



FUNCTIONAL PSYCHIATRY: GETTING TO THE ROOT CAUSE OF DEPRESSION AND ANXIETY

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OBJECTIVES

1. Define functional psychiatry and its importance in clinical practice.
2. Identify possible root causes that drive depression and anxiety.
3. Assess and treat root causes of anxiety and depression.



WHAT IS FUNCTIONAL PSYCHIATRY?

- **Functional medicine X psychiatry**
 - Using a root cause approach to address mental health concerns
 - Treating the whole person
 - Mind-body approach
- **Mental health disorders are multifactorial in nature**
 - Resulting from a combination of genetic, environmental, and lifestyle factors
 - Requiring a comprehensive and personalized approach
- **Goal:**
 - Restore balance in the body's
 - Optimize mental and physical well-being



CONVENTIONAL VS. FUNCTIONAL PSYCHIATRY

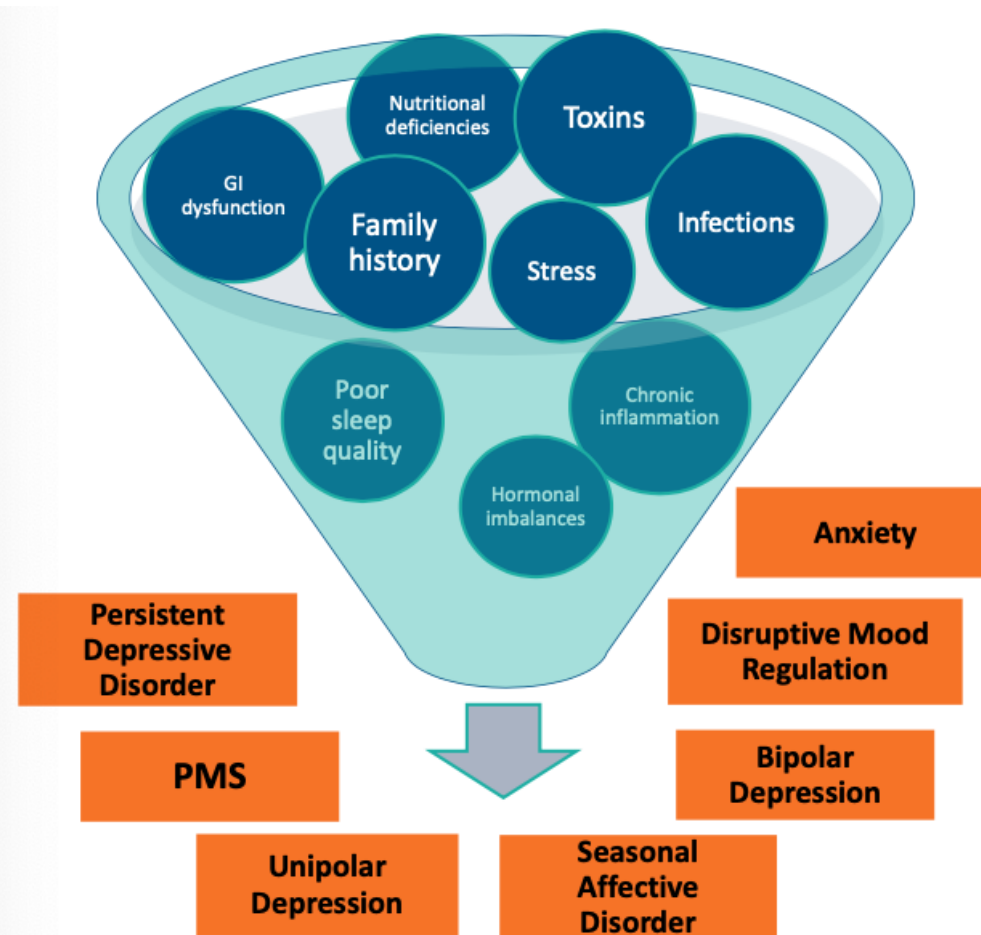
CONVENTIONAL PSYCHIATRY



FUNCTIONAL PSYCHIATRY



DEPRESSION AND ANXIETY



WHY DO WE CARE?

- All of our patients have a mental health component to their overall well-being
- Mental health concerns are often barriers to healing
 - They can also be mediators of disease
- Up to ½ of mood disorders contribute to future development of neurodegenerative disorders

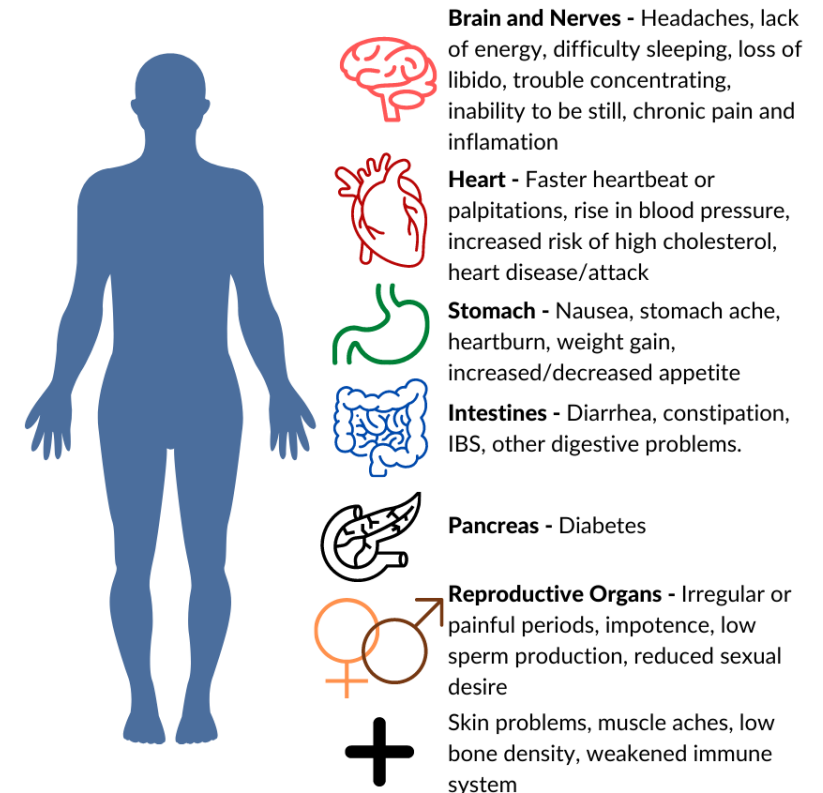


WHY DO WE CARE?

COMORBIDITIES:

- Alzheimer's dz
- Parkinson's dz
- Diabetes
- Metabolic syndrome
- Obesity
- Asthma
- Allergies
- Osteoporosis
- Traumatic brain injury
- Endocrine disorders
- Coronary artery disease
- HIV
- Cancer
- Autoimmune disease

The Effects of Anxiety and Depression on the Body



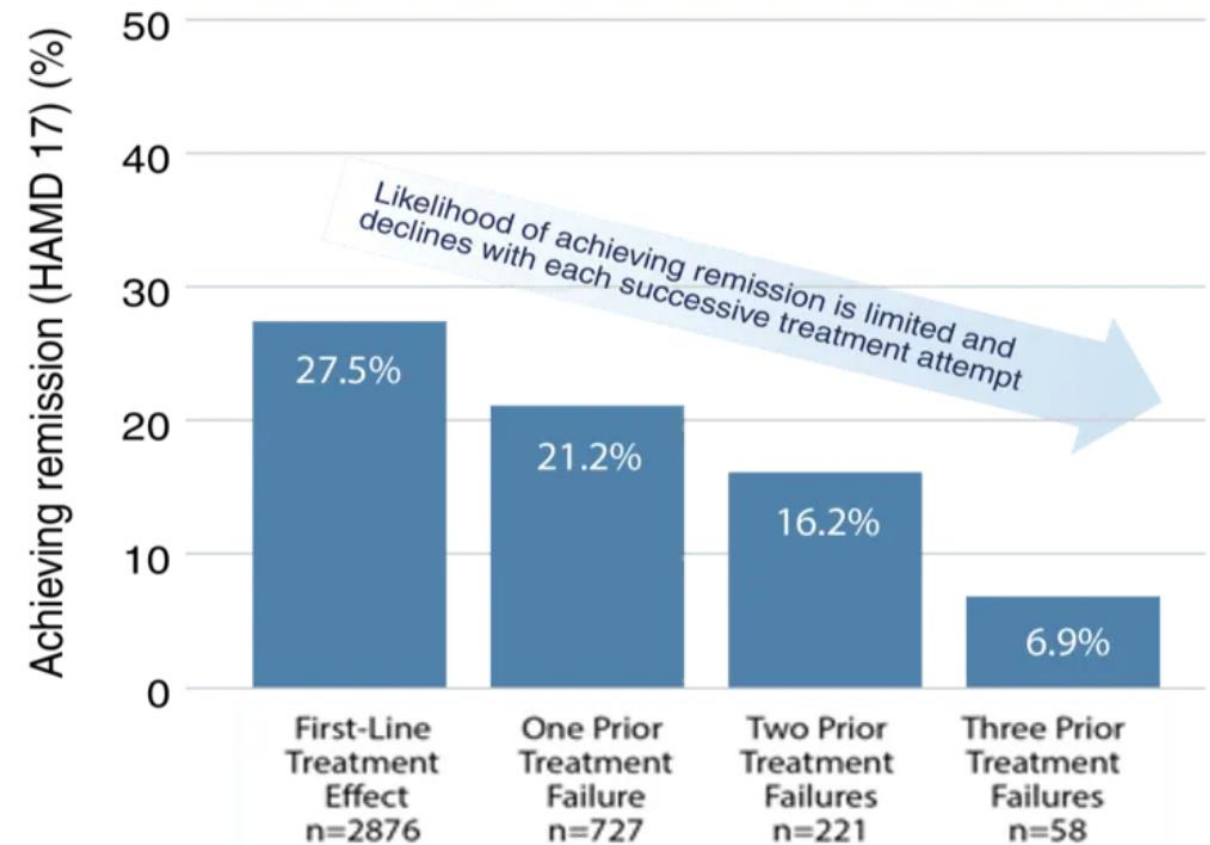
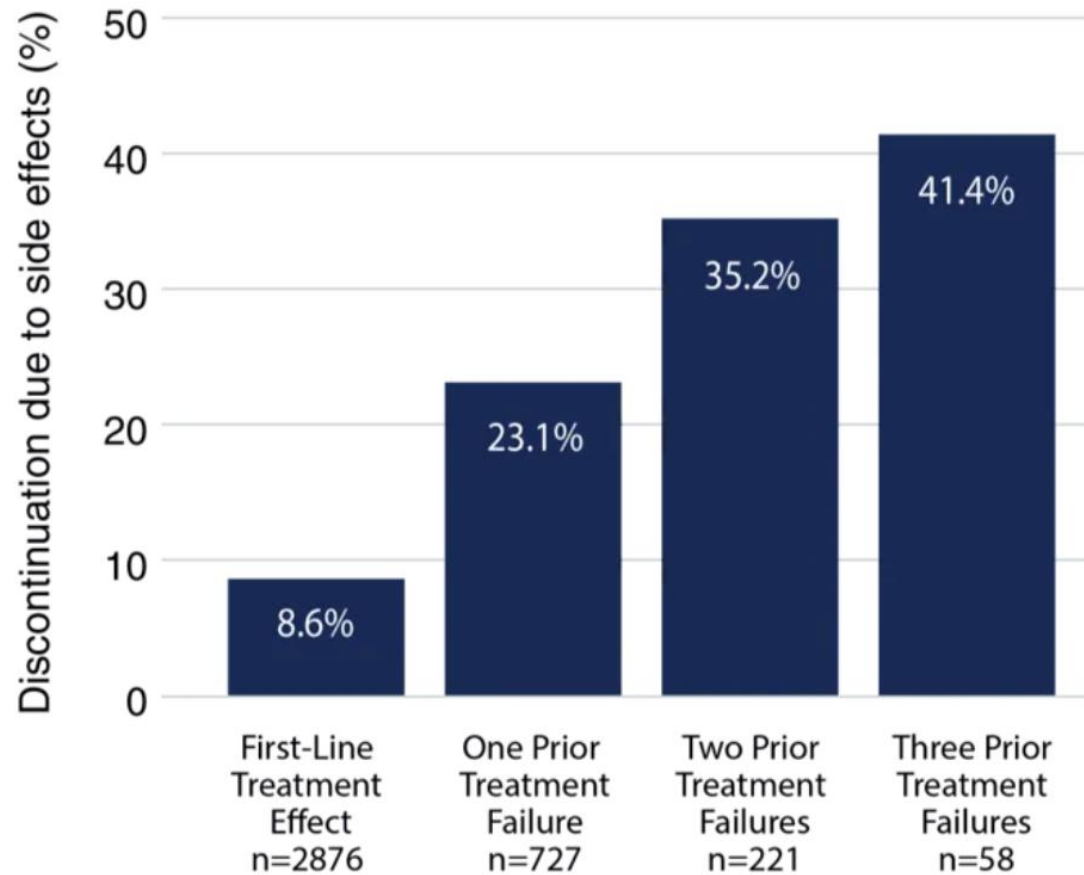
WHY DO WE CARE?

STAR*D Trial (Sequenced Treatment Alternatives to Relieve Depression)

- 50% of responders experienced treatment relapse within a year
- 25% experienced a long-term rate of remission
 - Full recovery rates are even lower



STAR*D Study





References: Why Do We Care?

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POSSIBLE ROOT CAUSES

- **Gut imbalances**
- **Inflammation**
- **Nutrient deficiencies**
- **Diet**
- **Exercise / sleep**
- **Thyroid / adrenal dysfunction**
- **Spiritual, social, emotional factors**



ROOT CAUSE: GUT IMBALANCES



GUT HEALTH AND MENTAL HEALTH

- **There is a significant correlation between gut health and mental health**
- Patients with depression are more likely to experience:
 - Increased intestinal permeability (AKA “leaky gut”)
 - Dysbiosis (altered microbiome)
 - Increased LPS antibodies
 - IBS (irritable bowel syndrome)



ANTIDEPRESSANTS AND GUT HEALTH

- 95% of the body's serotonin receptors are in the gut
 - SSRI GI side effects..?!
- Antidepressants have antimicrobial effects on the gut
- Long-term antidepressant use can change the gut microbiome



**IT IS CRUCIAL TO SUPPORT THE GUT IF A CLIENT
IS ON OR HAS BEEN ON AN ANTIDEPRESSANT!**

PSYCHOBOTICS

Psychobiotics = probiotics (live organisms) that improve mental health

- These organisms can help produce GABA, serotonin, and other neurotransmitters that improve anxiety and depression
- They can help stimulate the vagus nerve, calm the neuroendocrine system, and regulate the HPA axis
- They improve depression and anxiety
- They reduce overall cortisol and can be protective during stressful events
- They reduce inflammation
- They reduce chronic fatigue





References: Psychobiotics

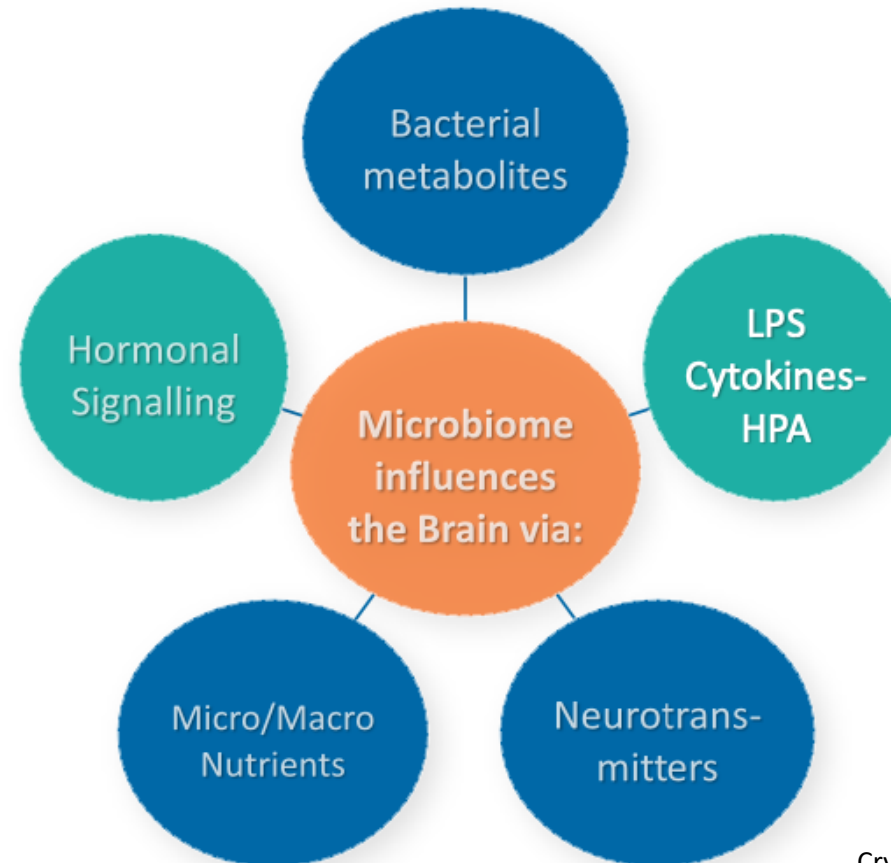
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GUT-BRAIN AXIS



GUT HEALTH AND MENTAL HEALTH

WHEN IN DOUBT, START IN THE GUT

TREATMENT

5-R PROTOCOL

TO RESTORE YOUR GUT HEALTH

- 1** Remove: Stressors & Gut Irritants
- 2** Replace: Nutrients, Bile & Stomach Acid
- 3** Reinoculate: With Pre- & Pro-biotics
- 4** Repair: Intestinal Wall
- 5** Rebalance: Your Lifestyle



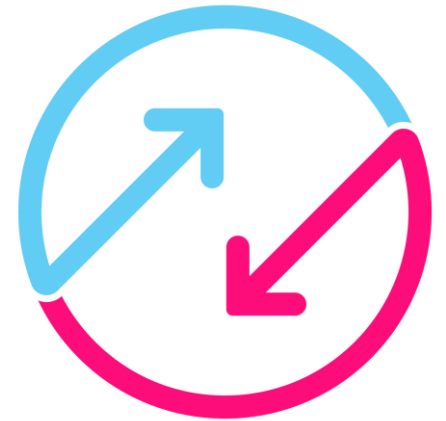


ROOT CAUSE: INFLAMMATION



INFLAMMATION AND MENTAL HEALTH

- There is a bi-directional relationship between inflammation and anxiety/depression
 - Inflammation can increase anxiety and depression
 - Anxiety and depression can increase inflammation
 - This occurs because of the release of pro-inflammatory cytokines
- Anti-inflammatory treatments have been shown to reduce symptoms of depression



ANTI-INFLAMMATORY BOTANICALS

- Turmeric
- Ginger
- Boswellia
- Bromelain
- Devil's Claw
- Quercetin
- Cayenne
- EGCG





References: Inflammation

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ROOT CAUSE: NUTRIENT DEFICIENCIES

NUTRIENTS INVOLVED IN DEPRESSION AND ANXIETY

- Vitamin D
- B12
- Zinc
- Copper
- Fatty acids
- Many more...



VITAMIN D

- "Normal" reference range: 30-100
- Optimal reference range: 60-100
- Low vitamin D levels not only correlates to higher depression rates but also to suicidality
- Supplementing with vitamin D has consistently been shown to improve depressive symptoms



Spedding S. (2014). Vitamin D and depression: a systematic review and meta-analysis comparing studies with and without biological flaws. *Nutrients*, 6(4), 1501–1518.

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B12

Low B12 ->

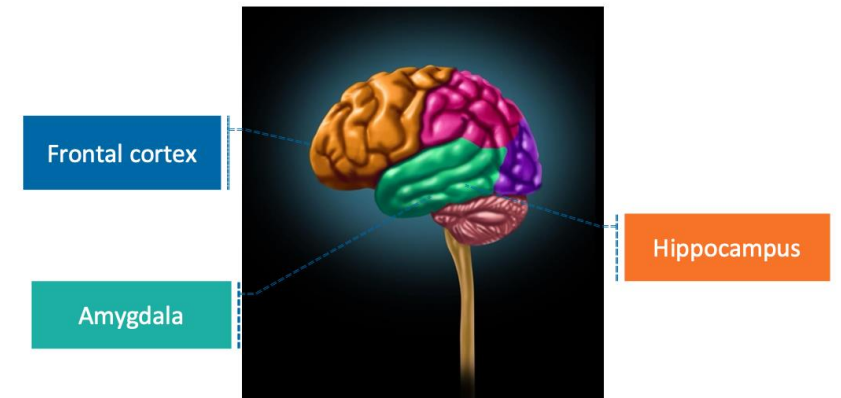
- 70% increased risk of depression
 - Panic attacks
 - Visual hallucinations
 - Fatigue
 - OCD
 - Bipolar disorder
 - PPD
 - Phobias
- Methylated B12 (methylcobalamin) is often better absorbed than other forms
 - B12 is critical in the methylation pathway



ZINC AND COPPER

- Zinc and copper have an inverse relationship
- Zinc modulates the glutathione / GABA balance
 - Zinc works as an antagonist of the glutamatergic pathway, allowing the GABAergic pathway to take over
- Zinc increases BDNF
- Zinc influences the serotonin receptor -> affects depression / anxiety
- Caution: zinc toxicity; copper depletion

Zn Localization in the Brain



Frederickson CJ. Neurobiology of zinc and zinc-containing neurons. Int Rev Neurobiol. 1989;31:145-238.



ZINC AND COPPER

- Patients with depression have been found to have lower levels of zinc and higher levels of copper
- It is estimated that 1/3 of people are deficient in zinc
- Supplementing with zinc can be an effective augmenting strategy in the treatment of depression and anxiety

Low zinc, high copper sx:

- Depression
- Anxiety
- Irritability / anger
- Hormonal issues (ex: PMS)

High zinc, low copper sx:

- Decreased BDNF
- Impaired memory
- Cognitive issues



References: Zinc and Copper

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Siwek M, et al. Zinc supplementation augments efficacy of imipramine in treatment resistant patients: a double blind, placebo-controlled study. *J Affect Disord*. 2009 Nov;118(1-3):187-95. doi:10.1016/j.jad.2009.02.014.

Yang Y, et al. High dose zinc supplementation induces hippocampal zinc deficiency and memory impairment with inhibition of BDNF signaling. *PLoS One*. 2013;8(1):e55384. doi: 10.1371/journal.pone.0055384.

OMEGA-3S

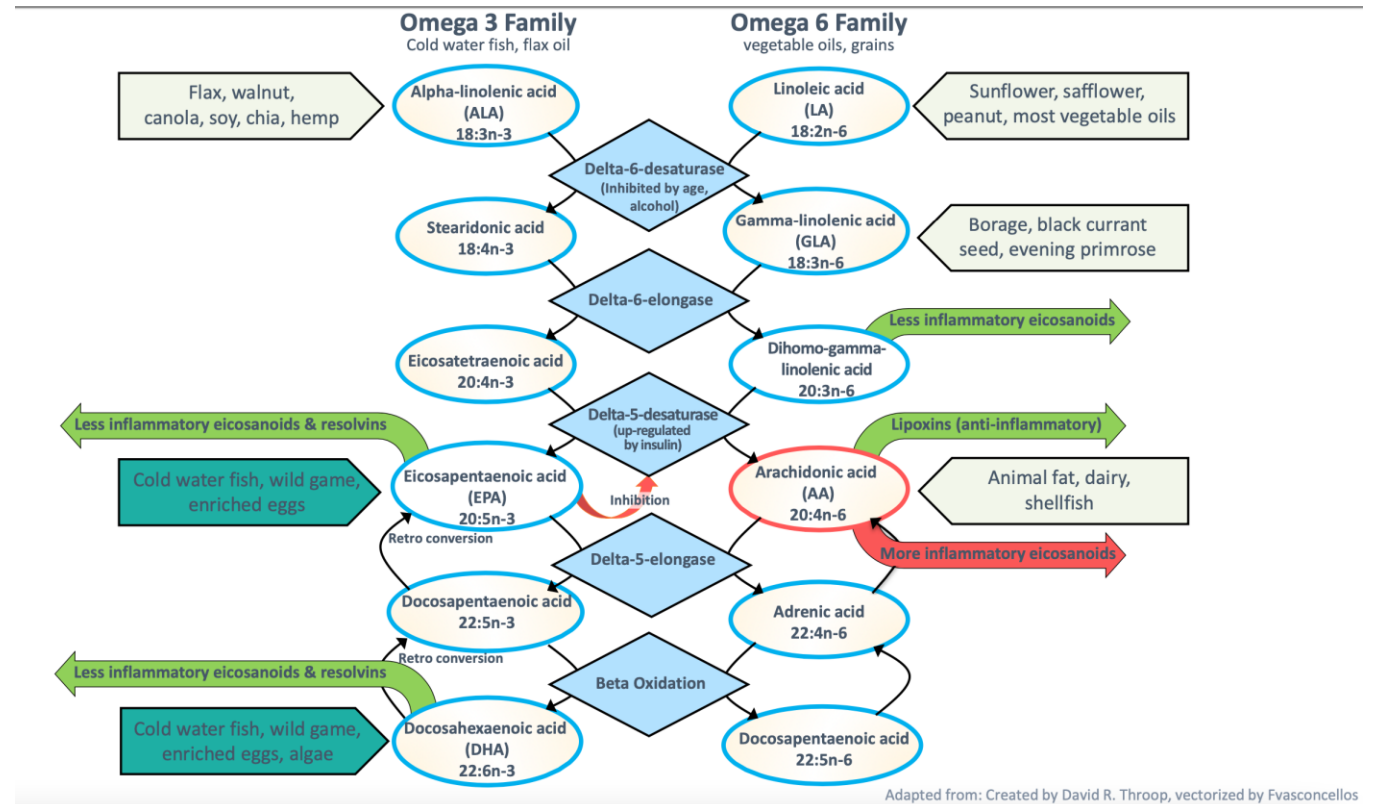
- Therapeutic dose of EPA: **1-2 grams/day**
- EPA in particular has been shown to improve depression when used as an adjunctive treatment
- Omega-3s have been shown to have anxiolytic effects
 - This effect was increased when using PUFA doses of >2 grams/day



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SOURCES OF PUFA

- **ALA:**
 - Flax
 - Walnut
 - Chia
 - Hemp
- **DHA:**
 - Same as EPA
 - Algae
- **EPA:**
 - Cold water fish
 - Eggs
 - Game meat



ADDITIONAL SUPPLEMENTS

ANXIETY SUPPORT

- Phosphatidylserine
- Adaptogens (ex: ashwaganda)
- GABA
- L-theanine
- Magnesium glycinate

DEPRESSION SUPPORT:

- 5-HTP
- Saffron
- Methylfolate
- SAMe
- Methylated B vitamins



References: Supplements

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ROOT CAUSE: DIET

DIET AND MENTAL HEALTH

- Studies have repeatedly shown an association between what we eat and our mental health
- Macronutrients have been shown to greatly affect both depression and anxiety by:
 - Controlling glucose supply to the brain
 - Influencing our microbiome
 - Providing anti-inflammatory benefits
 - Impacting our HPA axis



SUGAR AND MENTAL HEALTH

Processed sugar is full of downstream effects that can increase depression and anxiety

- Increases inflammation s/t pro-inflammatory cytokines
- Decreases BDNF
- Decreases neuronal plasticity
- Increases cortisol
- Decreases availability of B vitamins
- Increases brain fog
- Increases insomnia





BLOOD SUGAR AND MENTAL HEALTH

- **Blood sugar spikes can independently increase depression and anxiety**
- **Ways to balance blood sugar:**
 - Walk for 10 minutes post-meals
 - Drink bone broth
 - Reduce sodas / sugary drinks
 - Reduce processed carbs
 - Eat veggies then protein/fat then carbs
 - Use a CGM
- Consider supplements:
 - Berberine
 - Cinnamon
 - Magnesium





MEDITERRANEAN DIET

THE MEDITERRANEAN DIET IMPROVES OVERALL DEPRESSION AND ANXIETY



- Mediterranean diet:
 - Reduces inflammation
 - Improves methylation
 - Improves omega 6:3 ratio
 - Decreases insulin resistance and helps balance blood sugar
 - Improves gut microbiome diversity

References: Diet

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ROOT CAUSE: EXERCISE AND SLEEP

EXERCISE BENEFITS

- Decreases cortisol (stress hormone)
- Increases serotonin
- Increases BDNF
- Increases endorphins
- Increases endocannabinoids
- Decreases inflammation
- Improves sleep





EXERCISE

- All types of exercise improve anxiety / depression
 - Both aerobic/cardio and resistance/weight training have been found to be beneficial
 - Moderate-vigorous exercise is correlated with reduced distress
- Exercise alone has been shown to be beneficial in treating mild-moderate depression
- Exercise can prevent future anxiety and depression
- Exercise may protect against genetic SNPs that may make one more likely to experience anxiety and depression
 - Particularly promising research in regards to the COMT gene
- Exercise can help improve sleep, which directly impacts mood and anxiety

References: Exercise

Adapted with permission of Kowsar, from Depression and Exercise: A Clinical Review and Management Guideline, Ranjbar, E., Memari, A. H., Hafizi, S., Shayestehfar, M., Mirfazeli, F. S., & Eshghi, M. A., vol. 6, copyright 2015; permission conveyed through Copyright Clearance Center, Inc.

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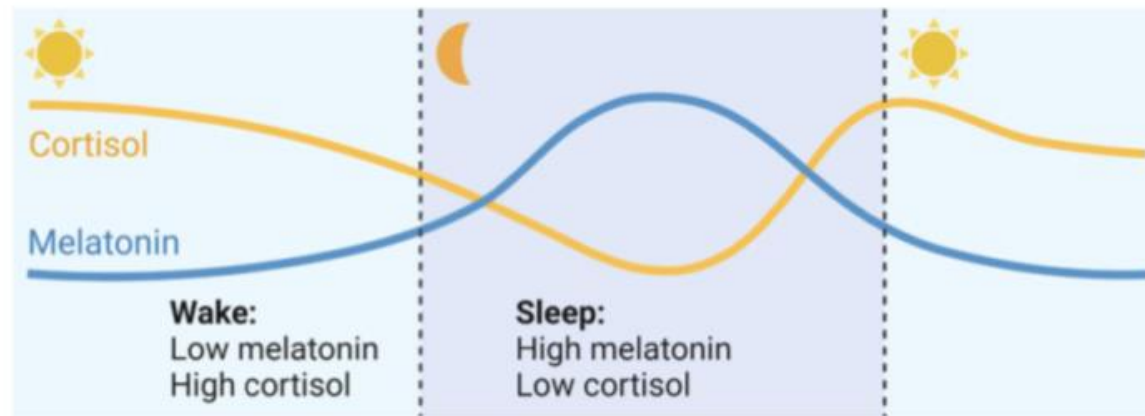
CIRCADIAN RHYTHM AND SLEEP

Circadian Rhythms

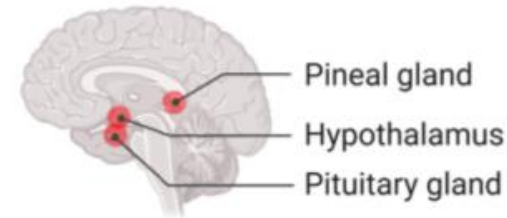


Circadian rhythm is part of the body's **internal clock**; it follows a 24-hour schedule and regulates the sleep-wake cycle.

During the 24-hour cycle, our hormone levels fluctuate in response to light, particularly **melatonin** and **cortisol**.




Regions of the brain that regulate the circadian rhythm include **pineal gland, hypothalamus** and **pituitary gland**.



SLEEP HYGIENE

Tips to improve sleep hygiene:

- Get morning sunlight between 7-11am
- Consider light therapy
- Reduce blue light exposure in the evening
- Wear blue light blocking glasses
- Reduce napping during the day
- Avoid caffeine after 12pm
- Eat dinner at least 2 hours before bedtime
- Maintain a stable blood sugar
- Consider meditation or yoga nidra
- Limit time in the bedroom
- Consider supplementation:
 - Melatonin
 - L-theanine
 - Phosphatidylserine
 - GABA
 - Adaptogens (ex: ashwaganda)



ROOT CAUSE: THYROID AND ADRENAL DYSFUNCTION



THYROID DYSFUNCTION AND MENTAL HEALTH

**THYROID FUNCTION DIRECTLY IMPACTS,
MOOD, COGNITION, AND ANXIETY**



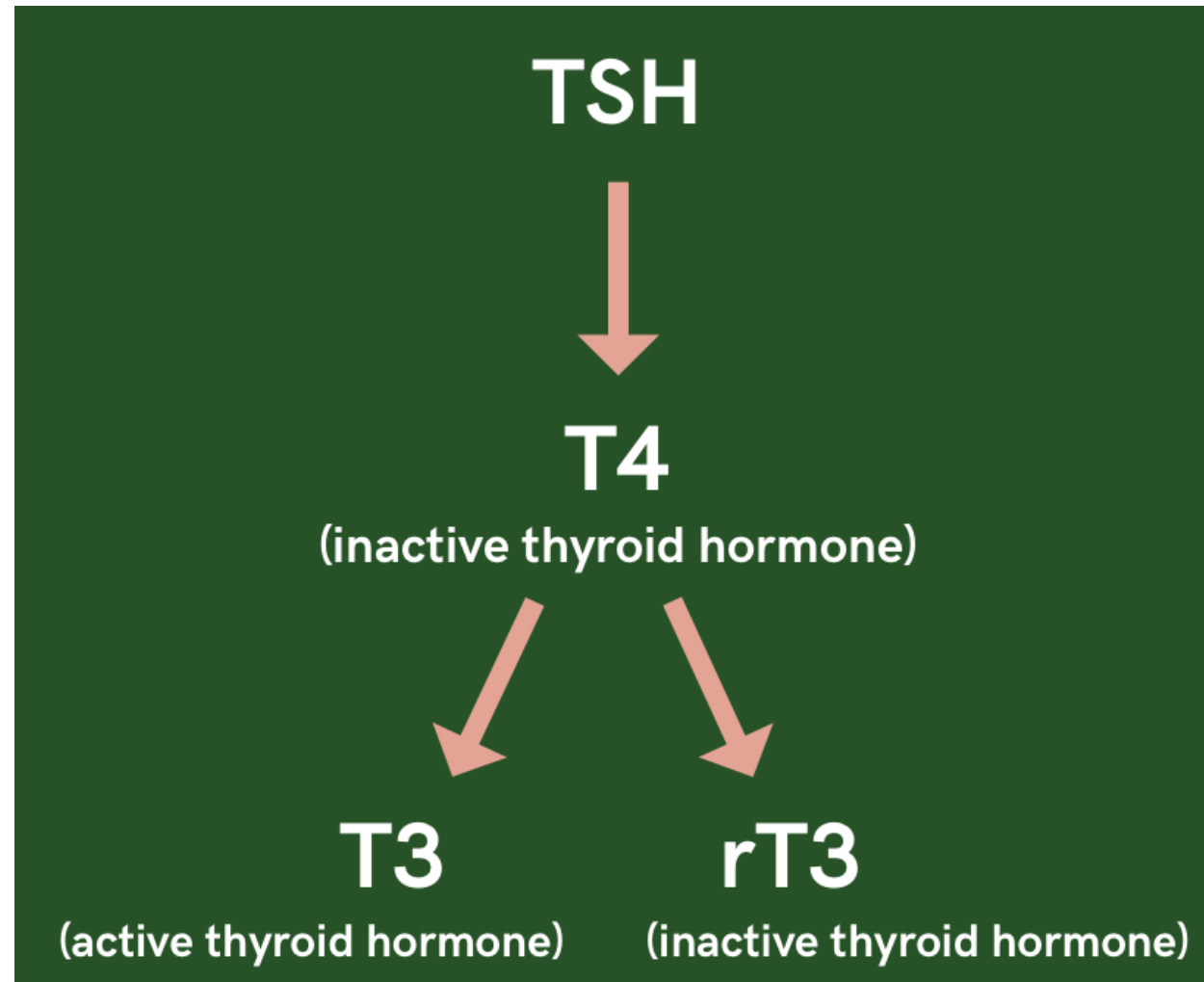
Hypothyroidism

- Hair loss
- Inability to think clearly
- Goiter (enlarged thyroid)
- Reduced heart rate
- Strong fatigue
- Sensitivity to cold
- Dry skin
- Weight gain
- Puffiness
- Memory problems
- Constipation
- Irregular menstrual periods
- Severe PMS
- Depression, mood swings
- Joint, muscle pain
- High cholesterol



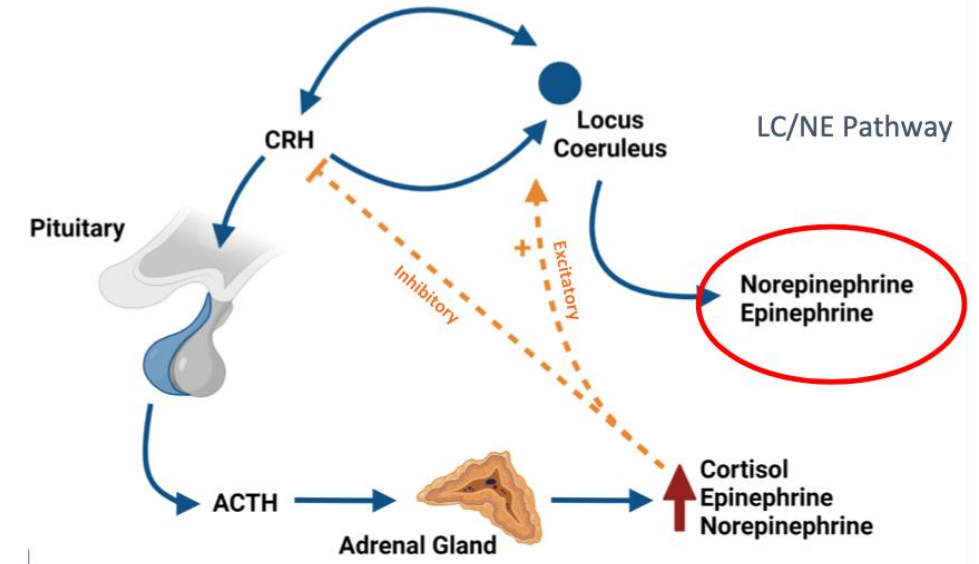
Hyperthyroidism

- Hair loss
- Bulging eyes
- Goiter (enlarged thyroid)
- Heart palpitations
- Tremors
- Heat intolerance
- Sleep disturbances
- Weight loss
- Shortness of breath
- Diarrhoea
- Increased appetite
- Irregular menstrual periods
- Muscle weakness
- Sweating
- Anxiety, nervousness
- Depression, mood swings



CORTISOL AND MENTAL HEALTH

- **HPA axis** = hypothalamic-pituitary-adrenocortical system
- The HPA axis is often dysregulated in depression and anxiety
 - Activation of the HPA axis -> increased cortisol secretion -> sympathetic response
 - Chronic stress -> chronic state of fight-or-flight
- Depression and anxiety are often associated with hypercortisolism
 - HPA axis hyperactivity
- Conventional treatments work to blunt the HPA axis

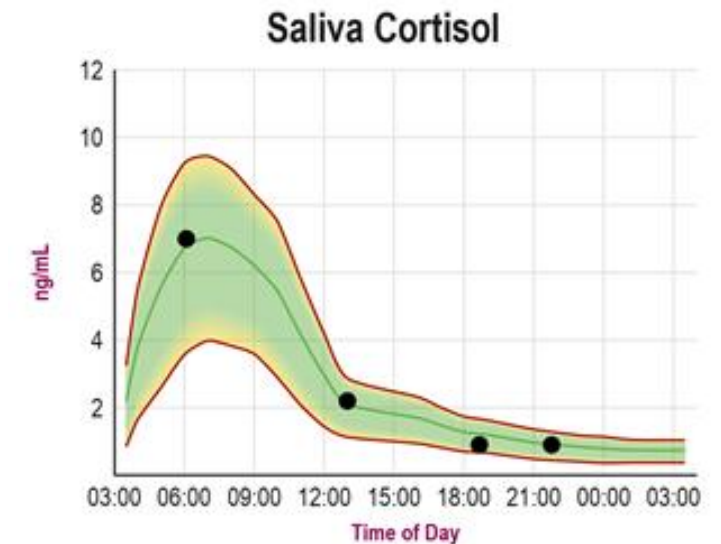


A specific PVN CRH pathway to brainstem noradrenergic nuclei independent of the HPA axis

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SIGNS OF DEPRESSION ASSOCIATED WITH HYPERCORTISOLISM

- Anxiety
- Irritability
- Anger
- Dread
- Impending doom
- Insomnia
- Loss of appetite
- Brain fog
- Fatigue
- Symptoms worse in the am



Source: ZRT Labs



CORTISOL AND ANTIDEPRESSANTS

ANTIDEPRESSANTS LOWER CORTISOL

- 2012 double-blind, placebo-controlled, cross-over study:
 - Citalopram 20mg vs. placebo
 - After 4 days of treatment or placebo, participants were give 30mg of PO cortisol
 - Treatment group experienced less impaired working memory disturbance and reduced EEG changes
- 2011 placebo-controlled study:
 - SSRI's significantly reduced cortisol
 - This cortisol reduction led to improvements in anxiety symptoms



BUT...

What happens when our adrenals give out ???

Salivary Cortisol in depressed patients				
	8 AM	11 AM	4 PM	11 PM
Normal	13-24n	4-10nM	3-8nM	1-4nM
Melancholic Agitated Depression	High	High	High	Marked increase
Atypical Depression and CFIDS	Low	Low	Low normal	Normal



LOW VS. HIGH CORTISOL ON DEPRESSION

TWO Subtypes of Depression	Atypical Depression	Melancholic Depression
Male/Female	F > M	M ≥ F
Sleep	↑	↓
Appetite/Body Fat	↑	↓
Immunity	Vulnerable to inflammation	Vulnerable to infection
Diurnal Variation in mood/energy	PM worse	AM worse
Reactivity to environment	Yes	No
Energy/LC activity (NE)	Reduced: Psychomotor Retardation Reduced central NE	Psychomotor Agitation Increased central NE PANIC /Anxiety
Prevalence	15-30% pure	25-30% pure
Heritability	Yes	Yes



References: Cortisol

Bschor T, Ising M, Erbe S, et al. Impact of citalopram on the HPA system. A study of the combined DEX/CRH test in 30 unipolar depressed patients. *Journal of Psychiatric Research*. 2012;46(1):111-117.

Gold PW, Chrousos G. P. Organization of the stress system and its dysregulation in melancholic and atypical depression: high vs low CRH/NE states. *Mol Psychiatry*. 2002;7(3):254-75.

Gold PW, Machado-Vieira R, Pavlatou MG. Clinical and biochemical manifestations of depression: relation to the neurobiology of stress. *Neural Plast*. 2015;2015:581976. doi:10.1155/2015/581976.

Hernandez MCADE, Mendieta D, Pérez-Tapia M, et al. Effect of Selective Serotonin Reuptake Inhibitors and Immunomodulator on Cytokines Levels: An Alternative Therapy for Patients with Major Depressive Disorder. *Clinical and Developmental Immunology*. 2013;2013:1-11.




References: Cortisol

Lenze EJ, Mantella RC, Shi P, et al. Elevated Cortisol in Older Adults With Generalized Anxiety Disorder is Reduced by Treatment: A Placebo-Controlled Evaluation of Escitalopram. *The American Journal of Geriatric Psychiatry*. 2011;19(5):482-490.

Tsigos C, Chrousos GP. Hypothalamic-pituitary-adrenal axis, neuroendocrine factors and stress. *J Psychosom Res*. 2002 Oct;53(4):865-71. doi: 10.1016/s0022-3999(02)00429-4. PMID: 12377295.

Pariante CM, Alhaj HA, Arulnathan VE, et al. Central glucocorticoid receptor-mediated effects of the antidepressant, citalopram, in humans: A study using EEG and cognitive testing. *Psychoneuroendocrinology*. 2012;37(5):618-628.



ROOT CAUSE: SPIRITUAL, SOCIAL, EMOTIONAL FACTORS



SPIRITUALITY

Studies on spiritual belief show:

- Decreased depression rate by almost 30%
- Decreased suicide rate by almost 85%
- Decreased substance use disorder
- Decreased all-cause mortality by up to 35%
 - 7 additional years of life
- Decreased divorce rate by up to 50%
- Increased happiness scores

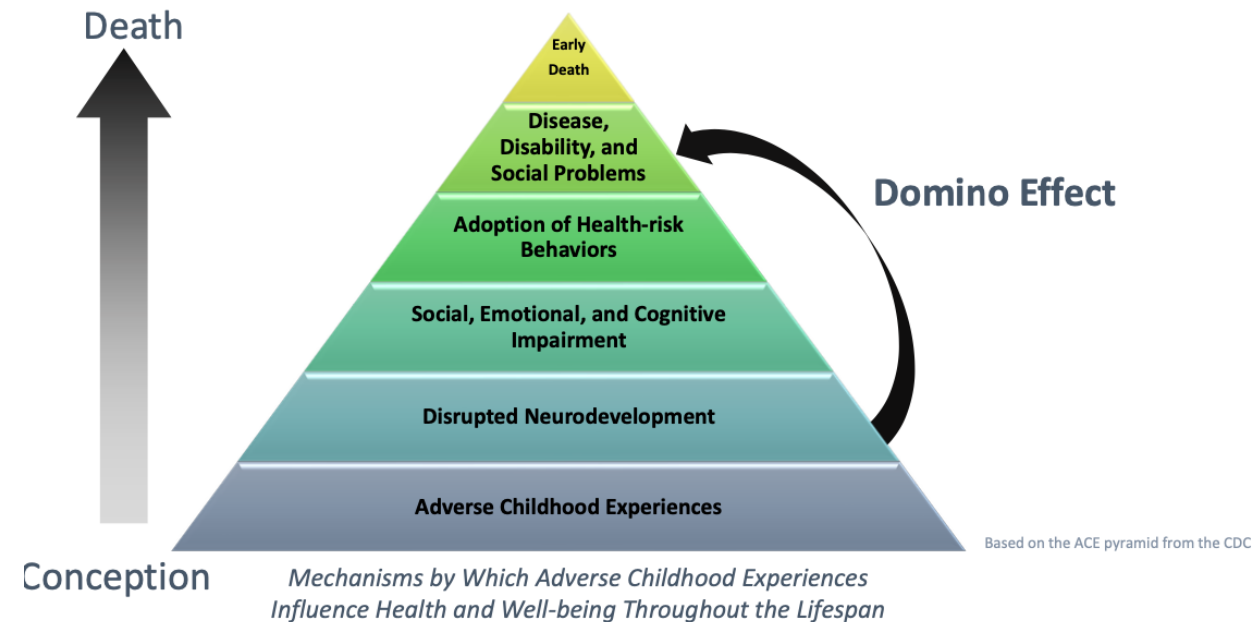
IMPORTANCE OF SUPPORT SYSTEMS

- A strong social support system reduces risk for depression
- Social connections improve vagal tone balance
- Social isolation can negatively influence gene expression and increase inflammation



CHILDHOOD EXPERIENCES ON DEPRESSION / ANXIETY

- **ACEs = adverse childhood experiences**
 - Socioeconomic disadvantage
 - Maltreatment
 - Social isolation
- 32 year prospective longitudinal study:
 - ACEs -> increased risk for metabolic disease, inflammation, and depression later in life
 - Highest risk: trauma, neglect, abuse





References: Support and ACEs

Ashida S, Heaney CA. Differential associations of social support and social connectedness with structural features of social networks and the health status of older adults. *J Aging Health*. 2008 Oct;20(7):872-93. doi: 10.1177/0898264308324626.

Cheong EV, Sinnott C, Dahly D, Kearney PM. Adverse childhood experiences (ACEs) and later-life depression: perceived social support as a potential protective factor. *BMJ Open*. 2017;7(9).

Denise A. Moffitt TE, Harrington H, Milne BJ, et al. Adverse Childhood Experiences and Adult Risk Factors for Age-Related Disease: Depression, Inflammation, and Clustering of Metabolic Risk Markers. *Arch Pediatr Adolesc Med*. 2009; 163(12): 1135-1143. doi:10.1001/archpediatrics.2009.214



References: Support and ACEs

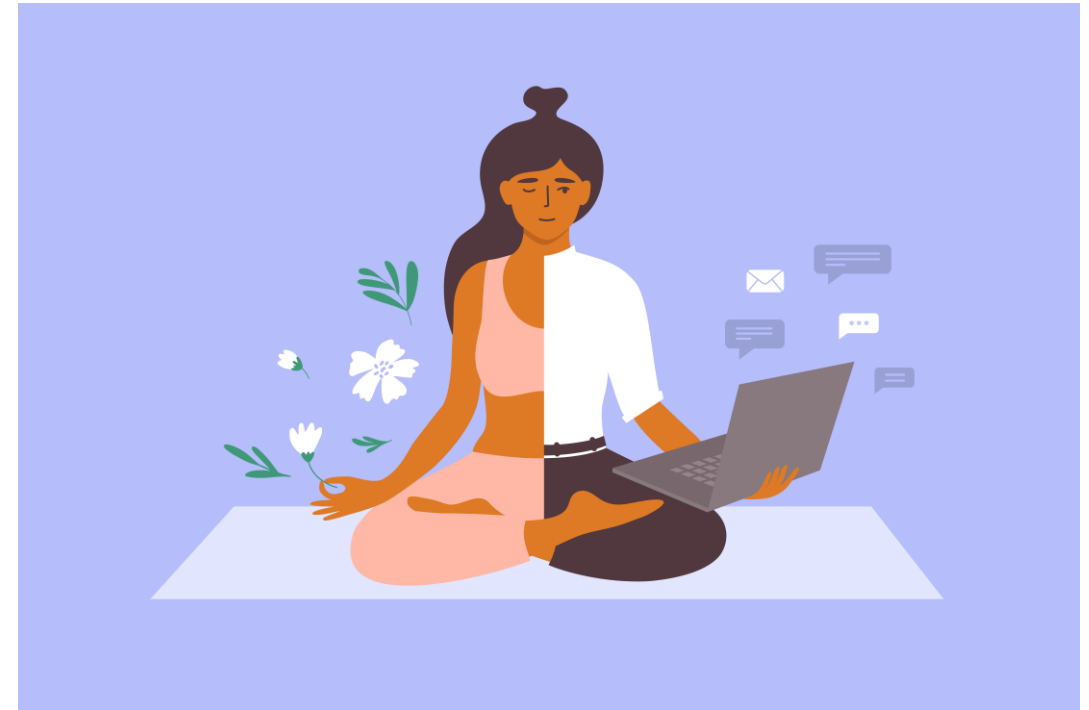
Kok BE, Coffey KA, Cohn MA, et al. How positive emotions build physical health: perceived positive social connections account for the upward spiral between positive emotions and vagal tone [published correction appears in Psychol Sci. 2016 Jun;27(6):931]. *Psychol Sci.* 2013;24(7):1123-1132. doi:10.1177/0956797612470827

Slavich GM, Cole SW. The Emerging Field of Human Social Genomics. *Clin Psychol Sci.* 2013 Jul;1(3):331-348. PubMed PMID: 23853742

MINDFULNESS

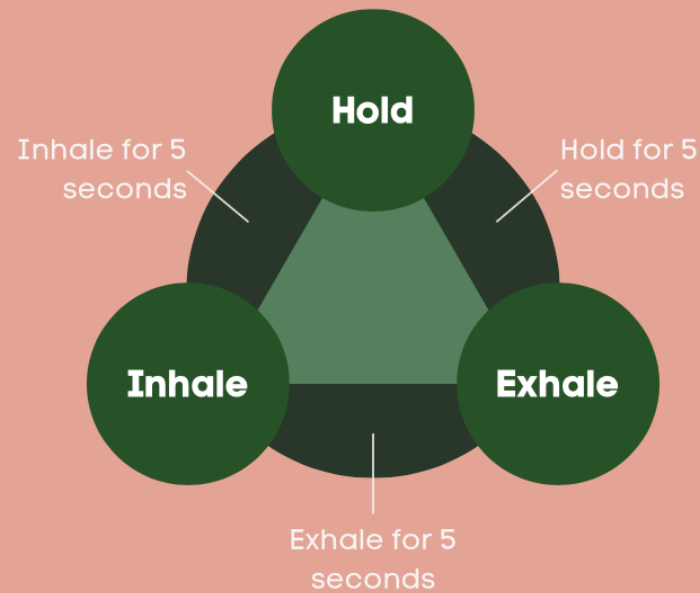
2018 randomized-controlled trial:

- Participants with generalized anxiety disorder were randomized to either a mindfulness intervention or control
- The mindfulness group had significantly greater reductions in stress response after performing a social stress test

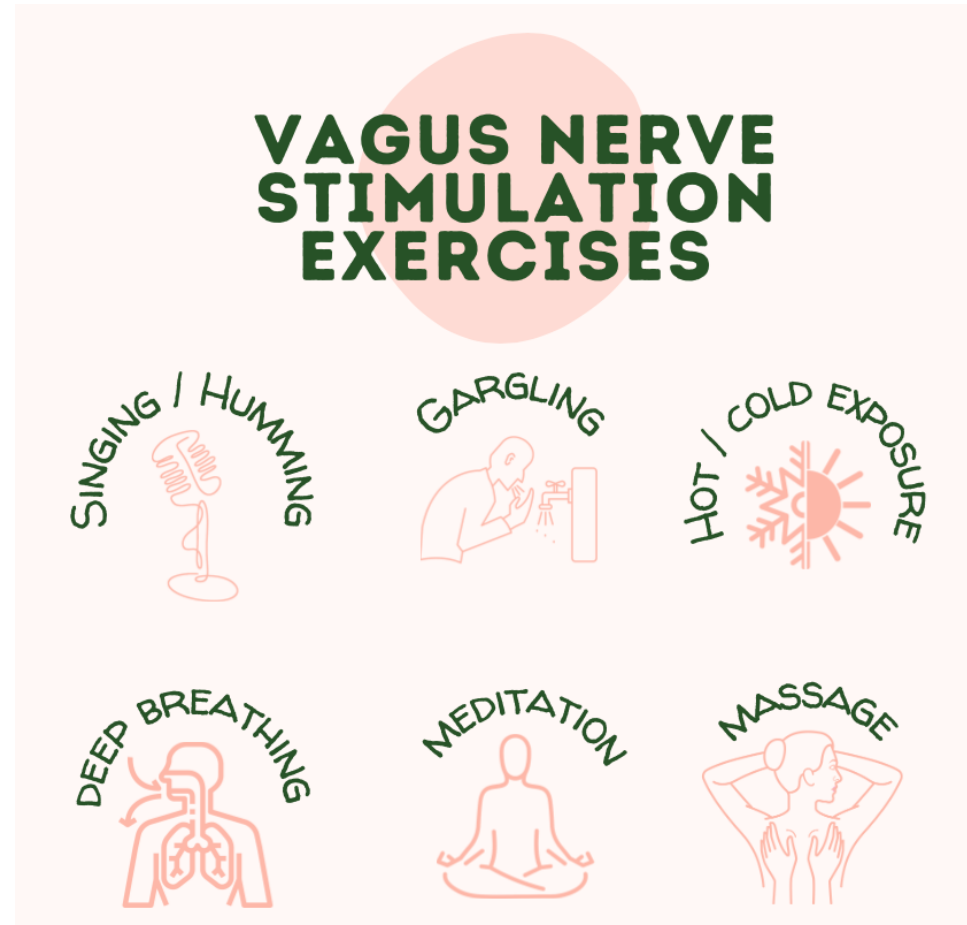


BREATHWORK

5 - 5 - 5 BREATHING TECHNIQUE FOR ANXIETY



VAGUS NERVE STIMULATION





MINDFULNESS-BASED PRACTICES

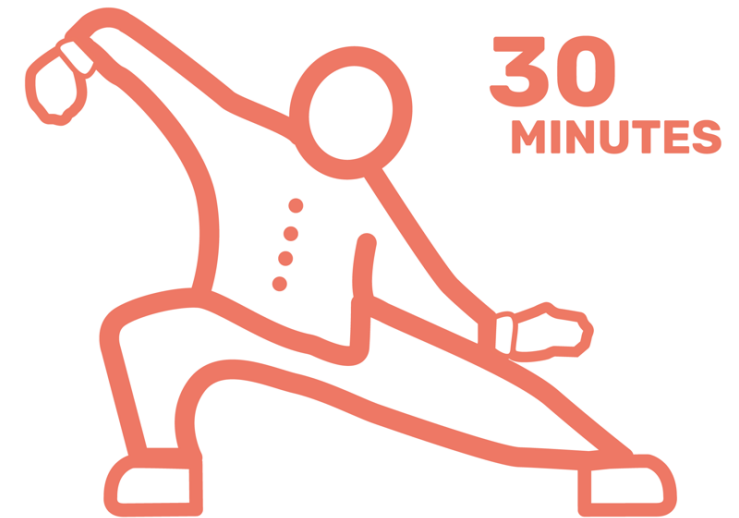
- Meditation
- Prayer
- Breathwork
- Biofeedback
- Guided Imagery
- Hot/cold exposure
- Therapy
- Tapping
- Nature-bathing
- Acupuncture
- Journaling
- Massage





TAI CHI

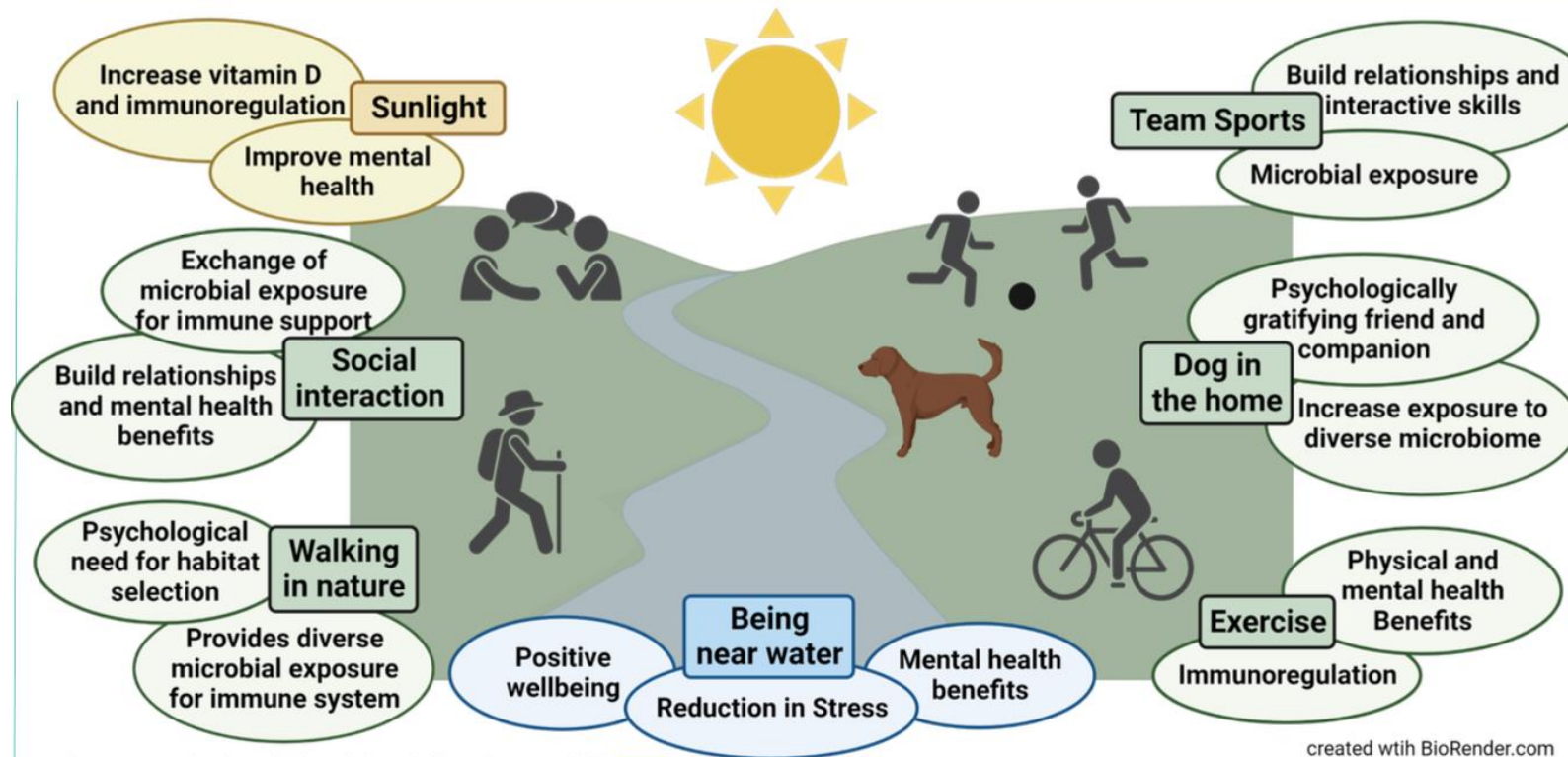
- Tai chi has been shown to improve emotional regulation
- Tai chi helps reduce and prevent further symptoms of depression



Practicing **Tai Chi** 30 minutes to 2 hours, 1 to 3 times per week, significantly **increases psychological well-being**, reduces stress, anxiety, depression, and low mood

NATURE

Physiological and Psychological Effects of Green and Blue Spaces





References: Nature

Rook GA. Regulation of the immune system by biodiversity from the natural environment: an ecosystem service essential to health. *Proc Natl Acad Sci U S A*. 2013;110(46):18360-18367.
doi:10.1073/pnas.1313731110

White MP, Elliott LR, Gascon M, Roberts B, Fleming LE. Blue space, health and well-being: A narrative overview and synthesis of potential benefits. *Environ Res*. 2020;191:110169.
doi:10.1016/j.envres.2020.110169



LAB TESTING



BASIC LABS TO CONSIDER

- CBC with differential
- Comprehensive metabolic panel
- Lipid panel
- Full thyroid panel
 - TSH, fT3, fT4, tT3, tT4, rT3 thyroid antibodies
- Heavy metals
- Hs-CRP
- GGT
- Testosterone
- Cortisol
- Vitamin D
- Magnesium
- B12
- Folate
- Homocysteine
- Iron panel
 - Iron, ferritin, TIBC, UIBC
- Fasting insulin
- HgA1c

SPECIALTY LABS TO CONSIDER

- Stool test
- Hormone test
- Salivary cortisol profile with CAR
- NutrEval
- SPECT Scans (Dr. Daniel Amen)
- Organic acids test
- Food sensitivity panel
- Tox screen
- Genetic testing *



REFERENCE RANGES

“References ranges are usually established by collecting results from a large population and determining from the data an expected average (mean) result and expected differences from that average (standard deviation).”

REFERENCE RANGES

OPTIMAL IS NOT THE SAME AS “NORMAL”

THE FUNCTIONAL PSYCHIATRY APPROACH TO LABS

- Look for patterns with each patient
- Look at the labs in relation to one another
- Use “optimal” reference ranges instead of just “normal” reference ranges
- Understand that labs are only one piece of the puzzle
- Consider each patient as an individual with a unique history, needs, and patterns



KEY TAKEAWAYS

KEY TAKEAWAYS:



- **Anxiety and depression:**
 - Are multifactorial in nature
 - Can be influenced by a range of factors that are not mutually exclusive
 - Need to be considered on an individual and case-by-case basis
 - Impact and are impacted by overall physical health

Q&A

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Thursday 2:45pm – 3:45pm

**Functional Psychiatry: Getting to the
Root Cause of Depression and Anxiety**

Please scan this QR code on you mobile
or tablet device to access the session feedback survey



Functional Psychiatry: Getting to the R
oot Cause of Depression and Anxiety