary fiber pectin structures on the gastrointestinal immune barrier: impact via gut microbiota and direct effects on immune cells. *Exp M Med.* 2020 Sep;52(9):1364-1376. doi: 10.1038/s1227 020-0449-2. Epub 2020 Sep 10. PMID: 32908213; PMCID: PMC8080816. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/). No changes made.





#### **Functional Medicine Deep Dive**

### The food-gutmood-brain axis:

The foods we take in become signaling agents for the brain

"The gut-brain axis [GBA] is a bidirectional information regulatory pathway composed of the central nervous system (CNS), neuroendocrine system, neuroimmune system, autonomic nervous system and enteric nervous system."

**Quote reference:** Liu, S.; Cheng, L.; Liu, Y.; Zhan, S.; Wu, Z.; Zhang, X. Relationship between Dietary Polyphenols and Gut Microbiota: New Clues to Improve Cognitive Disorders, Mood Disorders and Circadian Rhythms. *Foods* **2023**, *12*, 1309. https://doi.org/10.3390/foods12061309



#### **Functional Medicine Deep Dive**

### Short-chain fatty acids (SCFAs) for the gut-brain axis

- Stimulates the production of mucin
- Helps to promote manufacture of antibacterial peptides and tight junction proteins
- Provides energy source for colonocytes
- Signals from gut through G-protein coupled receptors to affect gut and immune function
- Reduce the production of cortisol
- Enhances the production of BDNF

1. van der Merwe, M. (2021). Gut microbiome changes induced by a diet rich in fruits and vegetables. *International Journal of Food Sciences and Nutrition*, 72(5), 665–669. https://doi.org/10.1080/09637486.2020.1852537. 2. Dalile, B., Vervliet, B., et al. (2020). Colon-delivered short-chain fatty acids attenuate the cortisol response to psychosocial stress in healthy men: A randomized, placebo-controlled trial. *Neuropsychopharmacology: Official Publication of the American College of Neuropsychopharmacology*, 45(13), 2257–2266. https://doi.org/10.1038/s41386-020-0732-x. 3. van de Wouw, M., Boehme, et al. (2018). Short-chain fatty acids: Microbial metabolites that alleviate stress-induced brain-gut axis alterations. *The Journal of Physiology*, 596(20), 4923–4944. https://doi.org/10.1113/JP276431. 4. Suda, K., & Matsuda, K. (2022). How microbes affect depression: Underlying mechanisms via the gut-brain axis and the modulating role of probiotics. International Journal of Molecular Sciences, 23(3), 1172. https://doi.org/10.3390/ijms23031172

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### Depressive symptoms reduce with increasing dietary fiber



**Image Credit** : Dreher ML. Whole Fruits and Fruit Fiber Emerging Health Effects. *Nutrients*. 2018;10(12):1833. Published 2018 Nov 28. doi:10.3390/nu10121833. <u>http://creativecommons.org/licenses/by/4.0/</u>. No changes made.



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# THE THREE NUTRITIONAL PILLARS OF **GUT HEALTH**

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#### Functional Medicine Deep Dive

# Improving Gut Health Through the Functional Medicine 5Rs

### THE 5R PROGRAM FOR GUT HEALTH\*





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# Potential Benefits of Probiotics



Image Credit: Swain MR, Anandharaj M, Ray RC, Parveen Rani R. Fermented fruits and vegetables of Asia: A potential source of probiotics. *Biotechnol Res Int.* 2014;2014:250424. doi:10.1155/2014/250424. No changes made. CC BY 3.0.



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### **Psychobiotics**

"...probiotics that can impact neuropsychiatric conditions, may influence depressive and anxiety phenotypes."

"...patients diagnosed with both IBS and major depression, a twice daily dose of *Bacillus coagulans* MTCC 5856 was administered, and treated patients demonstrated reduced depressive phenotypes on multiple scales (Majeed et al. 2018)."

Westfall S, Pasinetti GM. The Gut Microbiota Links Dietary Polyphenols With Management of Psychiatric Mood Disorders. Front Neurosci. 2019 Nov 5;13:1196. doi: 10.3389/fnins.2019.01196. PMID: 31749681; PMCID: PMC6848798.



#### **Functional Medicine Deep Dive**

### Potential Root Cause: Nutrient imbalance

- Unhealthy diets (brown, yellow, white)
- Lack of omega-3 fatty acids
- Lack of proper macronutrient quantity and quality for energy and neurotransmitter balance
- Lack of vitamins (vitamin C, D, B6, B9, B12, etc.)
- Lack of minerals (Mg, Zn, Fe, Se)
- Lack of phytonutrients for harmonizing cellular activities, hormone/neurotransmitter agonists

LaChance, L. R., & Ramsey, D. (2018). Antidepressant foods: An evidence-based nutrient profiling system for depression. World Journal of Psychiatry, 8(3), 97–104. https://doi.org/10.5498/wjp.v8.i3.97

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# Poor nutritional quality diets and increased risk of depression

- More studies indicating a relationship between food and mood
- Greater risk for depression with:
  - Fast food intake<sup>1</sup>
  - Ultraprocessed foods<sup>2</sup>
  - Higher added sugars & lower quality of carbohydrate<sup>3</sup>

1. Sánchez-Villegas, A., et al. (2012). Fast-food and commercial baked goods consumption and the risk of depression. Public Health Nutrition, 15(3), 424–432. https://doi.org/10.1017/S1368980011001856 PMID: 21835082; 2. Gómez-Donoso, C., et al. (2020). Ultra-processed food consumption and the incidence of depression in a Mediterranean cohort: The SUN Project. European Journal of Nutrition, 59(3), 1093–1103. https://doi.org/10.1007/s00394-019-01970-1 PMID: 31055621; 3. Sanchez-Villegas, A., et al. (2018). Added sugars and sugar-sweetened beverage consumption, dietary carbohydrate index and depression risk in the Seguimiento Universidad de Navarra (SUN) Project. The British Journal of Nutrition, 119(2), 211–221. https://doi.org/10.1017/S0007114517003361 PMID: 29268815





**Image Credit:** Dernini S, Berry EM. Mediterranean diet: From a healthy diet to a sustainable dietary pattern. *Front Nutr*. 2015 May 7;2:15. doi: 10.3389/fnut.2015.00015. eCollection 2015. No changes made. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution license CC BY 4.0.



#### Functional Medicine Deep Dive

# The Mediterranean Diet and Depression

- *N*=10,094 university graduates
- The greater the adherence to the MedDiet, the less incidence of depression.
- Inverse dose-response relationships for these dietary variables:
  - Fruit and nuts
  - $\circ$  Legumes
  - Monounsaturated to saturated fat ratio

Sánchez-Villegas A, Delgado-Rodríguez M, Alonso A, Schlatter J, Lahortiga F, Serra Majem L, Martínez-González MA. Association of the Mediterranean dietary pattern with the incidence of depression: the Seguimiento Universidad de Navarra/University of Navarra follow-up (SUN) cohort. Arch Gen Psychiatry. 2009 Oct;66(10):1090-8. doi: 10.1001/archgenpsychiatry.2009.129. PMID: 19805699.

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### Nuts are nutrient dense foods for mood



**Image Credit:** Ros, E.; Singh, A.; O'Keefe, J.H. Nuts: Natural Pleiotropic Nutraceuticals. *Nutrients* 2021, *13*, 3269. <u>https://doi.org/10.3390/nu13093269</u>. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution license CC-BY 4.0.



#### Functional Medicine Deep Dive

### **Gut health:** Elimination diet

### What is an "elimination diet"?

As used in functional medicine, a defined time period of removing typical dietary offenders: corn, soy, wheat, gluten, alcohol, sugar, eggs, shellfish, overly cooked foods, peanuts, dairy, processed oils, coffee; followed by a reintroduction period to observe symptoms.

- Useful in food allergy, atopy, eczema
- Migraine, headaches, neurological & behavioral issues (e.g., ADHD)
- Gut disorders and dysfunction (e.g., IBS, leaky gut)
- Fibromyalgia

Bunner, A. E., Agarwal, U., Gonzales, J. F., Valente, F., & Barnard, N. D. (2014). Nutrition intervention for migraine: A randomized crossover trial. The journal of headache and pain, 15(1), 69. <u>https://doi.org/10.1186/1129-2377-15-69</u>; Gonsalves, N., Yang, G. Y., Doerfler, B., Ritz, S., Ditto, A. M., & Hirano, I. (2012). Elimination diet effectively treats eosinophilic esophagitis in adults; food reintroduction identifies causative factors. Gastroenterology, 142(7), 1451–e15. <u>https://doi.org/10.1053/j.gastro.2012.03.001</u>; Lamb, J. J., Konda, V. R., Quig, D. W., Desai, A., Minich, D. M., Bouillon, L., Chang, J. L., et al. (2011). A program consisting of a phytonutrient-rich medical food and an elimination diet ameliorated fibromyalgia symptoms and promoted toxic-element detoxification in a pilot trial. *Alternative Therapies in Health and Medicine*, 17(2), 36–44.



#### **Functional Medicine Deep Dive**

### Case Study Dietary Intervention for Mental Health

Challenging Case in Clinical Practice: Qualitative and Quantitative Improvements in Overall Health and Mood Following a Three-Week Elimination Diet and a Four-Week Detox Food Plan

Claudia de la Espriella, MS, and Deanna Minich, PhD

Claudia de la Espriella and Deanna Minich. Alternative and Complementary Therapies. Oct 2018.ahead of printhttp://doi.org/10.1089/act.2018.29181.ces Published in Volume: 24 Issue 5: October 11, 2018; Online Ahead of Print: September 4, 2018



#### **Functional Medicine Deep Dive**

# **Chief Complaints**

- 35-year-old female presenting with hormonal imbalances, fatigue, brain fog, anxiety, bloating, gas, dizziness, eczema, and allergies, including sinus complaints
- She works at a busy café/restaurant and is also a kayak instructor part of the year
- High stress lifestyle due to work demands and not having healthy food available

Claudia de la Espriella and Deanna Minich. Alternative and Complementary Therapies. Oct 2018.ahead of printhttp://doi.org/10.1089/act.2018.29181.ces Published in Volume: 24 Issue 5: October 11, 2018; Online Ahead of Print: September 4, 2018



# Diet and Lifestyle History

- Activity level is high as she prefers hiking, biking, swimming, and yoga
- BL dietary analysis revealed high intake of alcoholic beverages, caffeine, high glycemic foods such as pizza and pasta, low water consumption, and few servings of fruits and vegetables
  - Daily caloric consumption averaged 1457 calories, with most from carbohydrates, mainly rice, pasta, and pizza.

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- Daily water consumption averaged 1233 g
- Fiber was low at 17.3 g on average
- Low intake of vitamin B1, folate, vitamin E, calcium, copper, iron, magnesium, and potassium

Claudia de la Espriella and Deanna Minich. Alternative and Complementary Therapies. Oct 2018.ahead of printhttp://doi.org/10.1089/act.2018.29181.ces Published in Volume: 24 Issue 5: October 11, 2018; Online Ahead of Print: September 4, 2018



### **Dietary Intervention**

- Elimination Diet, followed by Detox Food Plan
- By the end of the first week, she was experiencing improvements, but it took time to get accustomed to this new diet
- Her challenges:
  - The first week was difficult for her as she had the stress of dealing with smoke from a local wildfire.
  - Her busy schedule, sometimes 10- to 11-hour shifts on foot, made it challenging to prepare meals.
  - Socializing with alcohol required an adjustment

Claudia de la Espriella and Deanna Minich. Alternative and Complementary Therapies. Oct 2018.ahead of printhttp://doi.org/10.1089/act.2018.29181.ces Published in Volume: 24 Issue 5: October 11, 2018; Online Ahead of Print: September 4, 2018

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### Her progression through the weeks: Elimination Diet

FIGURE 2: Medical Symptoms Questionnaire (MSQ) for the IFM Elimination Diet phase

	Baseline	Week 1	Week 2	Week 3
Head	1	4	2	1
Eyes	5	8	5	2
Ears	1	1	0	0
Nose	11	6	1	3
Mouth/throat	0	0	0	0
Skin	3	3	2	1
Heart	0	0	0	0
Lungs	1	1	2	0
Digestive tract	5	5	4	3
Joints/muscle	3	3	0	1
Weight	6	2	2	2
Energy/activity	4	5	4	1
Mind	9	6	3	1
Emotions	4	3	1	0
Other	1	1	0	1
TOTAL	54	48	26	16
% Improvement		11.1%	51.85%	70.37%

Table modified from: Claudia de la Espriella and Deanna Minich. Alternative and Complementary Therapies. Oct 2018.ahead of printhttp://doi.org/10.1089/act.2018.29181.ces Published in Volume: 24 Issue 5: October 11, 2018; Online Ahead of Print: September 4, 2018

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### Her progression through the weeks: Detox Food Plan

#### FIGURE 3: MSQ scores for the Detox Food Plan phase

	Week 6	Week 7	Week 8	Week 9
Head	0	0	1	1
Eyes	1	1	1	1
Ears	1	1	1	1
Nose	1	3	2	2
Mouth/throat	1	0	0	0
Skin	0	0	1	1
Heart	0	0	0	0
Lungs	0	0	0	0
Digestive tract	1	1	0	0
Joints/muscle	1	0	0	0
Weight	0	0	0	0
Energy/activity	1	0	0	0
Mind	1	0	0	0
Emotions	0	0	0	0
Other	0	0	0	
TOTAL	8	6	6	6
% Improvement	85.1%	88.8%	88.8%	88.8%

Table modified from: Claudia de la Espriella and Deanna Minich. Alternative and Complementary Therapies. Oct 2018.ahead of printhttp://doi.org/10.1089/act.2018.29181.ces Published in Volume: 24 Issue 5: October 11, 2018; Online Ahead of Print: September 4, 2018



#### Functional Medicine Deep Dive

### MSQ Scores over time



Graph modified from: Claudia de la Espriella and Deanna Minich. Alternative and Complementary Therapies. Oct 2018.ahead of printhttp://doi.org/10.1089/act.2018.291 81.ces Published in Volume: 24 Issue 5: October 11, 2018; Online Ahead of Print: September 4, 2018



#### Functional Medicine Deep Dive

# **Final Comments**

- Overall mental-emotional benefits from the program
- Client reported feeling peaceful during the detox, no longer experiencing anxiety and feeling more headstrong and being able to "let things roll off her shoulders without stressing too much."
- She noted a shift in her work environment to one being more supportive rather than negative
- She was strengthening relationships and encouraging others to change their eating for improved wellness

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Claudia de la Espriella and Deanna Minich. Alternative and Complementary Therapies. Oct 2018.ahead of printhttp://doi.org/10.1089/act.2018.29181.ces Published in Volume: 24 Issue 5: October 11, 2018; Online Ahead of Print: September 4, 2018



### 12 Nutrients for Better Mood

- 1. Folate
- 2. Iron
- 3. Omega-3 fatty acids
- 4. Magnesium
- 5. Potassium
- 6. Selenium
- 7. Thiamin (vitamin B<sub>1</sub>)
- 8. Vitamin A
- 9. Vitamin B<sub>6</sub>
- 10.Vitamin B<sub>12</sub>
- 11.Vitamin C
- 12.Zinc

LaChance LR, Ramsey D. Antidepressant foods: An evidence-based nutrient profiling system for depression. World J Psychiatry. 2018 Sep 20;8(3):97-104. doi: 10.5498/wjp.v8.i3.97. PMID: 30254980; PMCID: PMC6147775.



### **Functional Medicine Deep Dive**

### Antidepressant foods from greatest to least score

- 1. Vegetables
- 2. Organ meats
- 3. Fruits
- 4. Seafood
- 5. Legumes
- 6. Meats
- 7. Grains
- 8. Nuts and seeds
- 9. Dairy

LaChance LR, Ramsey D. Antidepressant foods: An evidence-based nutrient profiling system for depression. *World J Psychiatr* 2018; 8(3): 97-104 Available from: URL: http://www.wjgnet.com/2220-3206/full/v8/i3/97.htm DOI: http://dx.doi.org/10.5498/wjp.v8.i3.97

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### Figure out patterns with clinical assessments

- Food & Mood Tracker
- Food journal tracking emotions & foods
- Eating Timeline (top 10 events)



#### FOOD & MOOD WEEKLY TRACKER

Track the 'colors' of your foods and moods through the week

#### DIRECTIONS:

 FOODS: Put an X in the circle when you have had at least one serving of the corresponding food color. Foods that count are whole, unprocessed fruits, vegetables, whole grains, legumes, nuts, and seeds. The colors below are listed as red, orange, yellow, green, blue-purple, brown, and white.
MOODS: Log your overall moods for the day. Red = Angry/Frustrated; Orange = Playful/Adventurous; Yellow = Joyful/Happy; Green = Loving/Grateful; Blue-Purple = Sad/Depressed; Brown = Worried/Anxious; White = Open-Minded/Hopeful



### FOOD & MOOD WEEKLY TRACKER

Identifying correlations between colors of foods and colors of moods





#### Functional Medicine Deep Dive

# Tracking emotional patterns

Difficulty identifying and making sense of emotional states and not knowing how to regulate emotions are implicated in the relationship between emotions and binge eating.<sup>1</sup>

- Be specific as to what you are feeling
- Identify "little and important hurts"
- Record what makes you feel strongly for 2 months
- Keep a journal
- HRV biofeedback device

1. Whiteside U, Chen E, Neighbors C, Hunter D, Lo T, Larimer M. Difficulties regulating emotions: Do binge eaters have fewer strategies to modulate and tolerate negative affect? Eat Behav. 2007 Apr;8(2):162-9. Epub 2006 May 22



### **Functional Medicine Deep Dive**

# Creating one's eating timeline

- In-depth life-story interviewing and narrative analysis revealed:
  - Distinct 'food mood' events based in childhood memories about dinnertime
  - Parental attitudes important

Hooper CM, Ivory VC, Fougere G. "Dinner's ready!" A qualitative exploration of the food domain across the lifecourse. Appetite. 2015 Sep;92:133-42. doi: 10.1016/j.appet.2015.04.073. Epub 2015 Apr 29.



# Eating strategies to help with mental health

- 1. Color
- 2. Creativity
- 3. Variety





# Colorful foods make for colorful moods!



**Functional Medicine Deep Dive** 

### Strategy #1:Color

Eating more fruits and vegetables has been associated with less psychological distress, better mood, greater happiness, flourishing, & well-being.

- Conner TS, Brookie KL, Carr AC, Mainvil LA, Vissers MC. Let them eat fruit! The effect of fruit and vegetable consumption on psychological well-being in young adults: A randomized controlled trial. PLoS One. 2017;12(2):e0171206. Published 2017 Feb 3. doi:10.1371/journal.pone.0171206
- Głąbska D, Guzek D, Groele B, Gutkowska K. Fruit and vegetables intake in adolescents and mental health: a systematic review. Rocz Panstw Zakl Hig. 2020;71(1):15-25. doi:10.32394/rpzh.2019.0097
- Holder MD. The Contribution of Food Consumption to Well-Being. Ann Nutr Metab. 2019;74 Suppl 2:44-52. doi:10.1159/000499147
- Mujcic R, Oswald AJ. Evolution of Well-Being and Happiness After Increases in Consumption of Fruit and Vegetables. Am J Public Health. 2016 Aug;106(8):1504-10. doi: 10.2105/AJPH.2016.303260.
- Nguyen B, Ding D, Mihrshahi S. Fruit and vegetable consumption and psychological distress: cross-sectional and longitudinal analyses based on a large Australian sample [published correction appears in BMJ Open. 2017 Apr 7;7(4):e014201corr1]. BMJ Open. 2017;7(3):e014201. Published 2017 Mar 15. doi:10.1136/bmjopen-2016-014201

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## Life Satisfaction and Fruit/Vegetable Servings



Image Credit: Dreher ML. Whole Fruits and Fruit Fiber Emerging Health Effects. *Nutrients*. 2018;10(12):1833. Published 2018 Nov 28. doi:10.3390/nu10121833. No changes made. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (http://creativecommons.org/licenses/by/4.0/)



#### **Functional Medicine Deep Dive**

# Why plant foods?

- High potassium and magnesium
- Micronutrients (vitamins, certain minerals)
- Fibers of all types
- Thousands of phytochemicals that play roles in insulin sensitivity, inflammation and stress response
- Absence of inflammatory precursors (unless laden in toxicants like pesticides)
- Will depend on how they are cooked/prepared

Houston M, Minich D, Sinatra ST, Kahn JK, Guarneri M. Recent science and clinical application of nutrition to coronary heart disease. *J Am Coll Nutr.* 2018 Mar-Apr;37(3):169-187. doi: 10.1080/07315724.2017.1381053. Epub 2018 Jan 9.



### Functional Medicine Deep Dive

# How many servings of fruits and vegetables are required?

- Fruit & vegetable intake > 5 servings/d is associated with the lowest risk of CVD
- Highest risk with an intake <3 servings/d.

Flock MR, Kris-Etherton PM. Dietary Guidelines for Americans 2010: Implications for cardiovascular disease. *Curr Atheroscler Rep.* 2011 Dec;13(6):499-507. doi: 10.1007/s11883-011-0205-0.



Journal of Nutrition and Metabolism Volume 2019, Article ID 2125070, 19 pages https://doi.org/10.1155/2019/2125070



#### **Review** Article

#### A Review of the Science of Colorful, Plant-Based Food and Practical Strategies for "Eating the Rainbow"

#### Deanna M. Minich ()1,2

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Over the past decades, thousands of published studies have amassed supporting recommend vegetables for physiological and psychological health. Newer research has emerged to suggest that t a plethora of not only vitamins and minerals, but perhaps, most importantly, phytonutrients. The pleiotropic effects on cellular structure and function, ultimately resulting in the modulation of p epigenetic modification in a manner that leads to improved outcomes. Even though eating fruits a feature of a healthy dietary pattern, population intakes continue to be below federal recommendat to include fruits and vegetables into their diet, an "eat by color" approach is proposed in this review. may have numerous effects based on its constituents, the goal of this simplified approach was benefits based on the preponderance of scientific data and known mechanisms of food-based consti a consumer-oriented categorization of these plant-based foods may lead to greater recognition of th throughout the lifespan. Other adjunctive strategies to heighten awareness of fruits and vegetab

#### 1. Introduction

#### organize the findings into a cat understanding and application. While there continues to be debate about the inclusion of

meat, dairy, grains, and legumes in a healthy diet, there would seem to be little disagreement in the scientific community that eating fruits and vegetables is beneficial for one's health. Eating plant-based foods is part of many diverse dietary patterns, including the well-studied Mediterranean diet [1], vegan and vegetarian approaches, the hunter-gatherer (Paleolithic) diet [2], and even the less well-studied, ketogenic diet [3]. The quantity and quality of in vitro, animal, and clinical data over several decades suggest that intake of fruits and vegetables is associated with reducing chronic disease risk, such as cardiovascular disease, diabetes, cataracts, cancer, dementia, obesity, and others [4-7].

The search strategy for this review article was to start with a scientific literature review of the health benefits of fruits and vegetables, along with the predominant issues surrounding deficiencies in intake. Secondly, the goal was to

1.1. Phytonutrient Gap. Despite benefits of consuming fruits and historically consistent, with rece havioral Risk Factor Surveillan most adults (particularly men, yc in poverty) consume insufficier percent and twelve percent of recommendations for vegetables Moreover, a report [9] based of from the National Health and Nu (NHANES) conducted in 2003that eight out of ten Americans phytonutrients (referred to as a pecially in the color category of people neglected to meet their c

Reference: Deanna Minich, Journal of Nutrition and Metabolism, 2019, https://doi.org/10.1155/2019/2125070



ORANGE FOODS FOR REPRODUCTIVE HEALTH





#### GREEN FOODS FOR CARDIOVASCULAR HEALTH





The Science of

the "Rainbow"

of Foods

Minich DM. J Nutr Metab. 2019;2019:2125070.

#### **Functional Medicine Deep Dive**

### First: Make the case for why, what, how, and where to eat more plant-based foods.

#### EAT THE RAINBOW OF PLANT FOODS

#### WHY?

- TO REDUCE RISK OF CHRONIC DISEASE
- TO HELP WITH BETTER MOOD
- TO OPTIMIZE HEALTH AND FUNCTION

#### WHAT?

- FRUITS
- HERBS AND SPICES
- JUICES (100% JUICE)
- LEGUMES
- NUTS AND SEEDS
- SALADS
- SMOOTHIES
- TEAS
- VEGETABLES
- WHOLE GRAINS

#### HOW?

- INCLUDE IN EVERY MEAL
- VARY YOUR CHOICES
- AIM FOR A MINIMUM OF 5 SERVINGS DAILY
- TRY A NEW FOOD EVERY WEEK
- BUY COLORFUL PRODUCE AT THE MARKET

#### WHERE?

- HAVE FROZEN AND FRESH FOODS AT HOME
- ASK FOR SUBSTITUTIONS WHEN EATING OUT
- BRING WHOLESOME SNACKS WITH YOU WHEN TRAVELING

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#### **Functional Medicine Deep Dive**
### Second, provide a tool to track intake



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#### **Functional Medicine Deep Dive**

## Third: Encourage with new ideas and input on foods.

RED	ORANGE	YELLOW	GREEN	PURPLE BLACK	BROWN TAN	WHITE
Adzuki beans Apples Beets Blood oranges Cherries Cranberries Currants Goji berries Guava Kidney beans Lingonberries Peppers Pink grapefruit Pomegranate Radicchio Radishes Raspberries Red beans Red cabbage Red carrots Red chards Red potatoes Red potatoes Red potatoes Red plums Red potatoes Red plums Red potatoes Red quinao Strawberries Tomato Tomato paste Tomato sauce Watermelon	Apricots Cantaloupe Carrots Kumquat Mandarins Mangoes Nectorines Orange bell peppers Orange lentils Oranges Pepaya Passionfruit Peaches Persimmons Pumpkin Sweet potato Tangerines Turmeric spice Yams	Apples Asian pears Bananas Chamomile tea Chickpeas Corn (hominy, kernels, on cob, popcom) Endive Ginger root Ginger root Ginger rea Golden heets Golden flaxseed Golden raisins Lemons Millet Mustard (Dijon, spice, yellow) Pineapples Plantains Quinoa Squash Starfruit Yellow cauliflow Yellow cauliflow Yellow cauliflow Yellow lentils Yellow noins Yukon potatoes	Artichokes Arugula Asparagus Avocado Bamboo shoots Beet greens Bell peppers Bok choy Broccollower Broccoll Brussels sprouts Celery Chard Cilantro Collards Cucumbers Fennel bulbs Green cabbage Green beans Green cabbage Green nethis Green onions Green noins Green nethis Green nethis Green nethis Green peas Green tea Herbs Kale Kiwis Leeks Lettuces Limes Mung beans Mung beans Shustard greens Olives Peppers Pickles Snow peas Soybeans Spinach Sprouts Thyme Turnip greens Zucchini	Acai berries Aronia berries Asparagus* Beans* Black beans Black lentils Black lentils Black rice Black tea Black tea Blackberries Buyberries Carots* Colong tea Popers Plums Rice* Sweet potato* * <i>Purple variety</i>	Almonds Barley Brazil nuts Brown lentils Brown rice Buckwheat Cacao nibs Cacao powder Carob Cashews Chai tea Cocca powder Coffee Dates Flaxseeds Hemp seeds Millet Mushroom seas Mushrooms Nuts Nuts Dutters Oats Peanuts Peanuts Peanuts Peanuts Peanuts Peanuts Peanuts Peanuts Peanuts Peanuts Peanuts Peanuts Peanuts Peanuts Peanuts Peanuts Peanuts Seed butters Seeds butters Seeds butters Seeds butters Seeds Dutters So y sauce Spelt Sunflower seeds Taro root Teff Tempeh Triticale Walnuts Wheat	Apples Applesouce Cauliflower Coconut water Daikon radish Garlie Hearts of palm Horseradish Jicama Kohlrabi Mushrooms Parsnips Pear (flesh) Pumpkin seeds (outer) Rutabaga Sauerkraut Sesame seeds Shallots Tarnips White potatoes White potatoes White papper White rice White tea

EAT THE RAINBOW SHOPPING LIST

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#### **Functional Medicine Deep Dive**

## "Eat a Rainbow" Tool Kit



WHITE

Applesous Couliflowe Caconut Caconut Caconut wa Dakon radi Garlis Hearts of po Horseradis

Jicama Jicama Kahirabi Mushroome Parsnips Pear (flesh)

Pumpkin see (outer) Rutobogo Souerkrout

Second Second Second Shallots Totu Turnips White potato White corror White corror







#### **Functional Medicine Deep Dive**

## Select Functions of Phytochemicals: Modulation of the gut-brain axis



- Lamming DW, Wood JG, Sinclair DA. Small molecules that regulate lifespan: evidence for xenohormesis. Mol Microbiol. 2004 Aug;53(4):1003-9. doi: 10.1111/j.1365-2958.2004.04209.x. PMID: 15306006.
- Banudevi S, Swaminathan S, Maheswari KU. Pleiotropic Role of Dietary Phytochemicals in Cancer: Emerging Perspectives for Combinational Therapy. Nutr Cancer. 2015;67(7):1021-48. doi: 10.1080/01635581.2015.1073762. Epub 2015 Sep 11. PMID: 26359767.

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Color-code for RED: Inflammation, prostate



Functional Medicine Deep Dive

## The Color Code of Red Foods

- High in antioxidants and red-food carotenoids (e.g., astaxanthin, lycopene)
- Anti-inflammatory properties
- Immune system modulation:
  - Red-colored foods such as acerola cherry, rosehips, red bell pepper and tomatoes are some of the highest vitamin Ccontaining foods
  - Cell, animal, and human studies have shown that red-colored foods and/or their compounds may assist with reducing inflammation and helping immune status: watermelon, apples, cherries, cranberries, pomegranate, raspberries

Minich DM, A Review of the Science of Colorful, Plant-Based Food and Practical Strategies for "Eating the Rainbow", *Journal of Nutrition and Metabolism*, vol. 2019, Article ID 2125070, 19 pages, 2019. https://doi.org/10.1155/2019/2125070.



#### **Functional Medicine Deep Dive**



Color-code for ORANGE: Fertility, reproductive health, protection



**Functional Medicine Deep Dive** 

## The Color Code of Orange Foods

- Abundant in carotenoids, especially beta-carotene and beta-cryptoxanthin
- Fat-soluble antioxidants, storage in adipose tissue, skin, breast, ovaries, brain
- Endocrine-regulating activities such as ovulation; may play role in reducing risk for insulin resistance
- Role in fertility through association with hormone levels (in animals) and reducing oxidative stress
  - Supplementation with beta-carotene and other antioxidants in women has shown reduced time to pregnancy
  - Important for viability of sperm; levels of beta-carotene associated with sperm concentration

Minich DM, A Review of the Science of Colorful, Plant-Based Food and Practical Strategies for "Eating the Rainbow", *Journal of Nutrition and Metabolism*, vol. 2019, Article ID 2125070, 19 pages, 2019. https://doi.org/10.1155/2019/2125070.



#### **Functional Medicine Deep Dive**



Color-code for YELLOW: Digestion, energy, metabolism



Functional Medicine Deep Dive

## The Color Code of Yellow Foods

- Bioflavonoids for healthy microorganisms and metabolic detoxification
- Rich in fibers to support a complex microbiome and for sustained release of simple carbohydrates to modify glycemic impact
- Assist in maintaining gastrointestinal health through gastric motility and/or digestive secretions

Minich DM, A Review of the Science of Colorful, Plant-Based Food and Practical Strategies for "Eating the Rainbow", *Journal of Nutrition and Metabolism*, vol. 2019, Article ID 2125070, 19 pages, 2019. https://doi.org/10.1155/2019/2125070.

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Color-code for GREEN: Circulation, cardiovascular



Functional Medicine Deep Dive

## The Color Code of Green Foods

- High in a variety of nutrients for cardiovascular health such as vitamin K (phylloquinone), folate, magnesium, potassium, and dietary nitrates
- Flavonoid antioxidants like vitexin (found in green leafy vegetables) may have cardioprotective benefit.
- Blood-vessel expanding
- Relaxing due to vasodilatory properties
- Binding and clearing

Minich DM, A Review of the Science of Colorful, Plant-Based Food and Practical Strategies for "Eating the Rainbow", *Journal of Nutrition and Metabolism*, vol. 2019, Article ID 2125070, 19 pages, 2019. https://doi.org/10.1155/2019/2125070.



#### **Functional Medicine Deep Dive**



Color-code for BLUE-PURPLE: Brain, cognition, memory



**Functional Medicine Deep Dive** 

## Blue-purple foods for brain health

- Polyphenol-rich
- Flavonoids have an anti-anxiety effect due to their ability to bind GABA-A receptors.
- Blueberries and grapes most well studied
- Assist with learning, memory, and mood
- Contain mood- and brain-modulating flavonoids:
  - Procyanidins (monomeric and oligomeric form)
  - Flavonols (i.e., kaempferol, quercetin, myricetin)
  - Phenolic acids (hydroxycinnamic acids & derivatives of stilbenes)

Minich DM. "A Review of the Science of Colorful, Plant-Based Food and Practical Strategies for "Eating the Rainbow"," Journal of Nutrition and Metabolism, vol. 2019, Article ID 2125070, 19 pages, 2019. https://doi.org/10.1155/2019/2125070.



#### **Functional Medicine Deep Dive**

### The Family of Phytochemicals: A spotlight on polyphenols



**Image Credit:** Blekkenhorst LC, Sim M, Bondonno CP, et al. Cardiovascular health benefits of specific vegetable types: A narrative review. *Nutrients*. 2018 May 11;10(5). pii: E595. doi: 10.3390/nu10050595. No changes made. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution license CC BY 4.0.

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### Mood modulation by flavonols: GABA-a agonist activity

Table 1. Flavonols with relevant GABAergic effects.

	7 5 6 Flavonol			
Compound	Properties	Reference		
	Quercetin acts as a negative allosteric GABA <sub>A</sub> R modulator with antipsychotic activity. These results justify further therapeutic development of the excitatory-inhibitory imbalance disorders.			
Quercetin (5,7,3'	Quercetin antagonistic actions on GABA <sub>A</sub> p <sub>1</sub> Rs are mediated through a redox-independent allosteric mechanism.			
,4'-tetrahydroxy)	GABA <sub>A</sub> a <sub>5</sub> R could be a mechanism for reducing seizure severity (at anticonvulsive doses) or even be used a marker of seizure severity.			
	Quercetin and its glycosides (rutin and isoquercitrin) are partially responsible for the anxiolytic and sedative-like effect of <i>Tilia americana</i> var. <i>mexicana</i> through the GABA/BZD and serotoninergic 5-HT <sub>1A</sub> receptors.			
Fisetin (7,3',4'-trihydroxy)	Treatment with fisentin can delay or correct neuropathic hyperalgesia and allodynia in mice with type 1 diabetes. The analgesia caused by fisetin may be linked with its antioxidant activity. Spinal GABA <sub>A</sub> Rs are likely rendered as downstream targets.	[73]		
Myricetin (3,5,7,3',4',5' -pentahydroxy)	Myricetin enhances GABA <sub>A</sub> R activity via the calcium channel/Ca <sup>2+</sup> /calmodulin-dependent protein kinase II dependent mechanism, which is distinctively different from that of most existing BZD-binding site agonists of GABA <sub>A</sub> R.	[74]		
Viscosine (5,7,4'-trihydroxy- 3,6-dimethoxy)	The anxiolytic and anticonvulsant actions of viscosine are likely mediated via its positive allosteric modulatory action at different GABAAR subtypes.	[75]		
	Glycosides			
Rutin (quercetin 3- <i>0-</i> rutinoside)	The anxiolytic-like effect involves GABAergic neurotransmission without implication of BZD receptors.	[76]		
Rutin (quercetin 3-O- rutinoside) Isoquercitrin (quercetin-3-O- glucoside)	Leaves of <i>Tilia americana</i> var. <i>mexicana</i> have anxiolytic and sedative-like effects and its flavonoids, quercetin, rutin and isoquercitrin, are partially responsible due to the involvement of GABA/BZD and serotoninergic 5-HT <sub>1A</sub> receptors.	[72]		

Apple, apricot, black tea, broccoli, green bean, green tea, kale, leek, onion, red wine, tomato

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Ríos JL, Schinella GR, Moragrega I. Phenolics as GABA<sub>A</sub> Receptor Ligands: An Updated Review. Molecules. 2022 Mar 8;27(6):1770. doi: 10.3390/molecules27061770. PMID: 35335130; PMCID: PMC8953830.



# Blue-purple fruits & vegetables, select phytochemicals & physiological effects

Color	Fruits	Vegetables	Select Phytochemicals	Physiological Effects
Blue- purple	Blackberries Blueberries Boysenberries Figs Huckleberries Plums Prunes Purple grapes Raisins	Eggplant Purple bell peppers Purple cabbage Purple carrots Purple cauliflower Purple kale Purple potatoes	Anthocyanidins Flavonoids Phenolic acids Proanthocyanidins Pterostilbene Resveratrol Stilbenes	Antioxidant Cognitive support Healthy mood balance Neuronal health

Minich DM. "A Review of the Science of Colorful, Plant-Based Food and Practical Strategies for "Eating the Rainbow"," Journal of Nutrition and Metabolism, vol. 2019, Article ID 2125070, 19 pages, 2019. https://doi.org/10.1155/2019/2125070.



#### Functional Medicine Deep Dive

## **Purple is precious:**

## Choose blue-purple varieties whenever possible for added neuroprotective polyphenols





#### **Functional Medicine Deep Dive**

# Concord grape juice (Resveratrol)

- Daily intake over 3-4 months shown to improve memory in adults with mild cognitive impairment.
- Can help with other parameters of cognition including reactive time on an attention measure and increased calm ratings
- An animal study suggests it may modulate BDNF, a neuronal growth factor.
- Grape polyphenols like resveratrol have been shown to have anti-inflammatory effects.

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Minich DM, A Review of the Science of Colorful, Plant-Based Food and Practical Strategies for "Eating the Rainbow", *Journal of Nutrition and Metabolism*, vol. 2019, Article ID 2125070, 19 pages, 2019. https://doi.org/10.1155/2019/2125070.



### Blueberries

- May help with cognition
  - Regular blueberry intake can prevent cognitive decline in those at risk.
  - Clinical trials shown to help cognition in older adults, such as delayed word recognition or recall.
- May help with mood
  - In addition to cognitive markers, may help with mood, as shown in children and young adults.
- May affect hippocampal BDNF mRNA expression (shown in rats)
- Frozen blueberries preserves antioxidant effects and anthocyanin levels.
  - Drying the fruit, however, will reduce total anthocyanin level by 41%, and dehydrating will reduce levels by 49%.

Miller MG, Hamilton DA, Joseph JA, Shukitt-Hale B. Dietary blueberry improves cognition among older adults in a randomized, double-blind, placebo-controlled trial. Eur J Nutr. 2018 Apr;57(3):1169-1180. doi: 10.1007/s00394-017-1400-8. Epub 2017 Mar 10. PMID: 28283823. Krikorian R, Skelton MR, Summer SS, Shidler MD, Sullivan PG. Blueberry Supplementation in Midlife for Dementia Risk Reduction. Nutrients. 2022 Apr 13;14(8):1619. doi: 10.3390/nu14081619. PMID: 35458181; PMCID: PMC9031005.Minich DM, A Review of the Science of Colorful, Plant-Based Food and Practical Strategies for "Eating the Rainbow", *Journal of Nutrition and Metabolism*, vol. 2019, Article ID 2125070, 19 pages, 2019. <u>https://doi.org/10.1155/2019/2125070</u>. Lohachoompol V, Srzednicki G, Craske J. The Change of Total Anthocyanins in Blueberries and Their Antioxidant Effect After Drying and Freezing. J Biomed Biotechnol. 2004;2004(5):248-252. doi: 10.1155/S1110724304406123. PMID: 15577185; PMCID: PMC1082901.

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## Select mechanisms of how blueberries support mood & cognition

- Involved in inflammation and cell survival; enhance neuroplasticity, neurotransmission
- Reduce glycation
- Reduce DNA damage
- Improves spatial memory, increases rate of learning, elevates BDNF (animals)
- Improves cognition in older adults and in children
- Improved positive affect/mood in children/young adults

Khalid S, Barfoot KL, May G, et al. Effects of acute blueberry flavonoids on mood in children and young adults. *Nutrients*. 2017;9(2):158. Published 2017 Feb 20. doi:10.3390/nu9020158.; Barfoot KL, May G, Lamport DJ, Ricketts J, Riddell PM, Williams CM. The effects of acute wild blueberry supplementation on the cognition of 7-10-year-old schoolchildren. *Eur J Nutr*. 2019;58(7):2911–2920. doi:10.1007/s00394-018-1843-6.; Fragua V, Lepoudère A, Leray V, et al. Effects of dietary supplementation with a mixed blueberry and grape extract on working memory in aged beagle dogs. *J Nutr Sci*. 2017;6:e35. Published 2017 Jul 12. doi:10.1017/jns.2017.33.; Rendeiro C, Vauzour D, Rattray M, et al. Dietary levels of pure flavonoids improve spatial memory performance and increase hippocampal brain-derived neurotrophic factor. *PLoS One*. 2013;8(5):e63535. Published 2013 May 28. doi:10.1371/journal.pone.0063535



#### Functional Medicine Deep Dive

## Strategy #2: Creativity

- Creativity enables for better expression of oneself<sup>1,2</sup>
- Reduces burnout and emotional stress<sup>3,4</sup>
- Cultivates resilience<sup>3,4</sup>
- Greater sense of purpose and meaning<sup>5</sup>
- Food cravings may be related to need for less boredom and more creativity.<sup>6</sup>

 Jackson L. T. (1991). Creative movement promotes health, self-expression. Provider (Washington, D.C.), 17(7), 35. PMID: 10114257; 2. Stuckey HL, Nobel J. The connection between art, healing, and public health: a review of current literature. Am J Public Health. 2010 Feb;100(2):254-63. doi: 10.2105/AJPH.2008.156497. Epub 2009 Dec 17. PMID: 20019311; PMCID: PMC2804629. 3. Reynolds, S. S., & Sova, C. (2022). Memes and poetry: A descriptive analysis on creative arts therapy to reduce health care worker burnout. Journal of Nursing Care Quality, 37(3), 245–248.
 https://doi.org/10.1097/NCQ.000000000000618 PMID: 35142729; 4. Ho AHY, Tan-Ho G, Ngo TA, Ong G, Chong PH, Dignadice D, Potash J. A Novel Mindful-Compassion Art-Based Therapy for Reducing Burnout and Promoting Resilience Among Healthcare Workers: Findings From a Waitlist Randomized Control Trial. Front Psychol. 2021 Oct 21;12:744443. doi: 10.3389/fpsyg.2021.744443. PMID: 34744918; PMCID: PMC8566679; 5. Liddle, J. L., Parkinson, L., & Sibbritt, D. W. (2013). Purpose and pleasure in late life: Conceptualising older women's participation in art and craft activities. Journal of Aging Studies, 27(4), 330–338. https://doi.org/10.1016/j.jaging.2013.08.002 PMID: 24300053; 6. Hill, A. J., Weaver, C. F., & Blundell, J. E. (1991). Food craving, dietary restraint and mood. Appetite, 17(3), 187–197. https://doi.org/10.1016/0195-6663(91)90021-j PMID: 1799281



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## Strategy #2: Creativity

- Food preparation
- Plays, acting, drama
- Designing (interior, graphic, fashion)
- Thinking strategically
- Physical movement
- Being in nature
- Playing or listening to music
- Journaling
- Crafts of various types
- Painting, drawing, coloring books





# Mental creativity can help one move out of restrained eating ruts

- Mindfulness meditation may help reduce binge eating and emotional eating<sup>1,2</sup>
- Relaxation response to modulate stress eating episodes<sup>3</sup>

1. Katterman, S. N., et al. (2014). Mindfulness meditation as an intervention for binge eating, emotional eating, and weight loss: A systematic review. Eating Behaviors, 15(2), 197–204. https://doi.org/10.1016/j.eatbeh.2014.01.005 PMID: 24854804; 2. Warren, J. M., et al. (2017). A structured literature review on the role of mindfulness, mindful eating and intuitive eating in changing eating behaviours: Effectiveness and associated potential mechanisms. Nutrition Research Reviews, 30(2), 272–283. https://doi.org/10.1017/S0954422417000154 PMID: 28718396; 3. Masih, T., et al. (2017). Stress-induced eating and the relaxation response as a potential antidote: A review and hypothesis. Appetite, 118, 136–143. https://doi.org/10.1016/j.appet.2017.08.005 PMID: 28789869



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## Strategy #3: Variety

- Greater variety of fruits and vegetables was associated with a higher MMSE and cognitive domains such as executive function, memory, and attention in adults<sup>1</sup>
- Children with less dietary diversity and dietary adequacy have greater anxiety<sup>2</sup>
- Women with lower dietary diversity had greater associations with anxiety<sup>3</sup> and depression<sup>4</sup>.
  - A one-unit increase in the Dietary Diversity Score was associated with a 39% reduced risk of depression

1. Ye, X., Bhupathiraju, S. N., & Tucker, K. L. (2013). Variety in fruit and vegetable intake and cognitive function in middle-aged and older Puerto Rican adults. The British Journal of Nutrition, 109(3), 503–510. https://doi.org/10.1017/S0007114512001183 PMID: 22717056; 2. McMartin, S. E., et al. (2013). Diet quality and feelings of worry, sadness or unhappiness in Canadian children. Canadian Journal of Public Health = Revue canadienne de sante publique, 104(4), e322–e326. https://doi.org/10.17269/cjph.104.3845 PMID: 24044473; 3. Poorrezaeian, M., et al. (2015). Association of dietary diversity score with anxiety in women. Psychiatry Research, 230(2), 622–627. https://doi.org/10.1016/j.psychres.2015.10.016 PMID: 26506017; 4. Poorrezaeian, et al. (2017). Depression is related to dietary diversity score in women: A cross-sectional study from a developing country. Annals of General Psychiatry, 16, 39. https://doi.org/10.1186/s12991-017-0162-2 PMID: 29176995

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## More variety of vegetables results in greater intake in children



#### 100% HED Condition

#### 60% HED Condition

Mean ( $\pm$  SEM) intakes of LED vegetables at a lunch meal across both HED portion sizes by vegetable condition. A significant main effect of vegetable condition was observed at p < 0.05. Within each variety condition the mean consumption of each individual vegetable type (carrot (orange), cherry tomato (red) and cucumber (green) has been shown.

Associated with Downsizing a High Energy Dense Meal Item be Offset by Increased Vegetable Variety in 3<sup>-5</sup>-yearold Children?. *Nutrients*.
2018;10(12):1879. Published 2018 Dec 3.
doi:10.3390/nu10121879.
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Image Credit: Carstairs SA, Caton SJ, Blundell-Birtill P,

Rolls BJ, Hetherington MM,

Cecil JE, Can Reduced Intake



#### **Functional Medicine Deep Dive**

## **Clinical Tool:** Variety Tracker





**Figure 3.** The author's "50-food challenge" chart is an example of a simple, but powerful data collection tool used in clinical practice to engage with patients in a light-hearted way so that they report back to their practitioner on their dietary diversity. The rationale is to motivate patients to vary the foods they have every day, so that they're increasing their micronutrient diversity, thereby feeding different classes of gut microbes.

"Increasing the diversity of brightly-coloured plant foods, even in small amounts, can have a dramatic effect on SCFA production."



Write in the foods that you are eating that respond to the respective categories. Note that you do not have to populate each category. At the end of the 7 days, tally up the number of unique entries to see whether you were able to get to the goal of 50 foods.

Vegetables	Fruit	Herbs/Spices	Nuts/Seeds	Whole Grains	Liquids
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Toribio-Mateas, M. Harnessing the Power of Microbiome Assessment Tools as Part of Neuroprotective Nutrition and Lifestyle Medicine Interventions. *Microorganisms* 2018, *6*, 35. https://doi.org/10.3390/micr oorganisms6020035



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## Putting it all together

- Focus on physiological reasons for mood issues by dealing with inflammation, the gut microbiome and nutrient imbalances
- Aim for more color, creativity, and diversity as general principles to engage healthy, happy eating
- Use tracking metrics and assessments to put people in touch with emotions & food intake

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- Ensure nutrient sufficiency and eating foods that are known to be dense in those nutrients
- Food & mood are interconnected: physically, emotionally, and mentally.





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