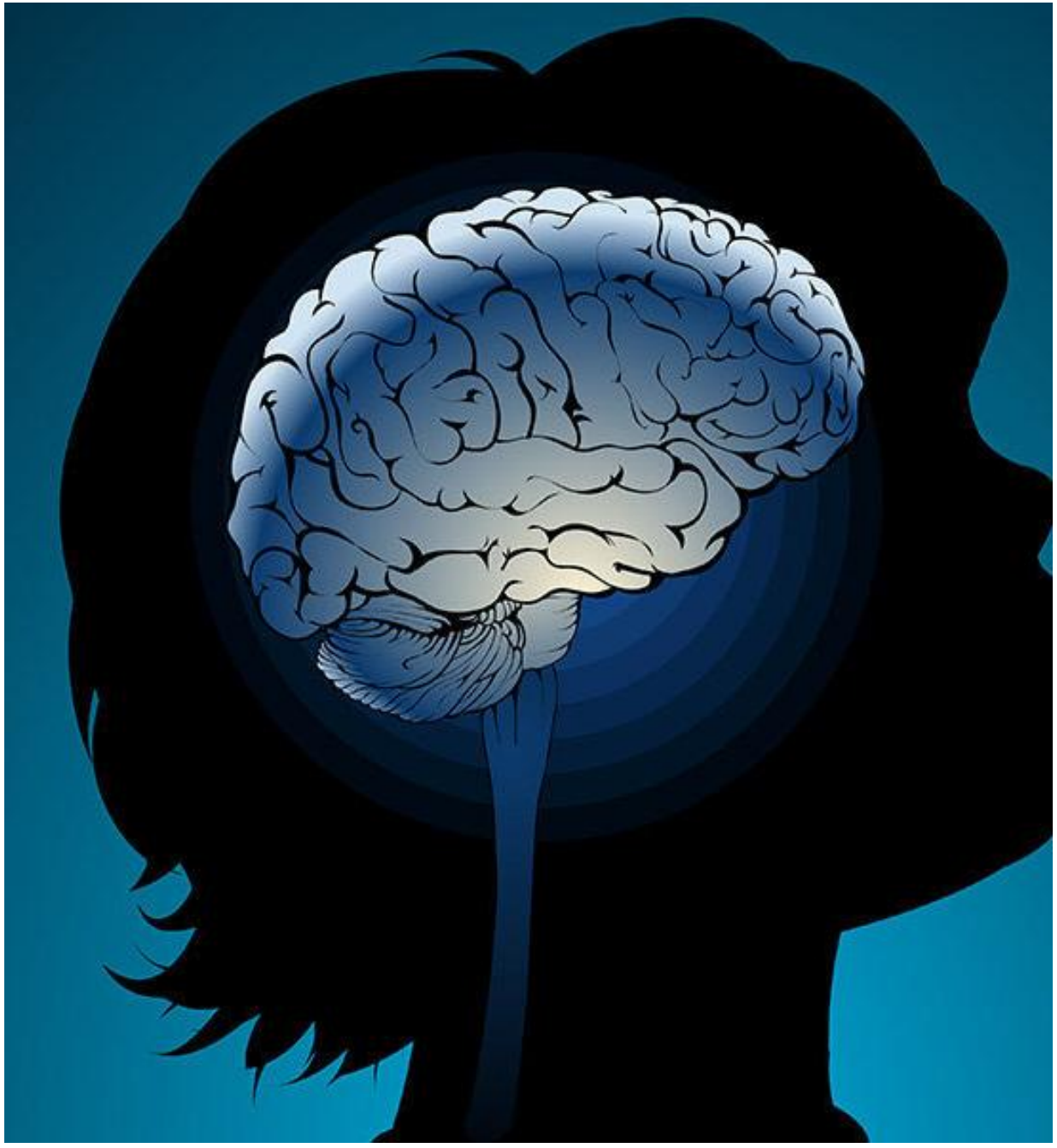


# COMBATING THE ESCALATING MENTAL HEALTH CRISIS HARMING OUR ADOLESCENTS

Debby Hamilton, MD, MPH, IFMCP

# THE ISSUE

# Mental Illness Rates in the UK

- In 2024
  - 1 in 4 adults experiencing a mental health problem annually
- **Young people- aged 16-24, are disproportionately affected**

- https://www.mind.org.uk/about-us/our-policy-work/reports-and-guides/the-big-mental-health-report-2024/

# Mental Illness Rates in the US

- Mental Health among Adults •
  - Among adults aged 18 or older in 2021, 22.8% (or 57.8 million people) had any mental illness (AMI) in the past year.
  - The percentage of adults aged 18 or older with AMI in the past year was **highest among young adults aged 18 to 25** (33.7% or 11.3 million people), followed by adults aged 26 to 49 (28.1% or 28.8 million people), then by adults aged 50 or older (15.0% or 17.7 million people). •
- Among adolescents aged 12 to 17 in 2021
  - 20.1% (or 5.0 million people) had a past year major depressive episode (MDE),
  - 14.7% (or 3.7 million people) had a past year MDE with severe impairment. •
- https://www.samhsa.gov/data/sites/default/files/2022-12/2021NSDUHFFRHighlights092722.pdf (National Institute of Mental Health)

# Treating a Diagnosis versus Treating Symptoms

## Diagnosis

Major Depressive Disorder
Generalized Anxiety Disorder
OCD
Behavioral Disorder
ADHD
Mood Disorder, NOS
Oppositional-Defiant Disorder

## Symptoms of Underlying Disease

- Issues with
  - Depression
  - Anxiety
  - Concentration
  - Memory
  - Cognitive Processing
  - Emotional regulation

# Review of Symptoms Acute vs Chronic vs Intermittent

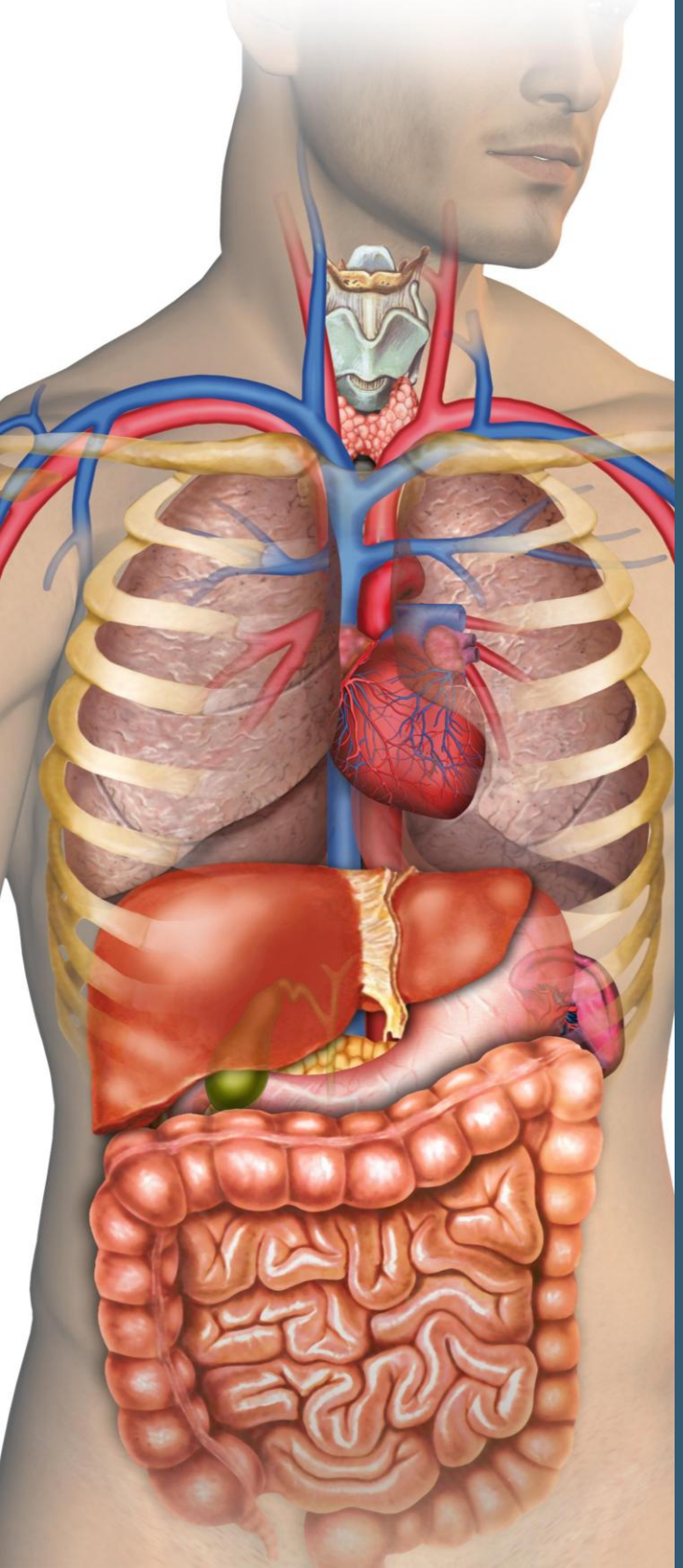
- Fatigue
- Poor endurance
- Pain
- Skin Rashes
- Headaches
- Allergies
- Eating disorders
- Weakness
- Dizziness
- Frequent infections
- Digestive symptoms
- Urinary symptoms
- Sleeping issues
- Neurologic symptoms- numbness/tingling/static shocks
- Sweating
- Cardiac-racing heart, chest pain, etc

- Family History:  mental health, autoimmune, thyroid, etc

# Social/Environmental Causes of Mood Issues

- Family Issues
- Work /School Issues
- Relationship stresses
- Financial Stresses
- Political Stresses
- Technology- Social isolation (amid connection by technology)
- Addiction
- Rapidly changing and uncertain world

- NOT the same world most adults grew up in



# Underlying Physical Causes of Mood Issues

- Nutrition
- Gut-Brain-Microbiome: Digestive issues
- Hypothalamic Pituitary Axis sympathetic overload
- Mitochondrial energy dysfunction
- Hormone imbalance
- Infections
- Immune Imbalance
- Toxin/mold exposure
- Genetics
- Trauma

# UNDERLYING BIOLOGICAL CAUSES, DIAGNOSIS, AND TREATMENT

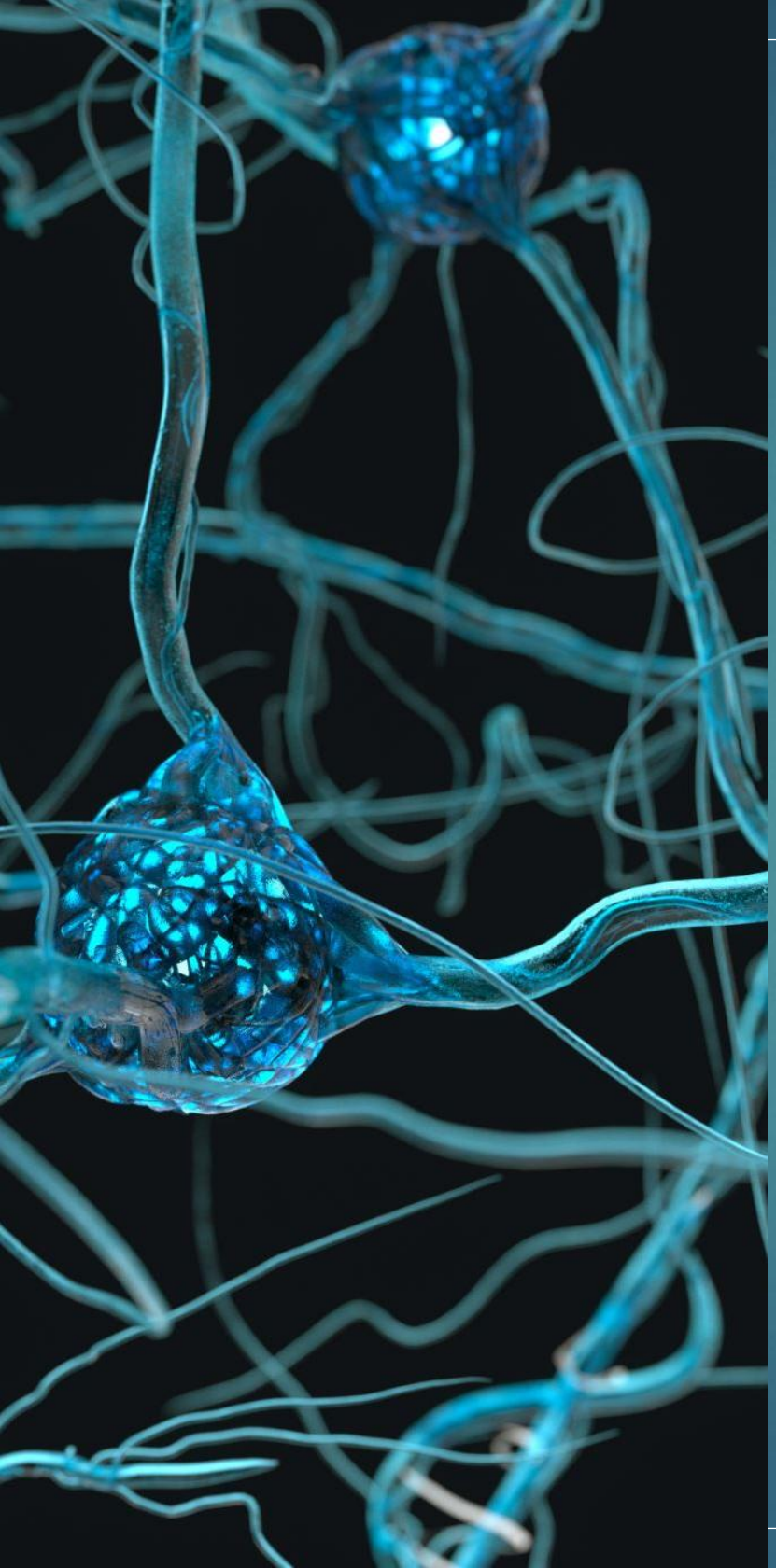
# Nutritional

- Diet:  What they are eating and not eating
- Mental health symptoms plus:
  - Skin issues
  - Nail changes
  - Digestive issues
  - Energy
  - Eating issues

# Nutritional Laboratory Testing



- Nutritional: Blood labs
  - B12
  - Vitamin D
  - RBC zinc or RBC minerals
  - iron panel: ferritin, iron, CBC
- Basic labs: metabolic panel, cholesterol
- Hair test- minerals including some trace minerals
- Organic acid test:
  - Nutrients: B6, B12, folate metabolites, vitamin C, biotin, CoQ10
- Food allergies/sensitivities
- Kryptopyrroles- Mg, Zinc, B6



# Magnesium Support of Mental Health



- Calms neurotransmission by regulating glutamate and GABA
- Modulates the HPA axis and cortisol levels
- Supports synthesis of serotonin and dopamine
- Increases brain-derived neurotrophic factor (BDNF)


- Botturi A. et al. The Role and the Effect of Magnesium in Mental Disorders: A Systematic Review. Nutrients. 2020 Jun 3;12(6):1661.

# Magnesium Malate

- 2 capsules 1 to 2 times daily-  serving size 200 mg
- Dimagnesium malate has malic acid used in the Krebs cycle to make ATP
- malic acid is utilized for energy production in the mitochondria and magnesium is simultaneously drawn through the cell membrane into the mitochondria, where it is most needed.

| SYMPTOMS OF ZINC DEFICIENCY | |
|---|---|
| **Marginal** | **Severe** |
| Developmental Delays<br>Loss of Taste & Appetite<br>Greater Risk for Infections<br>Mental Lethargy & Depression<br>Behavioral Problems | Stunted Growth<br>Reproductive Problems<br>Gastrointestinal Dysfunction<br>Hair Loss, Eye & Skin Lesions<br>Poor Wound-Healing<br>Neurological Disorders |

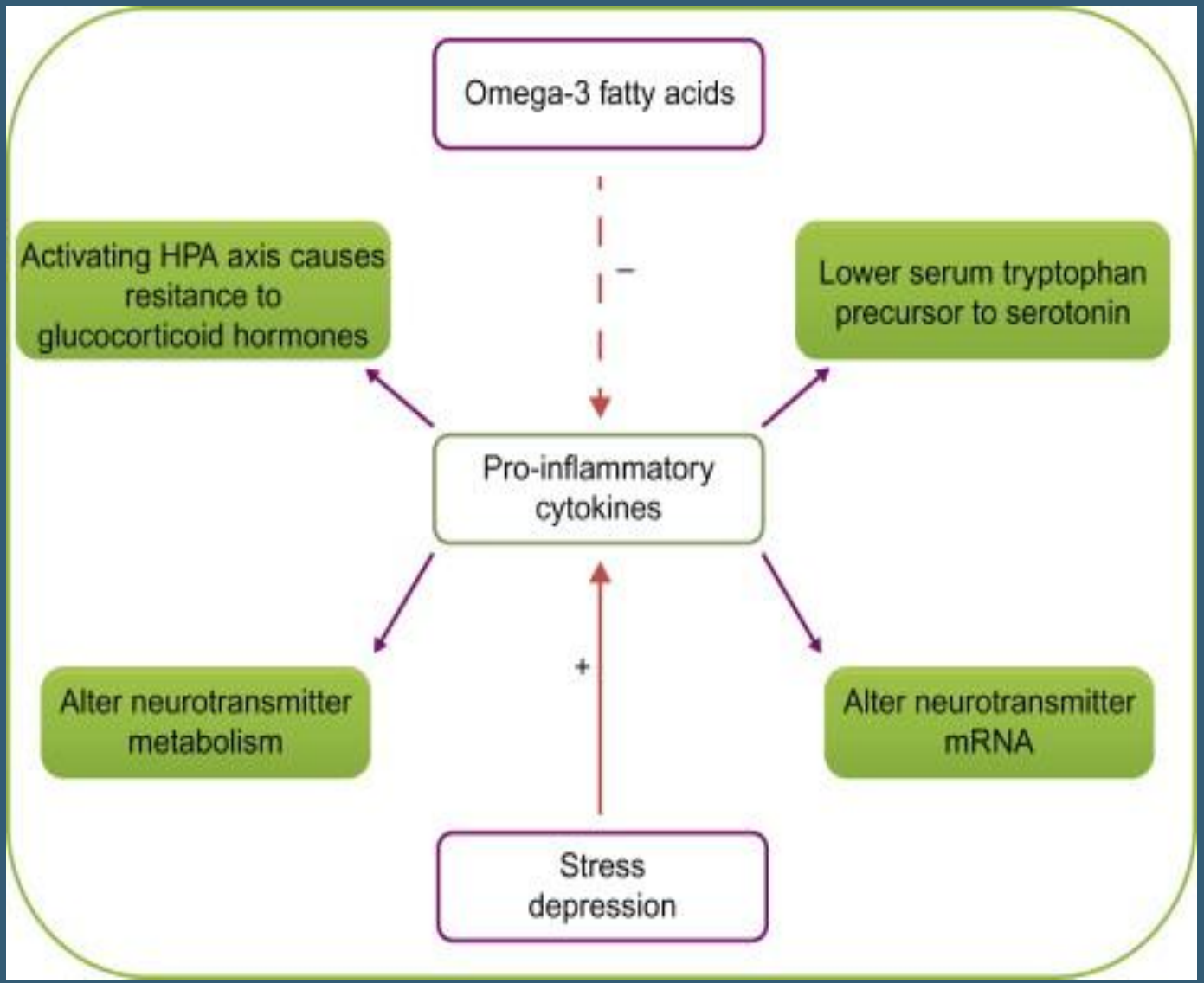
# Zinc: "No Zinc, No Think"

# Zinc Bisglycinate chelate

- 1 capsule 50 mg take with food away from other minerals
- Glycinate form highly bioavailable
- Zinc bound to glycine which has additional mood and sleep support benefits
  - Glycine calming neurotransmitter and support serotonin and sleep

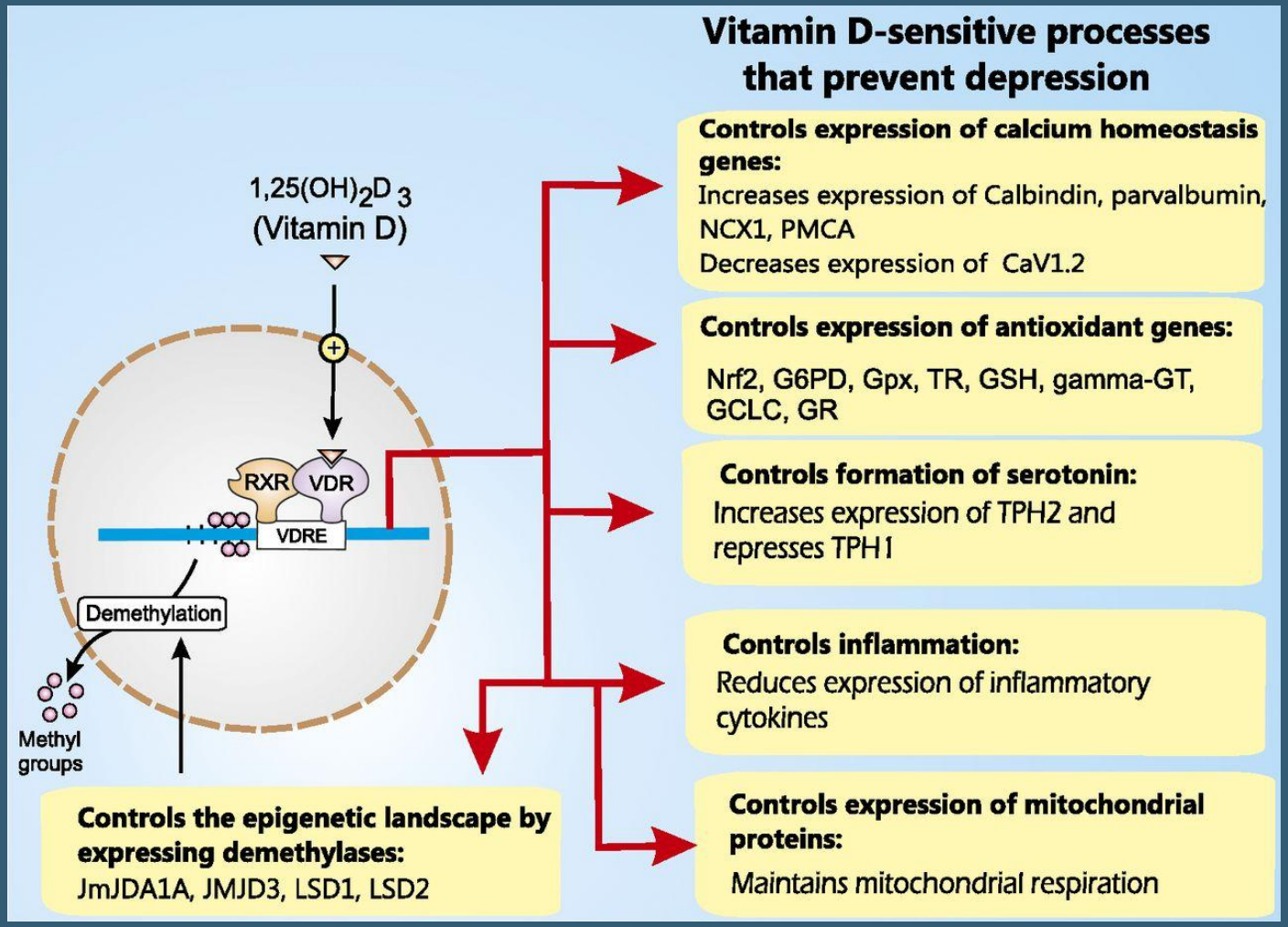
# Role of Omega-3 Fatty Acids in Brain and Neurological Health with Special Reference to Clinical Depression. Chandola M, et al.

Omega-3 Fatty Acids in Brain and Neurological Health
2014, Pages 163-179

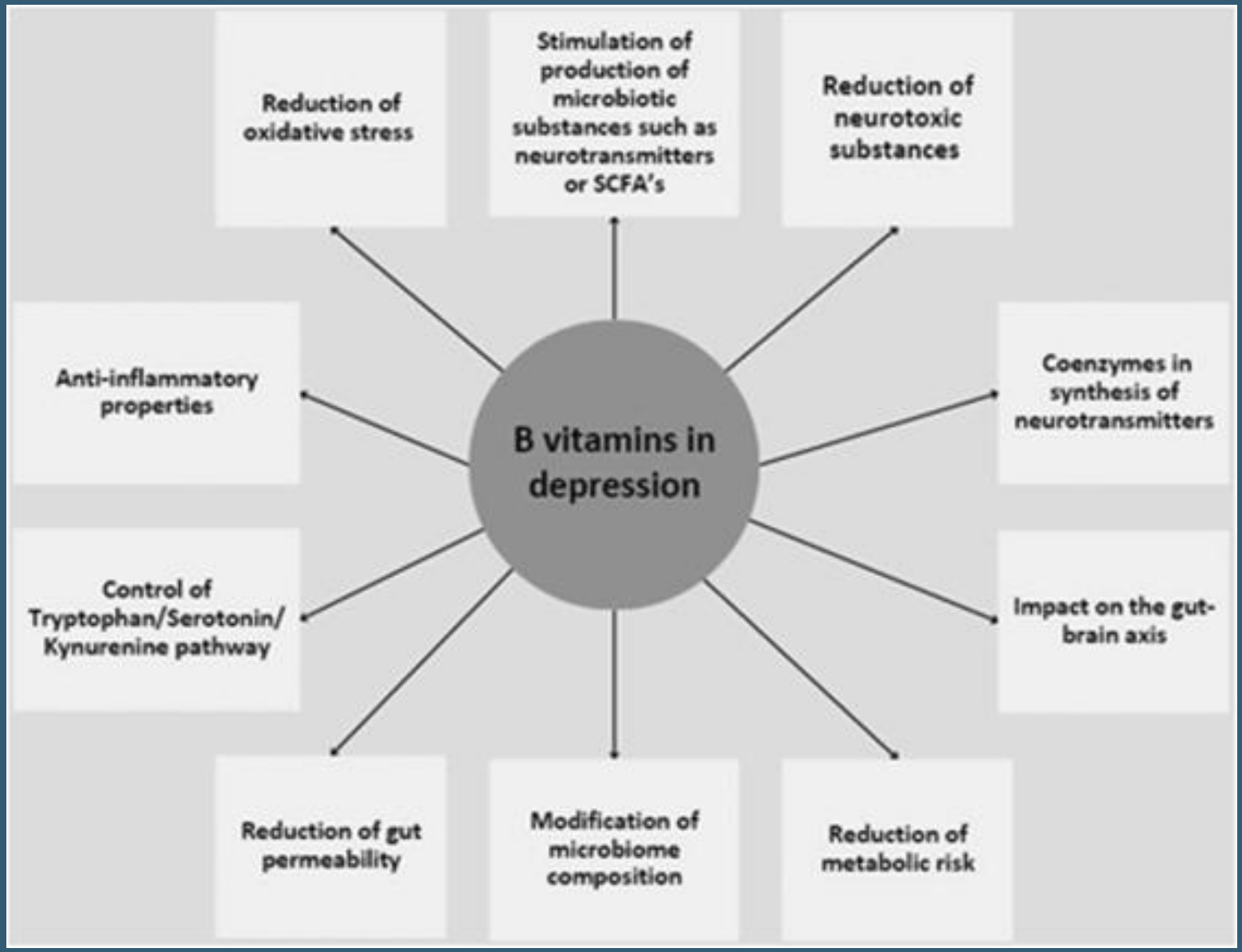


# Vitamin D and Depression: Cellular and Regulatory Mechanisms

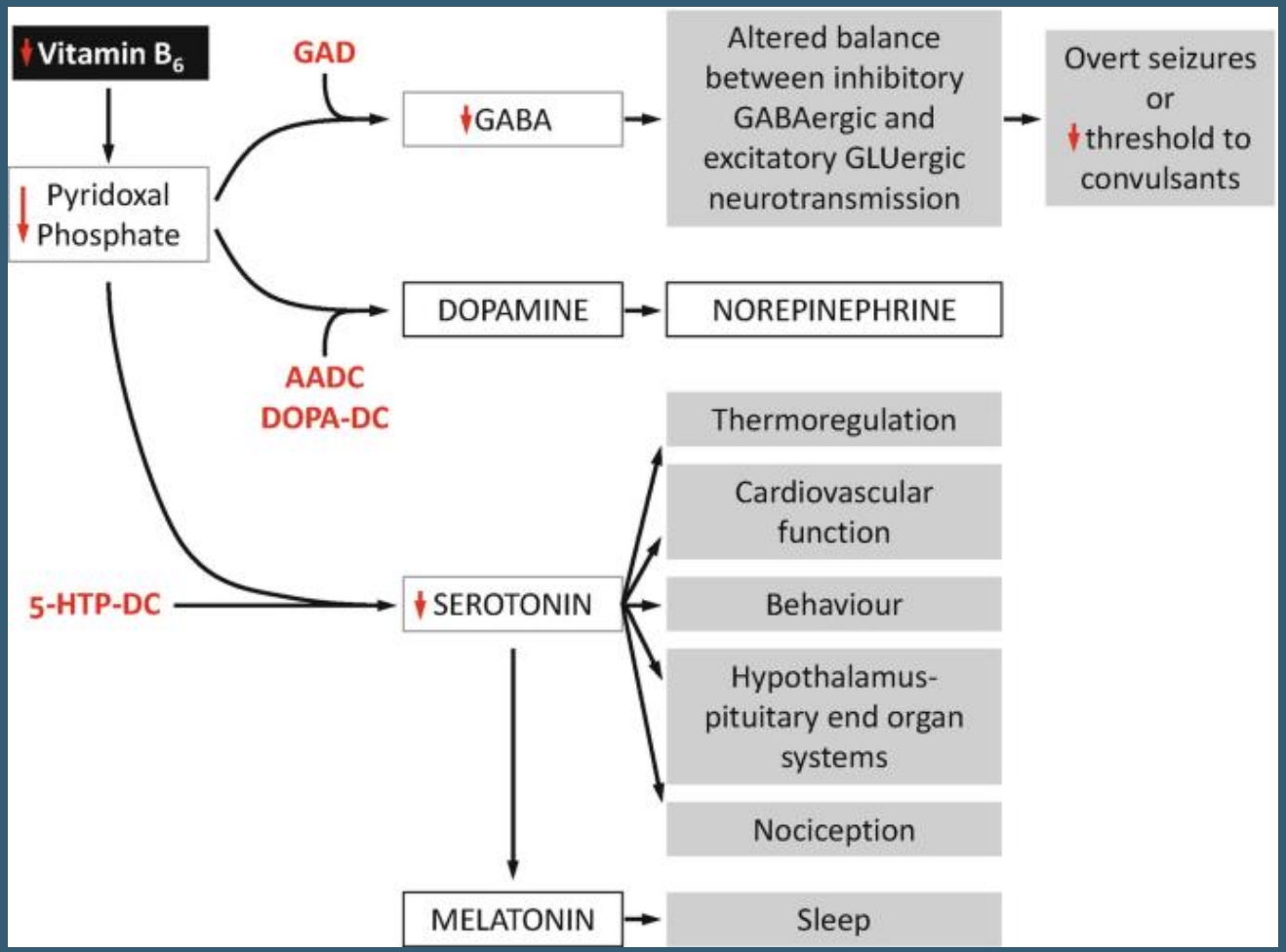
Michael J. Berridge. Pharmacological Reviews April 2017, 69 (2) 80-92;



# B Vitamins and Mood/Neurologic Issues



# B6 in active form Pyridoxal-5-Phosphate- Neurotransmitter synthesis

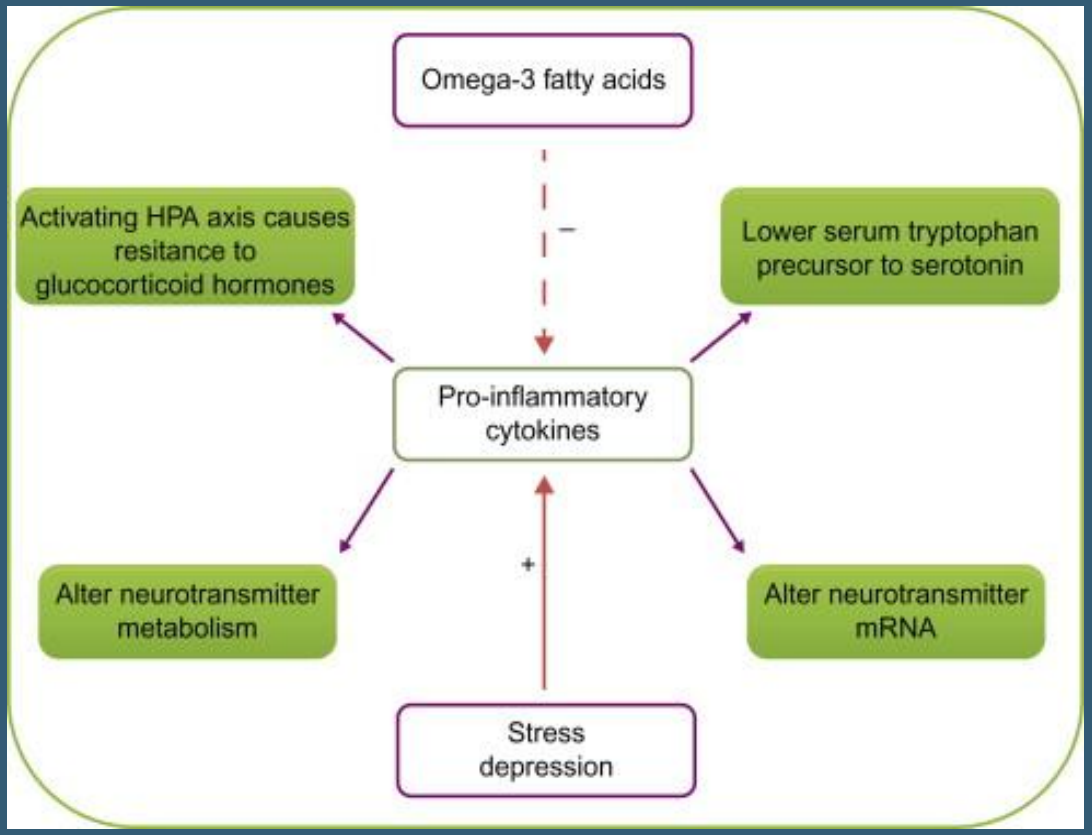


# Methylcomplete B complex: vitamins and cofactors needed to support methylation cycle

- Methylcomplete:  2 capsules
- Take in am or at lunch- gives energy
  - Vitamin B2-Riboflavin  20 mg
  - Vitamin B6 active form- P5P pyridoxal-5 Phosphate  20 mg
  - Folate-methylfolate  400 mcg
  - Vit B12-methylcobalmin  100 mcg
  - Creatine monohydrate  500 mg
  - Betaine Anhydrous (TMG- trimethylglycine) 500 mg

Role of Omega-3 Fatty Acids in Brain and Neurological Health with Special Reference to Clinical Depression.

Chandola M, et al. Omega-3 Fatty Acids in Brain and Neurological Health
2014, Pages 163-179




NutraMedix

# Antarctic Krill Oil:
# Dose: 1-2 capsules daily

- Anti-inflammatory
- Cardiovascular support
- Joint/muscle support
- Mood regulation
- Ocular support
- Neurologic support/cognitive support
- Skin health
- TBI repair

- Avoid if allergic to shellfish

GABA
TELEPSYCHIATRY

# PSYCHIATRIC SYMPTOMS OF VITAMIN-D DEFICIENCY

SUICIDALITY

ANXIETY

INATTENTION

INTRUSIVE THOUGHTS

DEPRESSED MOOD

POOR CONCENTRATION

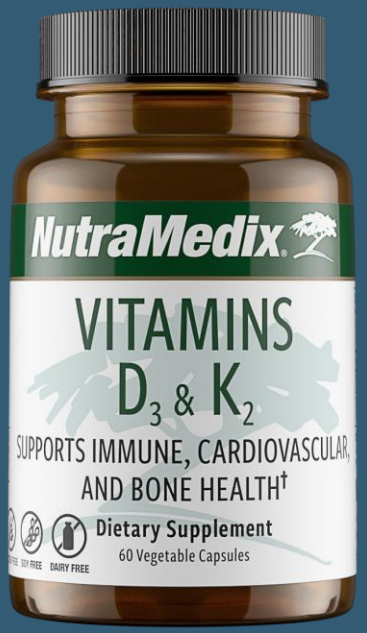
SLEEP DISTURBANCE

PANIC SYMPTOMS

www.gabapsychiatrist.com +1(833)312-4222

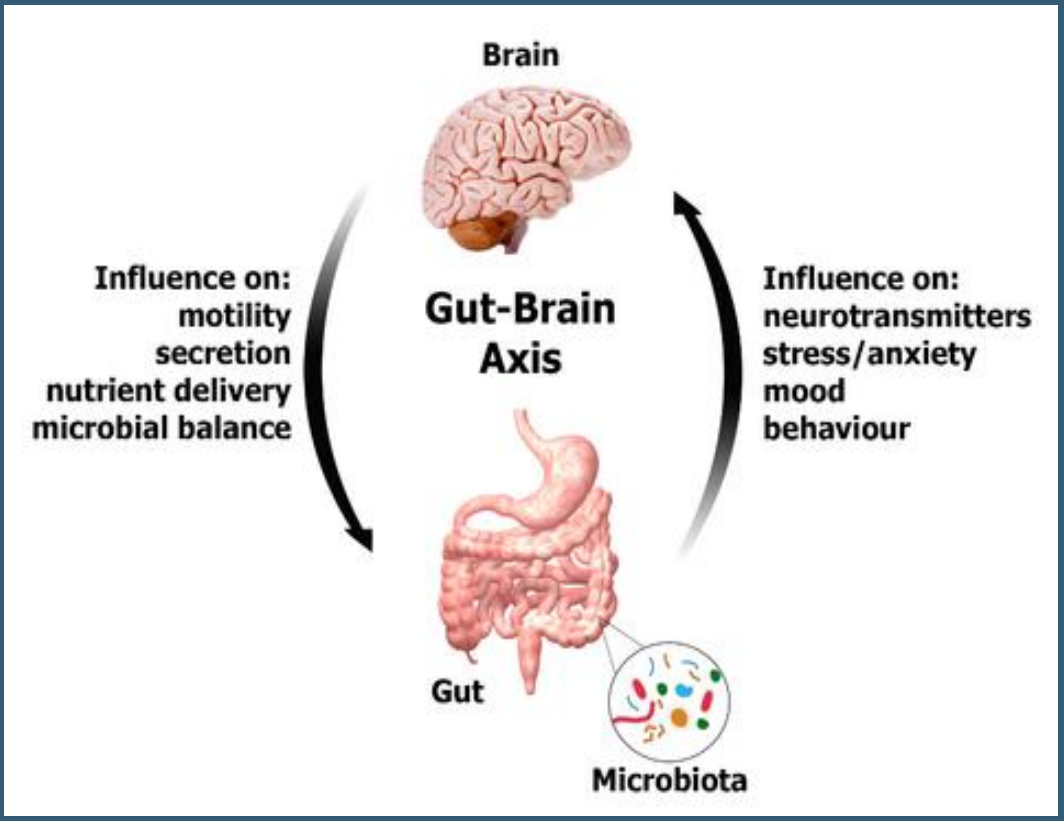
# Vitamin D3 K2

- 1 capsule daily
  - Vitamin D3:  125 mcg (5,000 IU's)
  - Vitamin K2:  150 mcg  (menaquinone form)




- Do not take with coumadin (warfarin) blood thinner-risk of bleeding other blood thinners okay

# Influence of Microbiome on Mood Psychobiotics



# General Nutritional Support for mood issues

- Multi-vitamin with active forms of B vitamins and minerals
- Zinc glycinate 25-50 mg
- Magnesium malate 200 mg +
- Vitamin D with K
- Omega 2 fatty acids: Antarctic Krill oil increased absorption of DHA/EPA plus astaxanthin and phospholipids
- Probiotic- mood support
- B6 in form of P5P 50 mg
- B complex-
  - MethylComplete 2-4 capsules

NutraMedix

# Adrenal Stress

Adolescents with mood issues often constant hypervigilant fight or flight mode

Difficult to treat mood issues

Without balancing cortisol and sympathetic hormones

# Physiologic Impact of Chronic Stress and Anxiety on the Body

- Lowers Brain Derived Neurotropic Levels (BDNF)
- Increased cortisol & inflammation levels
- Serotonin depletion
- Lower GABA levels
- Reduced metabolic functioning with elevated insulin and blood sugar
- Reduced mitochondrial function due to the higher inflammation and oxidative stress levels
- People end up in constant flight or fight mode

# Adrenal Support Options

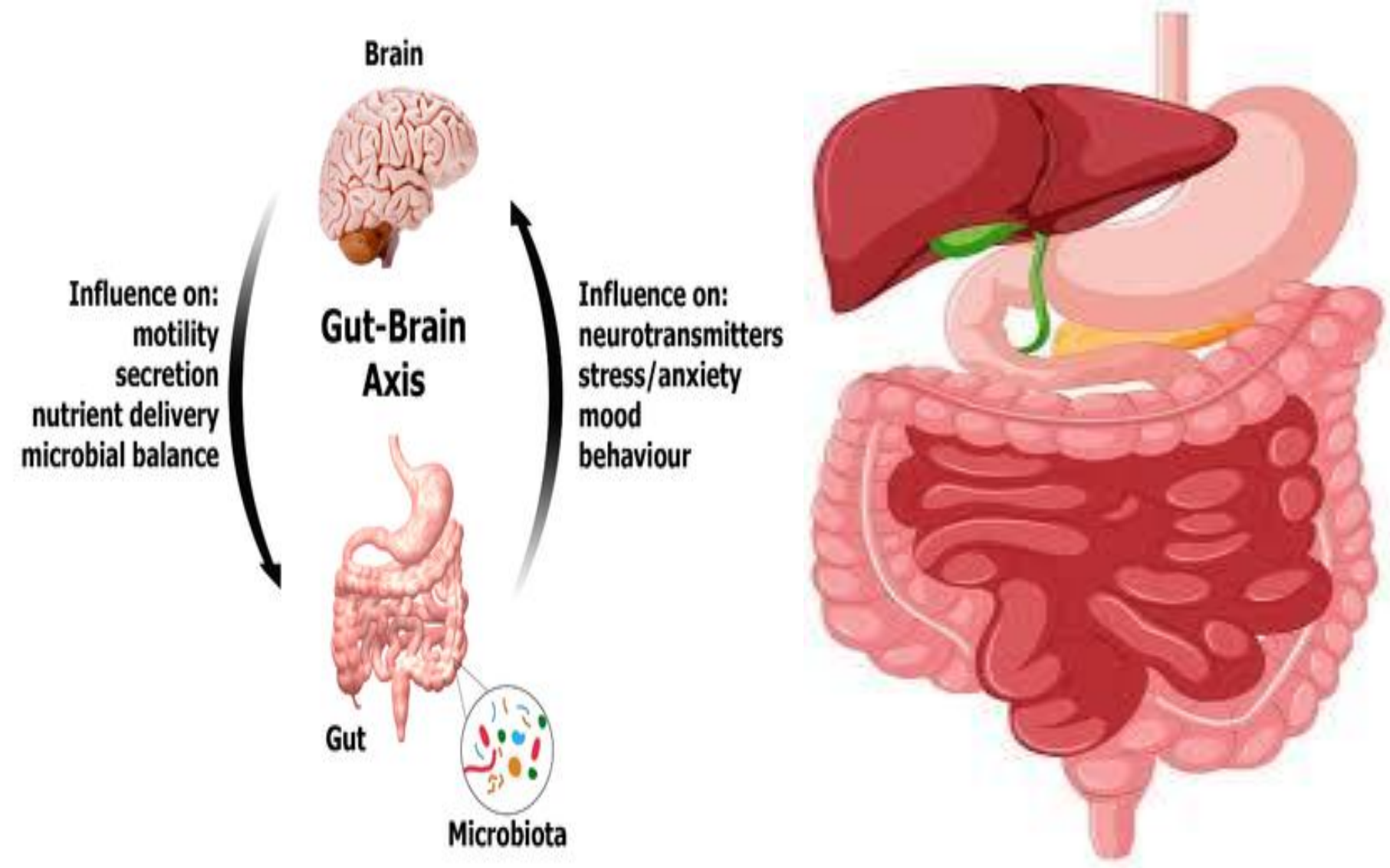


- B-vitamins: Methylcomplete
- Vitamin C: 1000 mg plus
- Adaptogens:
  - Ashwagandha: Lowers cortisol, decrease depression and anxiety
  - Adrenal Formula: Astragalus, Schisandra, Ginseng, Rhodiola, Holy Basil
- Phosphatidylserine: lowers cortisol and anxiety
- Calming herbs: Lavender, Magnolia, Hops, Passion Flower, Skullcap (American), Valerian, Lemon Balm, Chamomile
- Essential Oils: Immediate effects: citrus such as mandarin, lemon, lemon balm

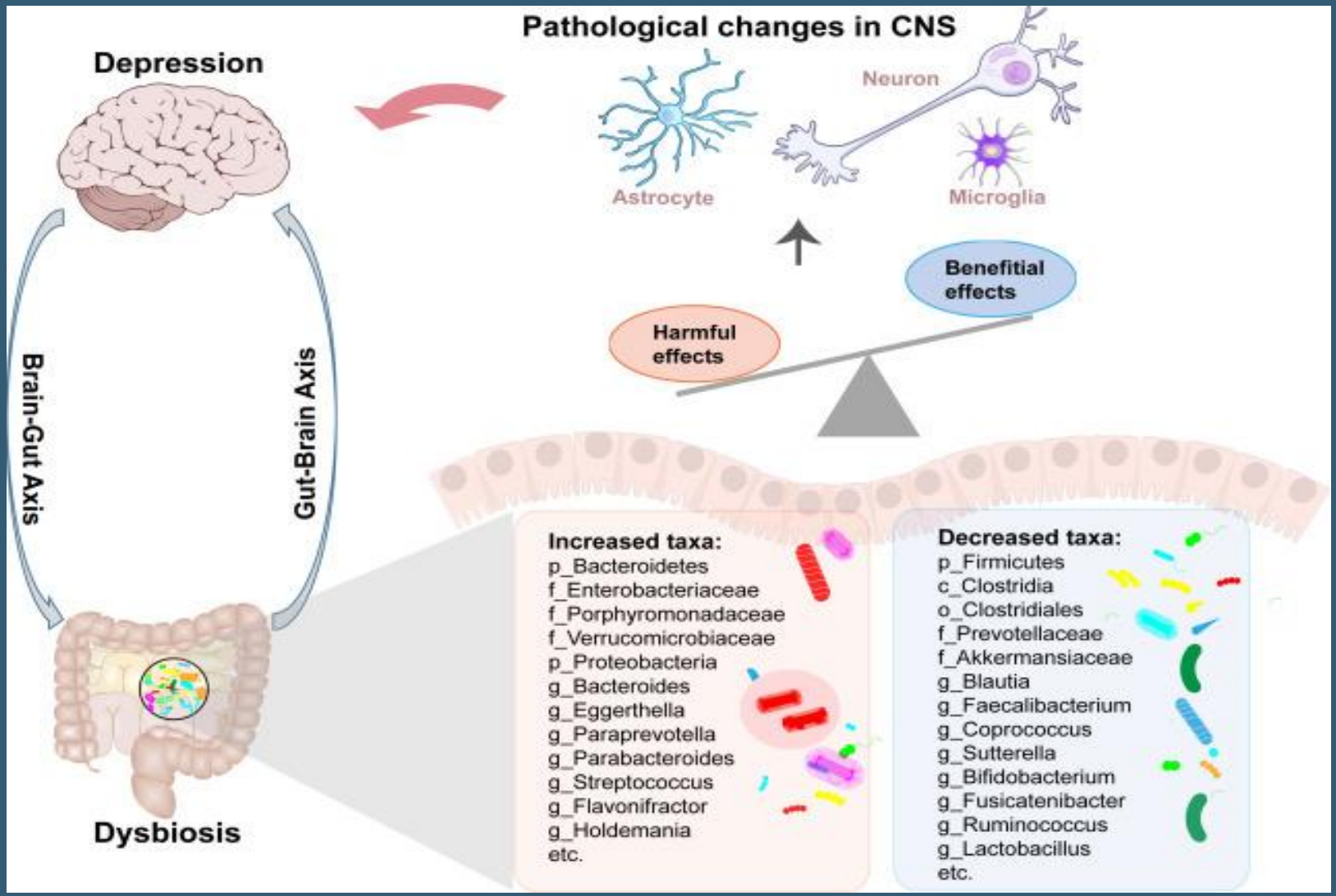
# Adrenal

- Astragalus root extract (Astragalus mongholicus)
- Rhodiola root extract (Rhodiola rosea)
- American Ginseng root extract (Panax quinquifolius)
- Schisandra berry extract (Schisandra chinensis)

# Gastrointestinal Influence of Microbiome on Mood



Liu L. et al. Gut microbiota and its metabolites in depression: from pathogenesis to treatment. EBioMedicine. 2023 Apr;90:104527.



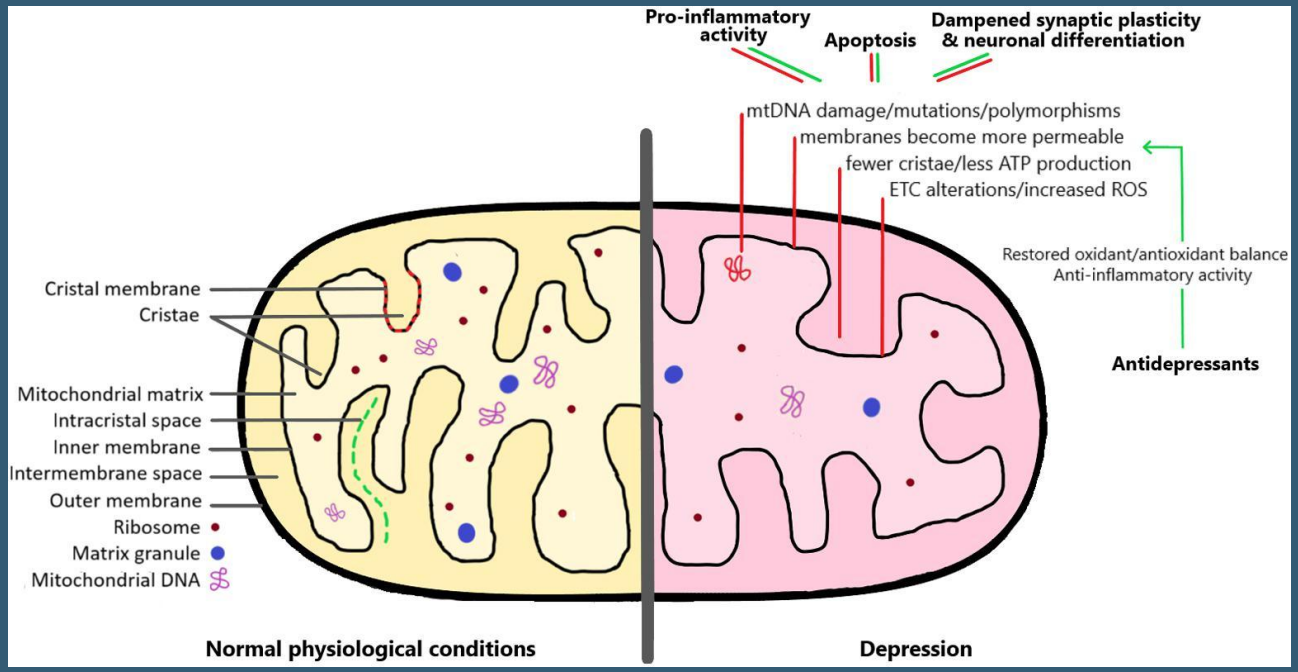
# Metabolic



- Mitochondrial Dysfunction
- Thyroid Dysfunction

# Mitochondrial Dysfunction Symptoms and Testing

- Symptoms
  - Poor Endurance
  - Poor exercise recovery
  - Low muscle tone:  hands, mouth
  - Attention deficits
  - Depression/mood issues
  - Slow processing
  - Fatigue
  - Constipation:  slow GI motility
- Testing:
  - Organic acid testing
  - Blood- lactate, pyruvate, CoQ10, acetyl carnitine panels
  - MitoSwab- genetic
  - Mitochondrial function testing




Mood and Mitochondrial Dysfunction

Allen J. et al. Mitochondria and Mood: Mitochondrial dysfunction as a key player in the manifestation of depression. Front. Neuroscience. 2018

## Medications That Cause Mitochondrial Dysfunction

Mitochondrial dysfunction is to blame for many toxicities caused by drugs and may explain the side effects of many medications. Even so, the Food and Drug Administration doesn't require mitochondrial toxicity testing for new drug approval.

Drugs can damage mitochondria in two ways: directly or indirectly. Medications can directly inhibit mtDNA transcription of electron transport chain complexes. Through other mechanisms, medications damage electron transport chain components, as well as block enzymes required for mitochondrial function.[64]

Indirect mitochondrial damage caused by medications occurs through the production of free radicals, causing a decrease in endogenous antioxidants such as glutathione. Medications may also deplete levels of nutrients needed for creating or proper functioning of mitochondrial enzymes or electron transport chain complexes.[64]

### Medications Documented to Cause Mitochondrial Damage[64]

| Drug Class | Drugs |
|---|---|
| Alcoholism medications | Disulfiram (Antabusem) |
| Analgesic (for pain) and anti-inflammatory | Aspirin, acetaminophen (Tylenol®), diclofenac (Voltaren®, Voltarol®, Diclon®, Dicloflex,® Difen, and Cataflam®), fenoprofen (Nalfon®), indomethacin (Indocin®, Indocid®, Indochron E-R® Indocin-SR®), Naproxen (Aleve®, Naprosyn®) |
| Anesthetics | Bupivacaine, lidocaine, propofol |
| Angina medications | Perhexiline, amiodarone (Cordarone®), Diethylaminoethoxyhexesterol (DEAEH) |
| Antiarrhythmic (regulates heartbeat) | Amiodarone (Cordarone®) |
| Antibiotics | Tetracycline, antimycin A |
| Antidepressants | Amitriptyline (Lentizol), amoxapine (Asendis), citalopram (Cipramil), fluoxetine (Prozac, Symbyax, Sarafem, Fontex, Foxetin, Ladose, Fluctin, Prodep, Fludac, Oxetin, Seronil, Lovan) |
| Antipsychotics | Chlorpromazine, fluphenazine, haloperidol, risperidone, quetiapine, clozapine, olanzapine |
| Anxiety medications | Alprazolam (Xanax®), diazepam (valium, diastat) |
| Barbiturates | Amobarbital (Amytal®), aprobarbital, butabarbital, butalbital (Fiorinal®), hexobarbital (Sombulex®), methylphenobarbital (Mebaral®), pentobarbital (Nembutal®), phenobarbital |
| (Luminal®), primidone, propofol, secobarbital (Seconal®), Talbutal®), thiobarbital | Mitomycin C, profiromycin, adriamycin (also called doxorubicin and hydroxydaunorubicin and included in the following chemotherapeutic regimens – ABVD, CHOP, and FAC) |
| Cholesterol medications | Statins – atorvastatin (Lipitor®, Torvast®), fluvastatin (Lescol®), lovastatin (Mevacor®, Altocor®), pitavastatin (Livalo®, Pitava®), pravastatin (Pravachol®, Selektine®, Lipostat®), rosuvastatin (Crestor®), simvastatin (Zocor®, Lipex®) bile acids – cholestyramine (Questran®), clofibrate (Atromid-S®), ciprofibrate (Modalim®), colestipol (Colestid®), colesevelam (Welchol®) |
| Cancer (chemotherapy) medications | Mitomycin C, profiromycin, adriamycin (also called doxorubicin and hydroxydaunorubicin and included in the following chemotherapeutic regimens – ABVD, CHOP, and FAC) |
| Dementia | Tacrine (Cognex®), Reminyl® |
| Diabetes medications | Metformin (Fortamet®, Glucophage®, Glucophage XR, Riomet), troglitazone, rosiglitazone, buformin |
| HIV/AIDS medications | Atripla®, Combivir®, Emtriva®, Epivir® (abacavir sulfate), Epzicom®, Hivid® (ddC, zalcitabine), Retrovir® (AZT, ZDV, zidovudine), Trizivir®, Truvada®, Videx® (ddI, didanosine), Videx® EC, Viread®, Zerit® (d4T, stavudine), Ziagen®, Racivir® |
| Epilepsy/Seizure medications | Valproic acid (Depacon®, Depakene®, Depakene syrup, Depakote®, depakote ER, depakote sprinkle, divalproex sodium) |
| Mood stabilizers | Lithium |
| Parkinson's disease medications | Tolcapone (Tasmar®, Entacapone (COMTan®, also in the combination drug Stalevo®) |

# Medicines associated with Mitochondrial Dysfunction

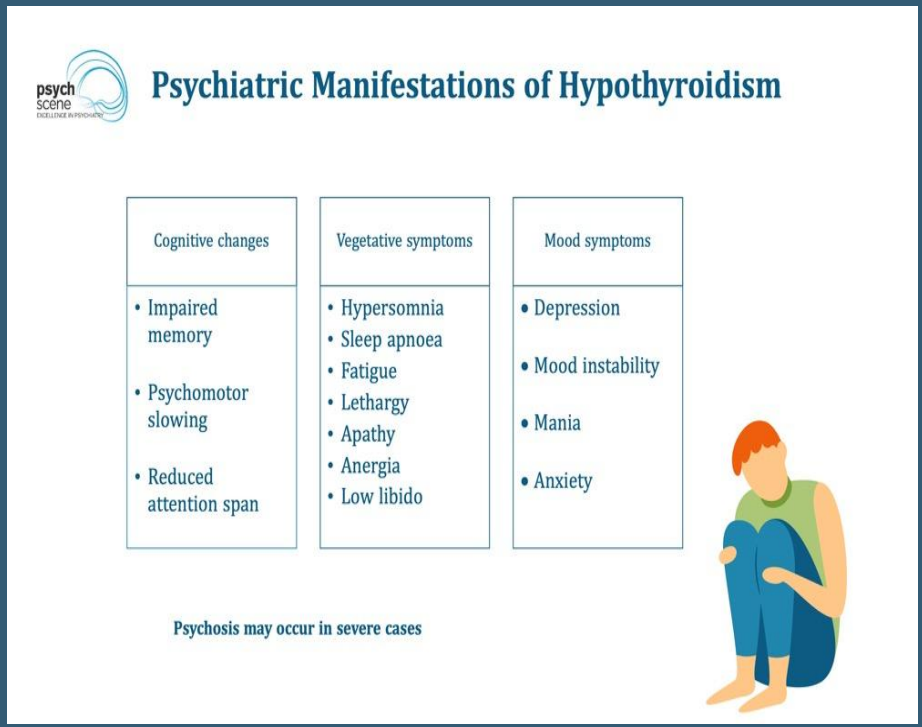
# Thyroid Dysfunction on Mood

Hypothyroid can present as depression

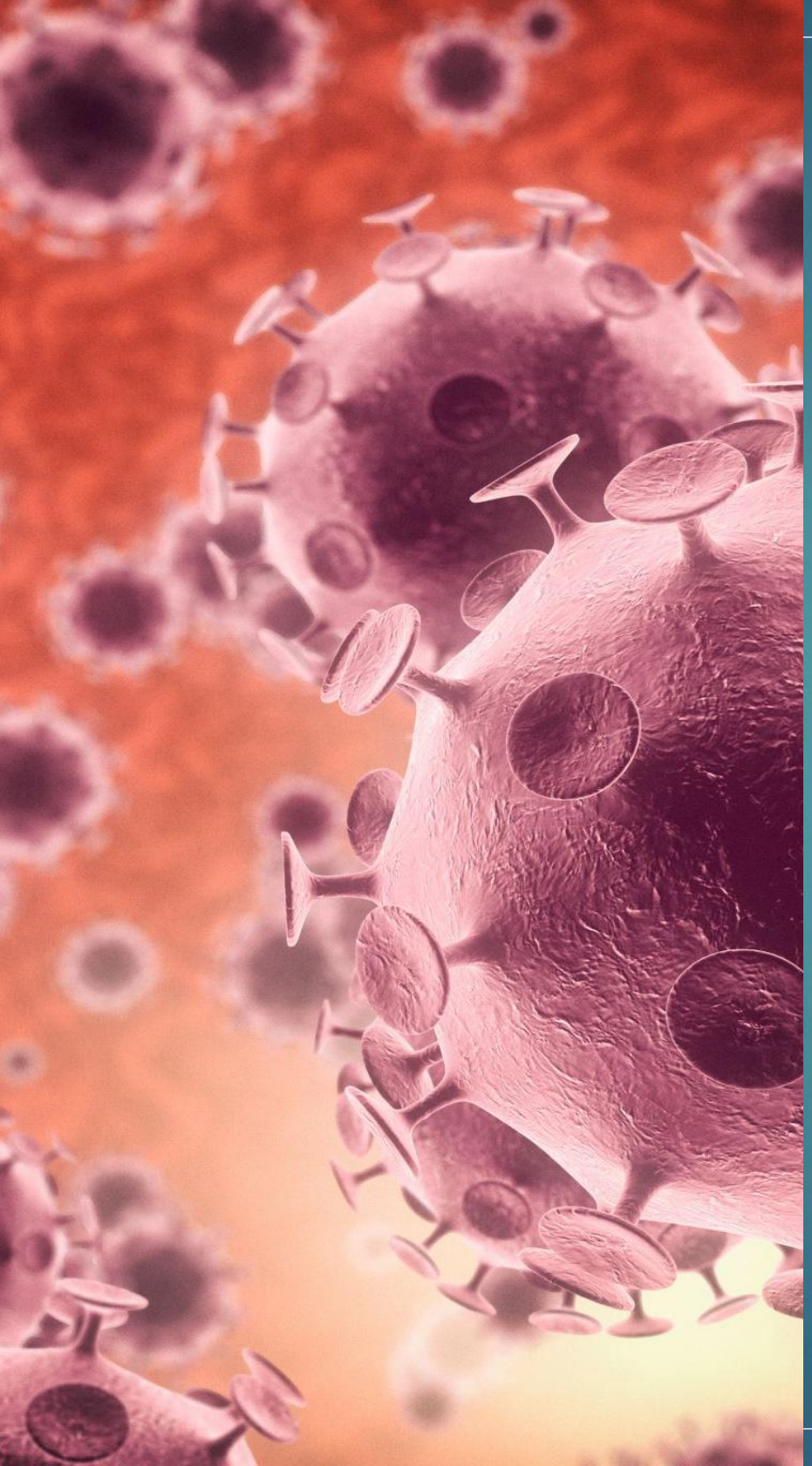
Hyperthyroid can present as ADHD and anxiety

Symptoms:  fatigue, constipation, dry skin, slow cognition

Lab testing:  TSH, free T3, free T4, reverse T3, thyroid autoantibodies




Singh B, Sundaresh V. Thyroid Hormone Use in Mood Disorders: Revisiting the Evidence. J Clin Psychiatry. 2022 Aug 15;83(5):22ac14590.



# Infections

# Inflammation

# Immune System Dysfunction

1. Presence of OCD and/or a tic disorder, as defined by the *DSM-IV-R* or *DSM-5*.

2. Symptom onset in children aged 3 years to prepuberty. Symptoms can include emotional lability, personality changes, separation anxiety, age-inappropriate behaviors, and noticeable handwriting decline.

3. Abrupt and severely dramatic onset of symptoms, within days to a week. Symptoms may also exhibit relapsing-remitting fluctuations.

4. Temporal relationship between group A streptococcal infection and symptom onset and exacerbation.

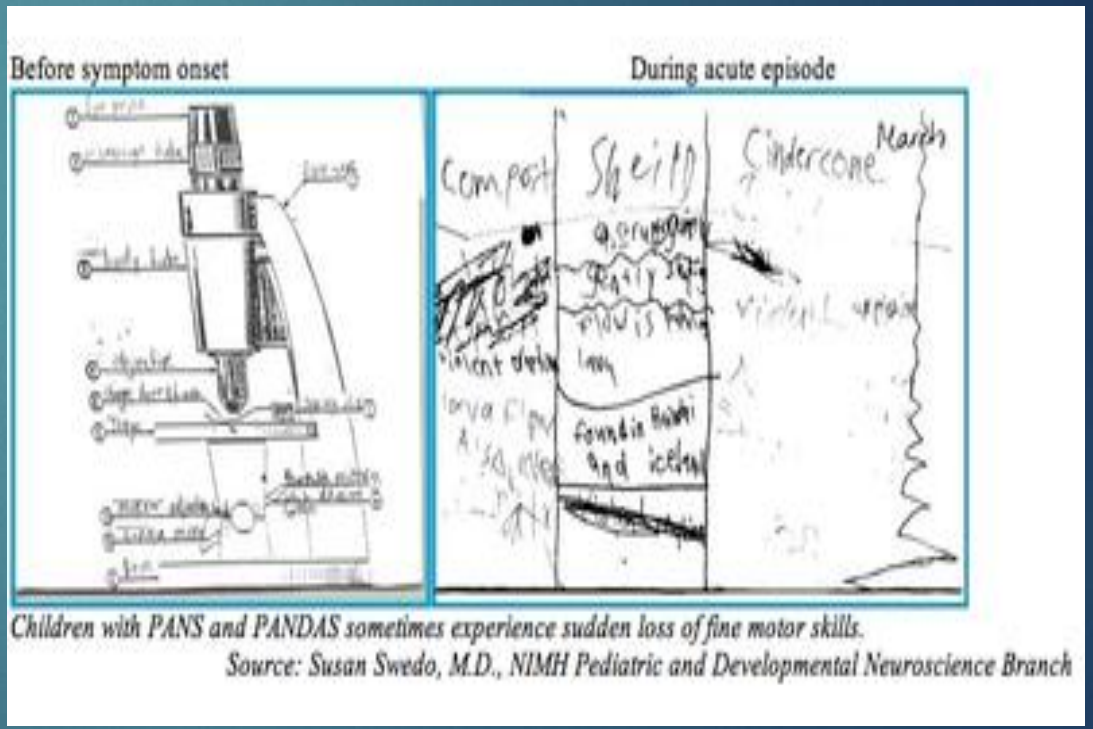
5. Neurologic abnormalities shown upon examination, most commonly as motoric hyperactivity and choreiform movements.

# PANS/PANDAS: Acute Onset Basal Ganglia Autoimmune Encephalitis

# Causes of PANS/PANDAS

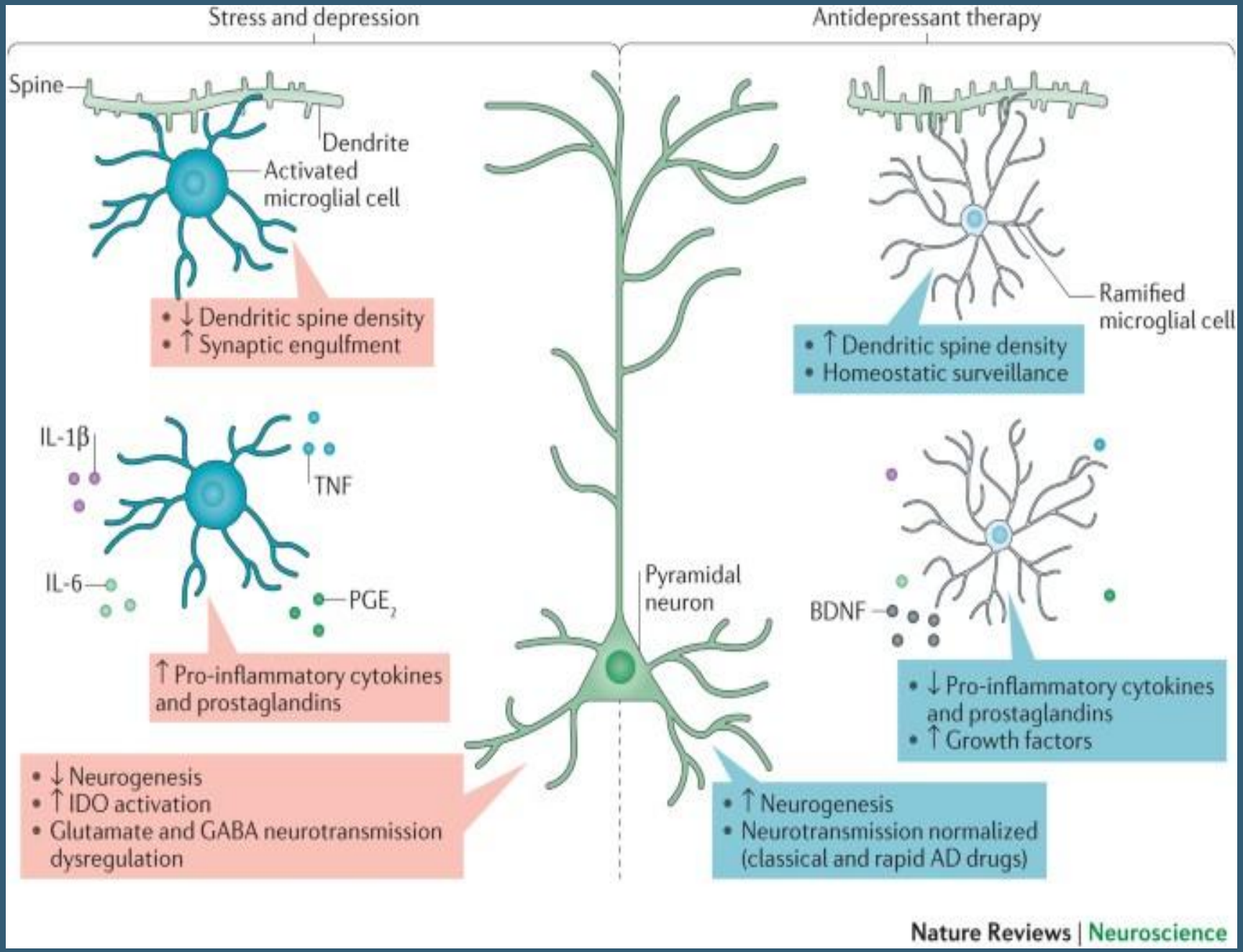


- Strep:  consider throat infections, perianal strep, dysbiotic strep species
- Staph: sinus infections
- Candida
- Mycoplasma
- Lyme
- Bartonella
- Viruses
- Toxins
- Mold




*Children with PANS and PANDAS sometimes experience sudden loss of fine motor skills.*
*Source: Susan Swedo, M.D., NIMH Pediatric and Developmental Neuroscience Branch*

Wohleb, E., Franklin, T., Iwata, M. *et al.* Integrating neuroimmune systems in the neurobiology of depression. *Nat Rev Neurosci* **17**, 497–511 (2016).

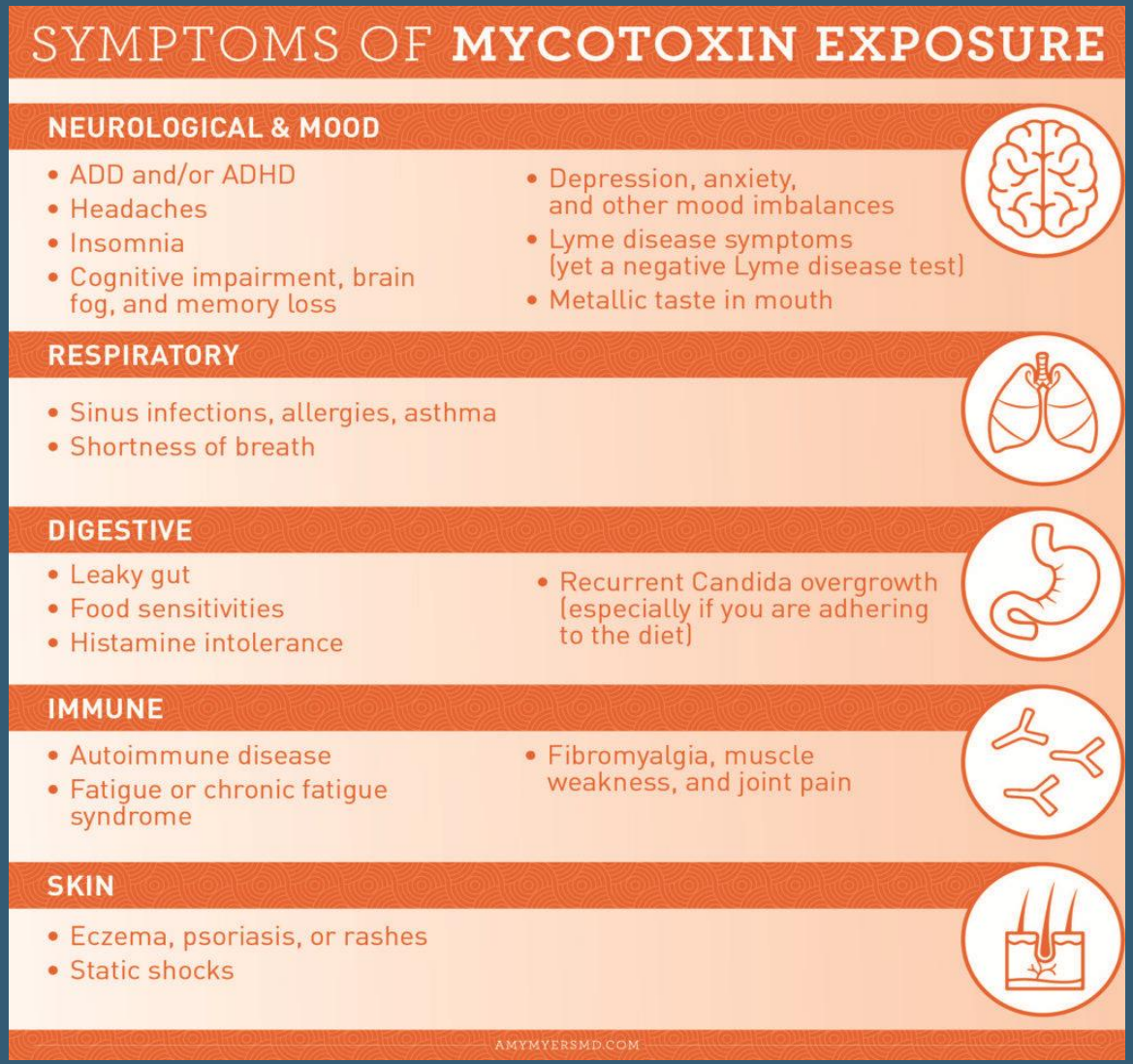



- Nonspecific symptoms with mood symptoms

- Testing:
  - Environmental toxin panels
  - Hair test
  - Urine challenge tests
  - Mold testing
  - Glyphosate testing

# Mycotoxin Exposure

https://www.amymyersmd.com/article/toxic-mold



# Effects of Mycotoxins on Child Development. Kadan F. Aral N. 2021. 14(5):770-781.

- Pregnancy Exposure:
  - Low birth weight: IUGR
  - Congenital anomalies
  - Neural tube defects
- Infancy Exposure
  - Growth retardation
  - Immune system damage
  - Cognitive developmental delay
  - Gastrointestinal illness
- Child and Adolescent Exposure
  - Developmental delay
  - Cognitive and neurological problems

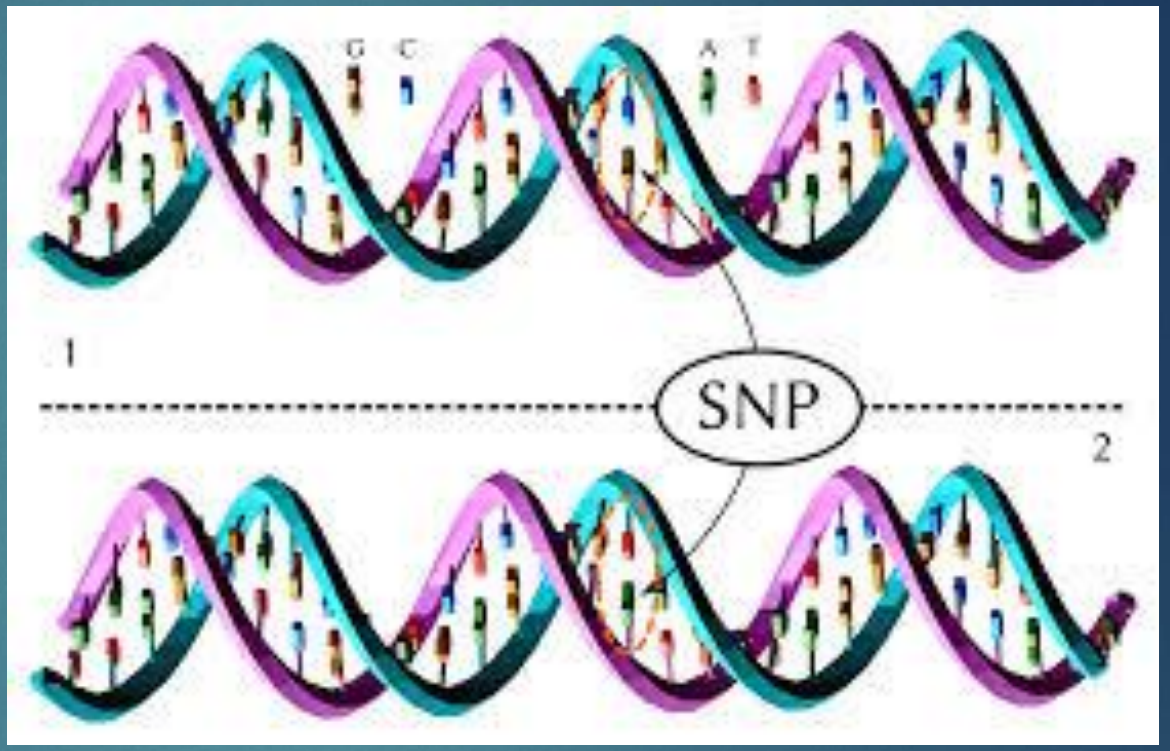
# Detoxification: Formulas to help remove toxins from the body

- **Algas**: Chondracanthus chamissoi extract- Red seaweed
- **Sealantro**: Mixture of chlorella, cilantro, and Chondracanthus chamissoi extract (in Algas)
- **Binder Plus capsules**: Mixture of activated charcoal, zeolite, inulin, aloe vera leaf, bentonite clay, fulvic minerals, and chitosan (from mushrooms so no risk of seafood allergy)

# Burbur-Pinella (Desmodium molliculum leaf and Pimpinella spp stems- Anise)

- Primary detoxification formula
- Primary herx prevention and treatment
- Herx:  may use every 10 min for acute herx symptoms
- Liver, kidney, lymph, ground matrix, nervous system, brain, spinal, peripheral nerves nervous system

# Genetics



# Issues with Genetic SNP's and Mood and Behavioral Issues

## Genomics panels
## Medication and metabolism panels

- Poor methylation (MTHFR, Folate and B12 cycle SNP's)
- Poor detoxification (GST)
- Problem with organophosphates (PON1)
- Glutamate issues (GAD): excitotoxicity
- Low vitamin D (VDR)
- Mood issues from neurotransmitters (COMT,GAD, MAO)
- Neuroplasticity- cognition, mood- BDNF
- Microbiome issues and difficulty maintaining Bifidobacterium (FUT2)
- Emotional regulation: ANK3 (sodium channel) and CACNAIC (calcium channel)- excitatory signaling in the brain

# Genetic SNP's for Excitatory Signaling in the Brain- Important for Mood Regulation

- ANK3- Sodium Channel
  - Associated with bipolar disorder, schizophrenia, autism spectrum disorder, and intellectual disability
- CACNAIC- Calcium channel
  - Associated with major psychiatric disorders- Schizophrenia, bipolar, MDD, ASD, migraines, cardiac issues

- Natural support:  Magnesium ( Calcium channel), lithium, omega 3 fatty acids


- Dickerson MR, Reed J. Pharmacogenetic testing may benefit people receiving low-dose lithium in clinical practice *J Am Assoc Nurse Pract*. 2023;

# Natural Support for BDNF

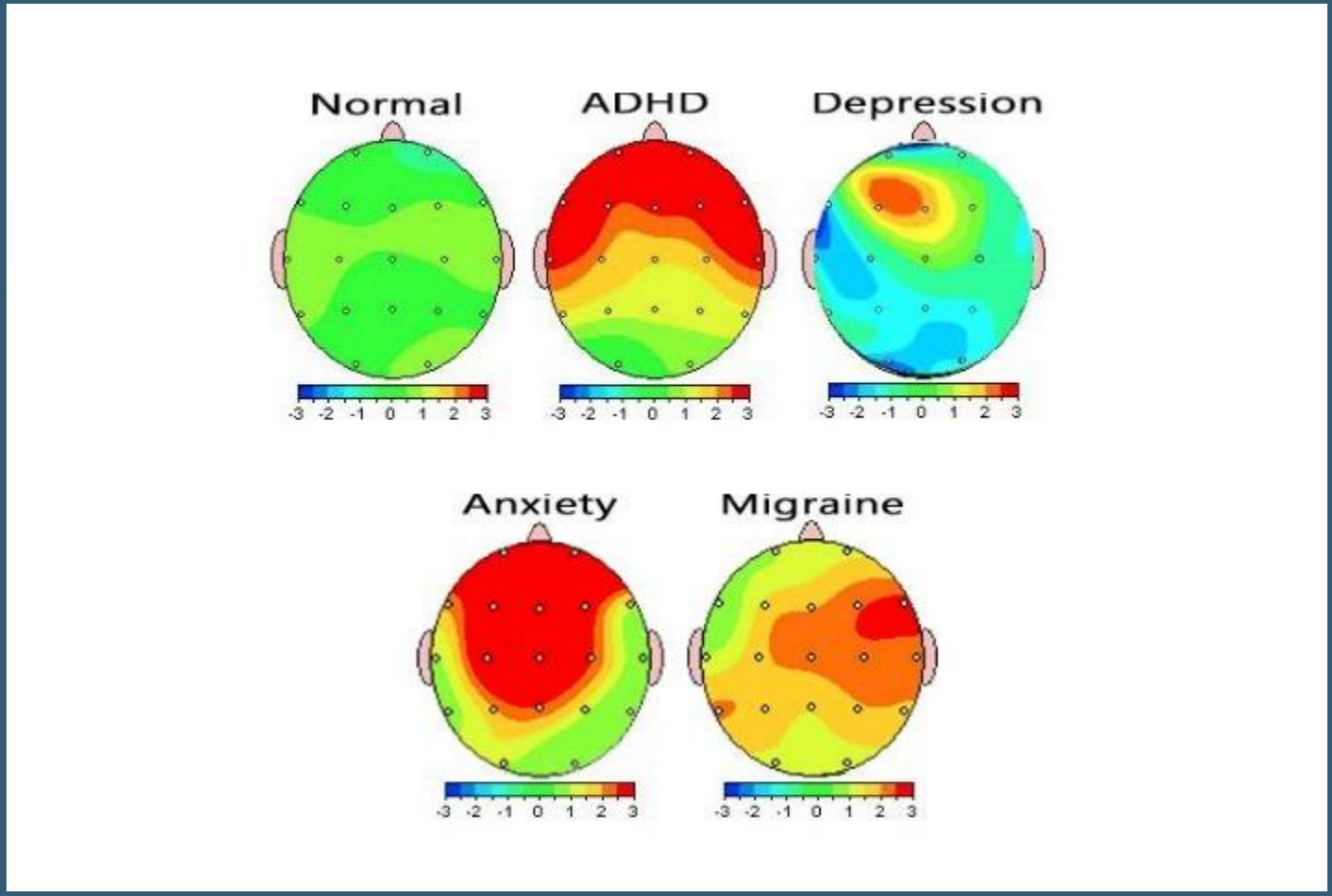
- Lion's Mane Mushroom
- Ashwagandha  (Withania somnifera )
- Baikal Skullcap  (Scutellaria baicalensis)
- American Skullcap (Scutellaria lateriflora)
- Avea:  Turmeric
- Ginkgo biloba
- Panax ginseng (part of Adrenal formula)
- Rhodiola rosea  (part of Adrenal formula)
- Bacopa monnieri


# Trauma

- Traumatic Brain Injury
- Self-injuries
- Accidents
- Abuse history

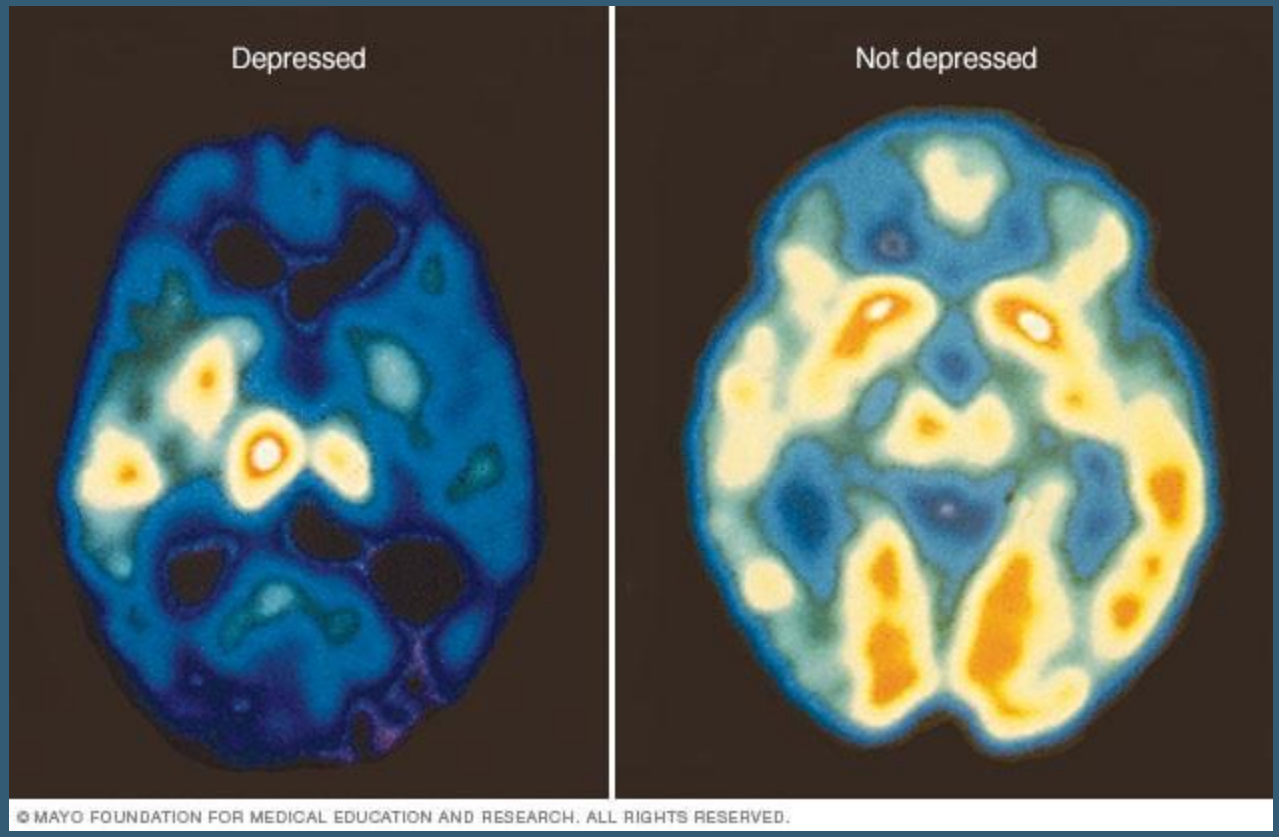
# qEEG

Kopanska M. et al. The role of quantitative electroencephalography in diagnostic workup of mental disorders. J Physiol Pharmacol. 2024 Aug;75(4).



# Evaluation for Depression: SPECT Scans

Gardner A. et al. Towards mapping the brain connectome in depression: functional connectivity by perfusion SPECT. Psychiatry Res. 2014 Aug 30;223(2):171-7.



# Additional Therapies:

## Trauma Therapy, Psychological Therapy, and Medications

- EMDR
- Brain Spotting
- Internal Family Systems (IFS)
- Cognitive Behavioral Therapy (CBT)
- Dialectical Behavior Therapy (DBT)
- Transcranial magnetic stimulation (TMS)
- Prescription medications

- **Comprehensive Treatment Important**

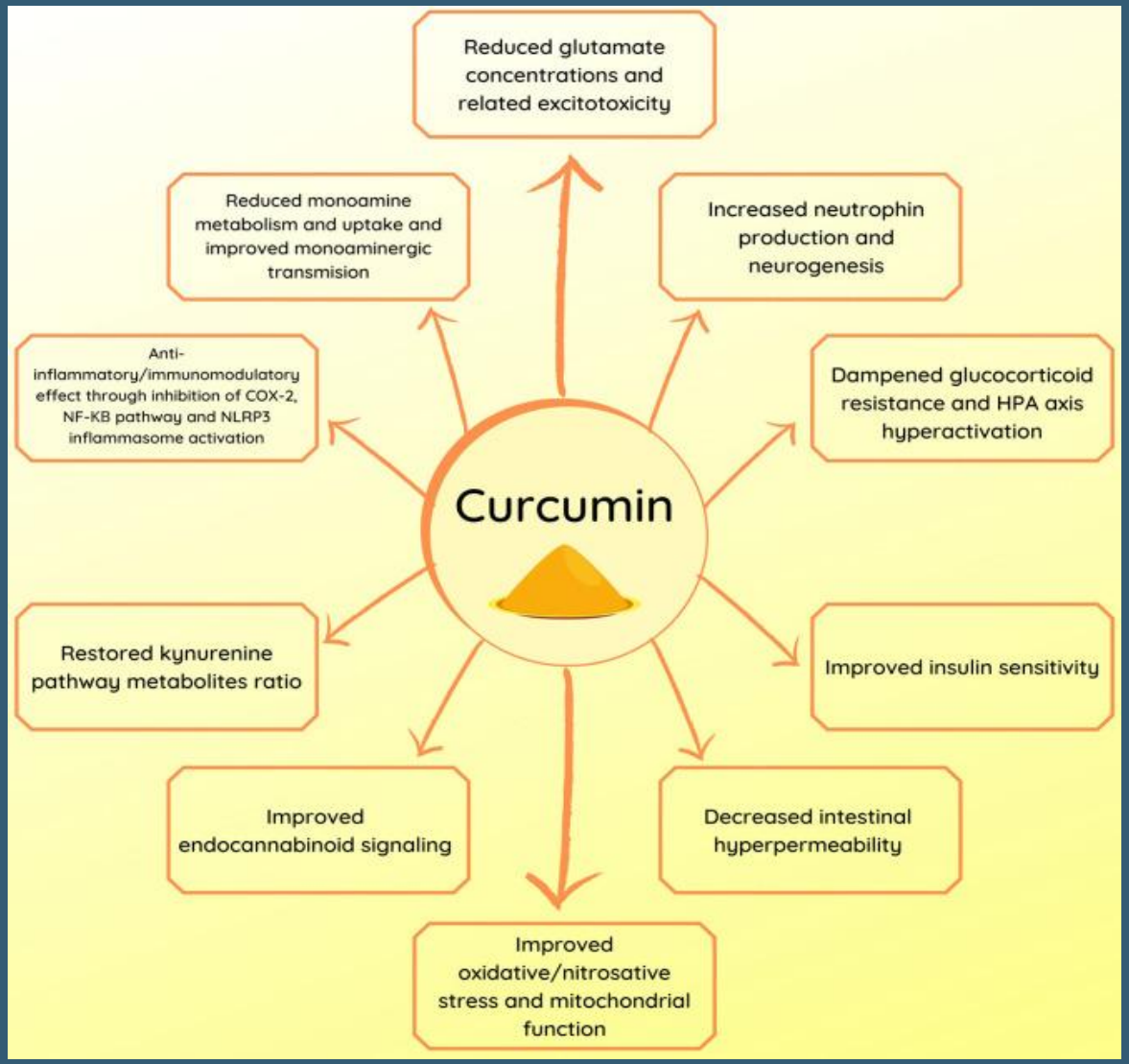
# Laboratory Testing: Summary of option: Depends on patient history

- Nutritional: B12, Vitamin D, zinc, ferritin, iron panel, cholesterol
- Thyroid panel
- Organic acid test:
  - neurotransmitter metabolites (help determine effects from MTHFR, COMT, etc.), dysbiosis markers, mitochondrial dysfunction, nutrients: B6, B12, folate metabolites, glutathione
- Adrenal Stress Panel
- Mitochondrial testing
- Digestive Stool analysis
- Food allergies/sensitivities
- Environmental toxins
- Mold- Mycotoxins
- Genetic SNP's (single nucleotide polymorphisms)
- Evaluation for chronic infections Lyme, Bartonella, EBV, HHV6 depending on history
- Kryptopyrroles
- Hormone evaluation depending on history


# Symptom Treatment for Mood Issues

# Turmeric /Curcumin

## Mechanisms of Action for Depression




Ramaholimihaso T. et al. Curcumin in Depression: Potential Mechanisms of Action and Current Evidence-A Narrative Review. Front Psychiatry. 2020 Nov 27;11:572533.

# Avea (Turmeric Root Extract)

- Anti-inflammatory: NFKB, Stat3, Nrf2, ROS, Cox2, TNF-alpha, CRP, IL-6, IL-1B, IL-8: primary anti-inflammatory cytokines
- Antioxidant
- Modulates transcription factors, kinases, cytokines
- Anti-carcinogenic and chemoprotective
- Mood and anxiety support
  - Can use for acute anxiety hourly
- Cardiovascular support: lipids, weight, blood sugar

# Babuna (Chamomile) Mood Effects

- Apigenin (primary flavonoid)
  - Binds to benzodiazepine receptors present in the brain. (GABA receptors)
  - Decreases seizure activity
  - Neuroprotective- increasing neurons in the brain (neuroplasticity)
  - Anxiolytic and sedative effects
  - Antagonist to the neurokinin-1 receptor
    - neuropeptide substance P binds to the neurokinin-1 receptor triggering the release of various substances leading to the onset of depression

# Babuna (Chamomile) Matricaria recutita

- Anxiolytic
- Anti-depressant
- Sleep induction
- Neuroprotective
- Stress-cortisol balancing
- Anticancer
- Anti-allergy (multiple flavonoids including apigenin,
  - luteolin, quercetin)
- Anti-infective
- Anti-inflammatory
- Antithrombotic
- Antioxidant
- Hypoglycemic
- Antihypertensive
- Digestive support

# Valerian (Valeriana officinalis)



- Increase GABA at A receptor
- Helps sleep initiation so helps fall asleep
- Improves overall sleep quality
- Supports serotonin
- Helps deep sleep
- Anti-anxiety
- Increase in frontal lobe alpha waves- anxiolytic effect
- Moderates stress response
- Increases serotonin levels
- Bind to GABA receptor-inhibitory neurotransmitter
  - Increases GABA

5-Hydroxytryptophan (5-HTP)

Amino Acid

Precursor of Serotonin and Melatonin

Improve sleep initiation

Improve overall sleep quality

Decrease depression

Decrease anxiety

# L-Theanine

- Amino acid
- Component of tea
- Improves overall sleep
- Decreases anxiety
- Improves attention
- Supports GABA
- Supports Serotonin
- Increases calming alpha waves in the brain

# St Johns Wort and Depression Treatment

Ng QX. Et al. Clinical use of Hypericum perforatum (St John's wort) in depression: A meta-analysis. J Affect Disord. 2017 Mar 1;210:211-221.

- 27 clinical trials with a total of 3808 patients were reviewed, comparing the use of St John's wort and SSRI.
- In patients with depression, St John's wort demonstrated comparable response (pooled RR 0.983, 95% CI 0.924-1.042, p<0.001) and
- Comparable remission (pooled RR 1.013, 95% CI 0.892-1.134, p<0.001) rate, and
- Significantly lower discontinuation/dropout (pooled OR 0.587, 95% CI 0.478-0.697, p<0.001) rate compared to standard SSRIs

- **Support its significant clinical efficacy in ameliorating depressive symptoms. Recommended use in mild to moderate depression**

# Saffron

Shafiee A. et al. Effect of Saffron Versus Selective Serotonin Reuptake Inhibitors (SSRIs) in Treatment of Depression and Anxiety: A Meta-analysis of Randomized Controlled Trials. Nutr Rev. 2025 Mar 1;83(3):e751-e761.

- Meta-analysis of 8 studies assessing depression outcomes revealed a **nonsignificant difference between saffron and SSR**Is in reducing depressive symptoms (SMD = 0.10l 95% CI: -0.09 to 0.29).
- Four studies reporting anxiety outcomes showed a **nonsignificant difference between saffron and SSRIs in reducing anxiety** symptoms (SMD = 0.04; 95% CI: -0.22 to 0.29).
- participants receiving saffron had **fewer adverse events** than the SSRI group (risk difference: -0.06; 95% CI: -0.09, -0.04; I2: 0%).

# HOPE FOR THE FUTURE