

Nutritional Neurochemistry

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Drs. Dale and Aida Bredesen's Story

- Dr Bredesen believed for many years that he would find a cure for Alzheimer's disease in the lab.
- He had joint appointments at the UCLA Brain Research Center and the Buck Institute on Ageing here in Marin County for over 25 years.
- He worked hard at his research for many years understanding what's going wrong in the brain in Alzheimer's Dz
- After many years he realized that there are so many things going wrong in the brain (36 holes) that there will never be a pill to fix all of it.
- He realized with the help of his wife, Dr. Aida Bredesen, that a comprehensive program, addressing all the underlying causes was the only approach that would work. So they started trying it! He wrote "The End of Alzheimer's."

Correctible causes of Alzheimer's and memory loss

- Type 1 Inflammation
- Type 1.5 Glycotoxic or high blood sugar and insulin
- Type 2 Atrophic or loss of support nutrients and hormones needed
- Type 3 Toxic or Infectious

- Type 4 Vascular – more difficult to correct
- Type 5 Traumatic – more difficult to correct

Type 1 Inflammatory

- Sign and symptoms of inflammatory issues:
- Joint pain, muscle pain or intestinal symptoms like bloating or constipation
- Elevated blood biomarkers such as CRP, IL 6, TNF alpha, ESR
- Dysbiosis (excess unfavorable bacteria) or markers of inflammation on stool testing
- Treatment may include:
- Anti inflammatory supplements such as Curcumin, Boswellia, Omega 3 oils and Specialized Pro Resolving Mediators
- Dietary changes to remove inflammatory foods: (Sugar, gluten, dairy, alcohol, and possibly many other foods in select patients)
- Probiotics, digestive enzymes for poor digestion, and other modalities to improve intestinal function and repair the unhealthy microbiome.

Type 1.5 Glycotoxic: High sugar

Signs and symptoms:

- Overweight and/or increased abdominal adiposity (increased girth)

Labs supporting this diagnosis include:

- High fasting blood sugar, (optimal 79-86)
- high Hgb A1c,(optimal 4.9 -5.2)
- high insulin (optimal 2.6-5.5)

Treatment may include:

- Ketogenic diet
- exercise
- Berberine, Cinnamon
- R lipoic acid
- Exogenous ketones

Type 2 Atrophic: lack of support molecules

Signs or symptoms: Weight loss, loss of muscle mass, loss of strength, fatigue

Insufficient nutrients may occur with aging or intestinal malabsorption:

- Protein, healthy oils or other nutrients
- Vitamins and minerals (Hugh list, most can be tested)
- Antioxidants, phytochemicals, collagen, healthy fats, protein

Loss of hormonal support can occur with aging:

- Thyroid
- Pregnenolone
- DHEA
- Testosterone
- Estradiol
- Cortisol

Type 3 Toxic and infectious

- Heavy Metal toxicity: Mercury, Lead, Arsenic, Tin, Cadmium
- Chemical toxin overload: pesticides, plastics, MTBE, styrene, others
- Mold related illness: Chronic Inflammatory Response Syndrome, also called Inhalation Alzheimer's Disease
- Infectious Diseases: Lyme Disease, Co-infections like Babesia and Bartonella occurring with Lyme
- Chronic viral infections: Epstein-Barre, Herpes simplex 1 and 2, Human Herpes Virus 6

The lifestyle foundation: DESS

- Diet:

 - Ketogenic, no sugar, low carbohydrate, high fat (high quality fats)

- Exercise

 - Aerobic or Cardio-Pulmonary

 - Strength Training

- Sleep Optimization

 - 8 hours of restful sleep without sleep apnea (oxygen drops)

- Stress Reduction

A Patient

- 72 year old woman who had gradually deteriorating memory for 3 years.
- She previously was an expert bridge player and could still play but like a beginner.
- She gradually lost her speech and had trouble getting a sentence out.
- Her husband read Dale Bredeesen's book: *The End of Alzheimer's*

And before they came in to see me he started her on a ketogenic diet and supplements: within 6 or 7 days she was speaking in full sentences and then within 14 days in full paragraphs. Her memory was still poor but slightly better.



Physical Methods

Key Physical Interventions for the Brain

- **Provide a complete array of nutrients.**
- **Get the gut right.**
- **Optimize serotonin.**
- **Increase GABA/glutamic acid ratio.**
- **Enhance excitatory neurotransmitters.**

And exercise!



Provide a Complete Array of Nutrients

Perspectives on Natural Methods

■ Potential benefits:

- Often highly effective
- Minimal side effects (pure molecules that the body knows how to metabolize)
- Readily available

■ But use wisely:

- Gather information.
- Don't do on your own with psychotropic meds.
- Start with low doses.
- If something does not feel good, stop.
- Make sure other co-factors are adequate (e.g., B-6, iron).
- Consider further testing (e.g., amino acids).

Key Functions of Nutrients

- Build tissue
- Act as substrate for metabolic processes
- Act as co-factors for enzymes that facilitate metabolic steps
- Act as anti-oxidants

Patient: “What do you think about the blood type diet?”

Jan: “I love it. But I don’ t think it matters what type you pick.”

Nutrients from Food - 1

- Protein:
 - 3 servings a day, the size of the palm of your hand
 - Animal protein: well absorbed, hypoallergenic
 - Nuts and seeds
 - Protein powder
 - Vegetarians: consider an amino acid supplement
- Vegetables and fruits:
 - Vegetables: at least several cups a day
 - Primary source of carbohydrates
 - Fruit: eat whole fruit; be mindful of sugar content¹⁶

Nutrients from Food - 2

- Oils:
 - Primary oil is olive
 - No trans-fats
 - Be mindful of saturated fats, but not afraid
 - Good fat is good for the brain
 - Good oil sources: olive, coconut, grass-fed beef, nuts and seeds, wild salmon, whole (pasture raised) eggs, avocado, fish oil supplements

Nutrients from Food - 3

- Dairy:
 - Try to eliminate cow dairy -- a major allergen
 - Goat and sheep products are best
 - Substitute with almond milk, coconut milk, etc.

Nutrients from Food - 4

- Grains:
 - Not so much
 - Whole kernel grains, not made into flour
 - Gluten-free (gluten = wheat, oats, rye, barley, spelt, kamut)
 - Cooked grains all contain about 20grams of carbohydrate in a half cup – that's a lot.

Nutrients From Food - 5

- Eat No Sugar and little refined flour . . .
- If you must, eat as little sugar as possible.
 - The average American eats 158 lbs per year.
 - Sugar raises and dysregulates blood sugar.
 - Sugar raises insulin and puts you on the road to diabetes.
 - High insulin is inflammatory.
 - Increased risk of Alzheimer's disease, Parkinson's and depression with diabetes.
 - Decreases cognitive performance

Nutrients From Food - 6

■ Carbohydrates

- Eat less! Probably the most important diet instruction for Americans.
- Weight loss: 60 gr. of carb or less
- Brain health, via David Perlmutter: 80gr.
- Jan's loosey-goosey: 100 – 120 gr.max

Nutrients from Food - 7

- Go paleolithic!
 - Eat like the hunter-gatherers did -- that is your evolutionary heritage.
 - Animal protein, vegetables, fruit, eggs, nuts, healthy oils.

Yummy Meal



Yummy Meal



Supplement B-Vitamins

- Start with a good multi-vitamin/mineral supplement, with high B-vitamins (10x DVs for B' s and 800 mcg folic acid, as 5-methyl-tetrahydrofolate)
- Folate, B-12, and B-6 cut brain shrinkage in half in older mildly cognitively impaired adults with high homocysteine. Take B-12 under the tongue.
- Low folate predisposes people to depression.
- Folic acid + SSRI almost doubles success rate over SSRI alone.

Supplement Minerals

- The multi should have the DV or more of zinc, copper, selenium, manganese, molybdenum, chromium, iodine.
- Typically add calcium and magnesium:
 - At least 400 mg. mag. Citrate laxative / glycinate not
 - Women should consume 600 - 1000 mg. calcium.
- Iron:
 - A critical brain nutrient, but toxic if you get too much
 - Carnivorous men usually shouldn't add iron.
 - Menstruating women usually do need iron.
 - It's best to test for iron with an iron panel or serum ferritin. A blood count helps, but can miss low iron.
 - If you have fatigue and/or depression, test.

Supplement Essential Fatty Acids

- Much DHA (docosahexaenoic acid) in the brain
- DHA & EPA (eicosapentaenoic acid) are important regulators of inflammation.
- EPA & DHA negatively correlate with depression (DHA has more data)
- EPA: anti-inflammatory; DHA: brain structure.
- May be preventive for Parkinson's and Alzheimer's.
- Fish oil: 500 mg. each of EPA and DHA

Supplement Vitamin D

- Co-factor in synthesis of serotonin, dopamine, and norepinephrine
- Low levels of D are implicated in depression.
- Major support for the immune system
- May be helpful in preventing dementia and Parkinson's disease
- Made in the skin from unprotected sunlight
- Get 10 - 15 minutes sun mid-day; do not burn.
- Goal for D: 50 - 60 ng./ml. The correct test is "25-OH-vitamin D."
- If you cannot test, try 2000 I.U./day.

About Supplements

Most supplements are available at health food stores.

Some products might be hard to find. If so, you can get them at my website, www.JanHealth.com. Or call me, at 415/472-3663.

If you want to check the formulas of vitamin, mineral, or amino acid products at health food stores, etc., you can compare them to products on my website.

For comparisons, look at the Twice Daily Multi (Designs for Health), and BAM or All Basic Plus amino acid mixes.



Get the Gut Right

The GI Tract and the Brain

- The road to health is paved with good intestines.
 - Our gastrointestinal (GI) tract has a huge effect on our brain.
 - We can have a huge effect on our GI tract.
 - Key issues: cytokines, malabsorption, dysbiosis
- GI tract effects on the brain via the immune system:
 - 60 - 70% of the immune system is in the GI tract.
 - When the GI tract is inflamed, it sends messengers called ***cytokines*** throughout the body - including the brain - causing inflammation and trouble.
 - By activating a particular enzyme, cytokines deplete the brain of serotonin.
 - Cytokines stimulate hypothalamic-pituitary stress pathway, resulting in higher stress hormones, including cortisol.

GI Malabsorption

- When the intestines are inflamed, malabsorption of nutrients occurs.
- Malabsorption decreases amino acids, iron, folic acid, and fats. (And probably all nutrients).
- We need these nutrients for brain health.

Increase Beneficial Microflora - 1

- There are trillions of bacteria in the intestines.
 - Beneficial bacteria protect intestinal walls, help build vitamins, and decrease inflammation and bad microbes.
 - Pathogenic bacteria cause inflammation.

- Increase beneficial bacteria:
 - Eat a low sugar, low refined flour, high fiber diet.
 - Bad bugs like sugar; good bugs like fiber.
 - Supplement probiotics:
 - Lactobacillus GG (Culturelle)
 - Saccharomyces boulardii (Florastor)
 - Bifido-bifidus (particularly for kids, but everyone)
 - Lactobacillus paracasei, casei, plantarum, rhamnosus, and salivarius

Increase Beneficial Microflora - 2

- Dosing multi-strain probiotics
 - Must sustain treatment: probiotics bloom then leave within two weeks
 - 5 billion CFUs (colony forming units) per day for ongoing healthy GI support
 - 25-50 billion CFUs for GI repair
 - 450 billion - 3.6 trillion CFUs: ulcerative colitis (VSL #3)
- Make your own yogurt or kefir
 - Dairy-free recipes using coconut milk are on-line.
 - Add your own probiotics.
 - Most supermarket brands have no active probiotics.

Decrease Pathogenic Microbes

- Get rid of bad bugs: parasites, yeast overgrowth, and bacterial overgrowth: large and small intestine.
- You may need to test to identify pathogens. A comprehensive stool test is offered by integrative practitioners.
- Treat microbes as appropriate. If possible use natural products. Parasites usually require prescription medication, and perhaps a long treatment.

Eliminate Food Allergens

- Food allergens cause inflammation and reactivity all over the body.
 - No down side, except giving up your favorite foods
 - Dramatic effects on mood and energy
 - Particularly noticeable in children
- The worst offenders are gluten and dairy, then soy.
 - Gluten: wheat, oats, rye, barley, spelt, kamut
 - Dairy: cow is usually worse than goat and sheep.
- Test:
 - Try a couple weeks off.
 - Or you can do an IgG antibody test, but lots of false positives and negatives – take with a lump of salt!.



Optimize Serotonin

Working with Neurotransmitters

- Two core functions of neurotransmitters:
 - Calming down - Inhibitory
 - Energizing up - Excitatory
- You can supplement neurotransmitters or their co-factors - in a context of overall health.
- Individual differences:
 - More benefit from inhibitory neurotransmitters

Inhibitory and Excitatory Neurotransmitters

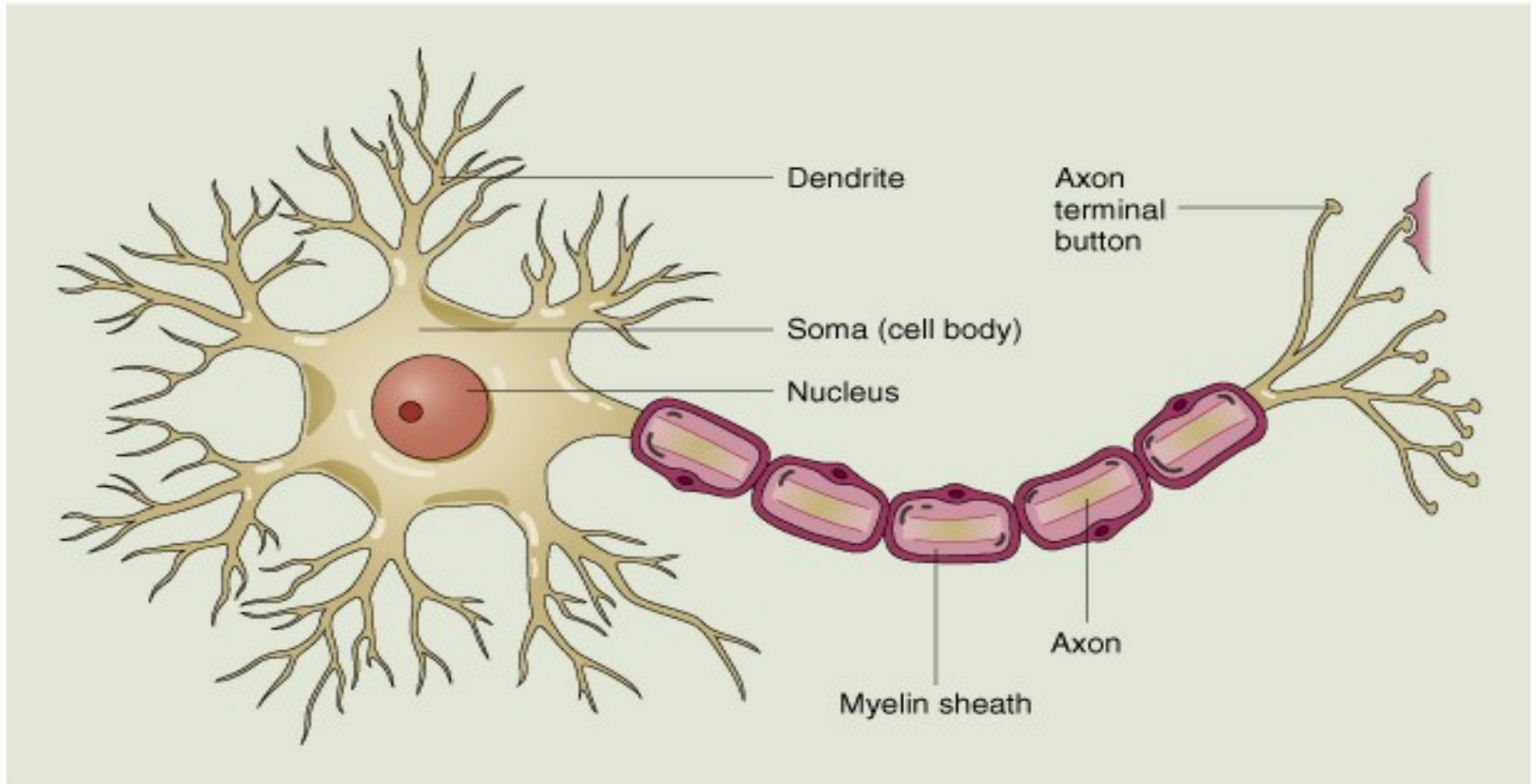
■ Inhibitory:

- Serotonin
- GABA

■ Excitatory:

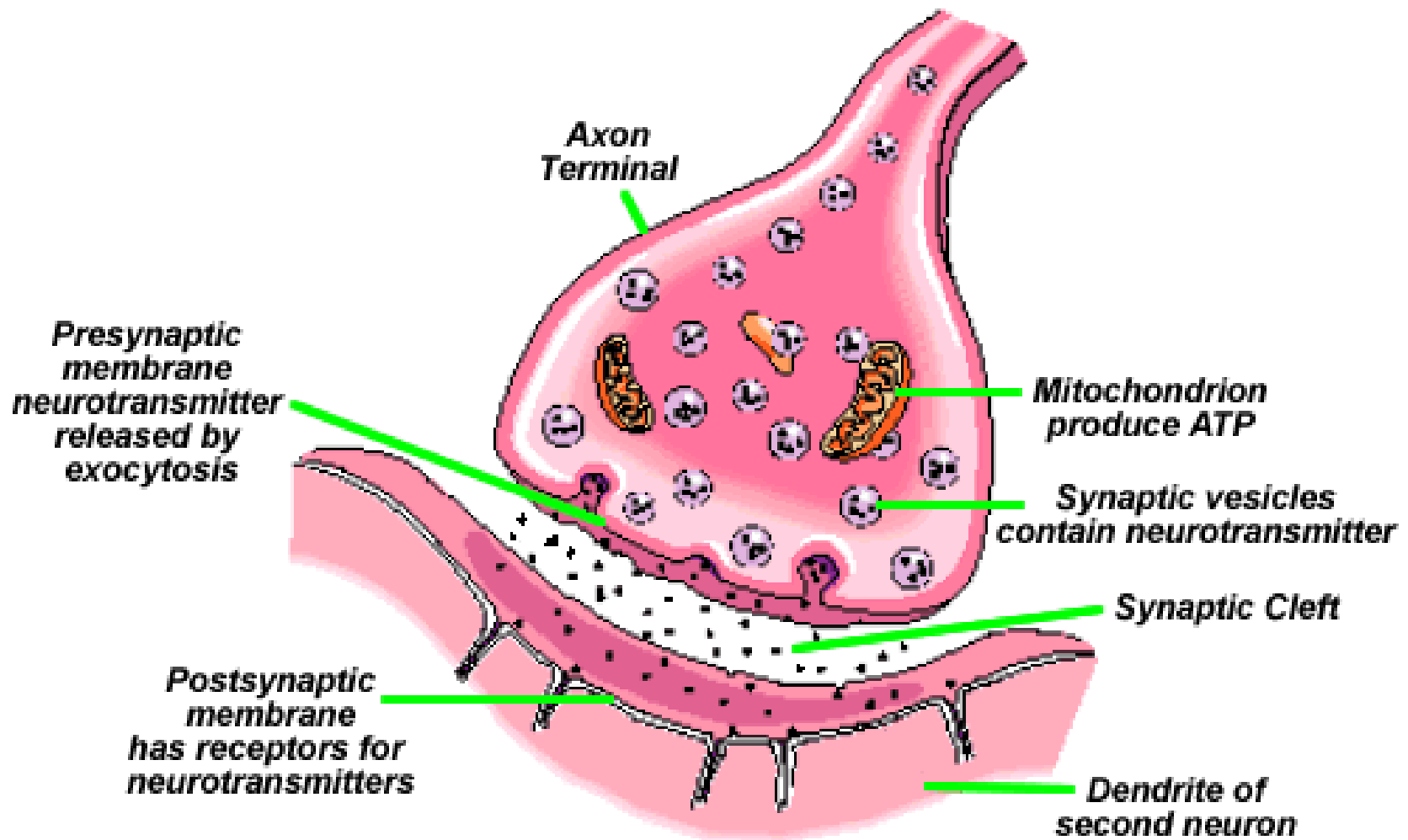
- Norepinephrine
- Dopamine
- Acetylcholine
- Glutamic acid (glutamate)

A Neuron



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A SYNAPSE



Serotonin Effects

- Serotonin is the key neurotransmitter for “happy and relaxed.”
- Serotonin is a neuro-modulator of GABA that increases its effects, and also helps decrease overactive norepinephrine, dopamine, adrenaline, and cortisol.
- Major effect on depression and anxiety

Serotonin Production and Supplementation

- Tryptophan (with iron) -> 5-hydroxytryptophan (5-HTP) (with B-6 [P-5-P]) -> **serotonin**
|----> melatonin
- Options for increasing serotonin:
 - 5-HTP, 50 - 200 mg./day; empty morning stomach
 - Tryptophan: 500 - 1500 mg./day; before bed (great for sleep)
- Stop if it doesn't feel good.

St. John's Wort

- Neurochemistry:
 - Many pathways of action due to molecular complexity
 - Uptake inhibitor of serotonin and probably dopamine and norepinephrine; mild MAO inhibitor
 - If the drug companies could make this, they would!
- Dosing: 300 mg. 3 times per day
- Concerns about decreasing the effectiveness of other medications:
 - Do not use with protease inhibitors for HIV.
 - Unproven concern with birth control pills, but be mindful

Increase GABA/Glutamic Acid Ratio

GABA and Glutamic Acid: Overview

- GABA and glutamic acid (GA) have a dance in the brain. GABA is Yin (inhibitory) and Glutamic Acid is Yang (excitatory).
- Too much GA feels like a monosodium glutamate (MSG) overdose.
- High GA and/or low GABA are associated with:
 - Anxiety, depression, bipolar disorder
 - Migraines, seizures
 - Parkinson's disease
 - Schizophrenia

Supplement Magnesium

- Supplementing magnesium increases GABA.
- Studies on migraines, seizures, and preeclampsia found magnesium to be effective.
- Take 400 - 1000 mg. magnesium.
 - Magnesium citrate will likely be a laxative.
 - Magnesium glycinate is not usually a laxative.

Supplement Vitamin B-6

- Glutamic acid --> GABA
- Vitamin B-6 as Pyridoxal-5-Phosphate (P-5-P) is the key nutritional co-factor that shifts the balance in the direction of GABA.
- Take 50 mg./day of P-5-P on an empty stomach.
- Many don't make P-5-P from pyridoxine effectively.
- Often deficient in women on birth control pills

Supplement Taurine

- Taurine binds to GABA receptors, thus stimulating GABA-like activity.
- It stimulates enzymes that make GABA, and inhibits enzymes that break it down.
- It's typically a benign amino acid, also depleted during breastfeeding.
- It is an inhibitory neurotransmitter.
- Consider 1000 mg./day (maybe more).

Supplement Melatonin

- Melatonin blocks the main glutamate receptor.
- Get good sleep. Take the time. Sleep is perhaps the most restorative activity for the brain.
- For sleep, use 1 - 3 mg. melatonin before bed, or a smaller amount for middle-of-the-night waking. Try sublingual preparations.
- Melatonin Zn Se – distributes melatonin throughout the night.

Supplement Theanine

- Theanine is an amino acid found in green tea and added to soft drinks in Japan (!).
- It is “antagonistic” to glutamic acid.
- Consider 100 - 200 mg./day.

Supplement GABA

- Theoretically, GABA does not cross the blood-brain barrier, but many people do report a calming effect.
- Possibly there is a “leaky brain syndrome” allowing GABA to get through.
- Several studies show efficacy of GABA with anxiety.
- Consider 250 - 750 mg./day, or more, on an empty stomach.

Supplement Progesterone

- For women only . . .
- Progesterone stimulates GABA receptors, triggering a GABA-like effect.
- Approaching menopause, progesterone decreases before estrogen does, so supplementing progesterone may be helpful.
- Consider Pro-Gest cream, during the second half of your cycle.

Possible Daily Supplements for Enhancing GABA/Glutamic Acid Ratio

- Magnesium: 400 - 1000 mg. citrate (lax.) or glycinate (non-lax.)
- Vitamin B6 as P-5-P: 50 mg. on an empty stomach
- Taurine: 1000 mg. (or more) on an empty stomach (in a.m.)
- Melatonin 1-3 mg.
- Theanine: 100 – 200 mg.
- GABA: 250 - 750 mg.
- Progesterone cream (women only)
- Tryptophan or 5-HTP to enhance serotonin --> modulates GABA⁵⁴



Enhance Excitatory Neurotransmitters

Enhance Dopamine, Norepinephrine

- Increase dopamine and norepinephrine, which support attention, energy, and mood.
- Phenylalanine (with iron) -> tyrosine (with P-5-P) -> dopamine -> norepinephrine
- Tyrosine also builds thyroid hormone.
- On a foundation of good serotonin, supplement:
 - 500-1000 mg./day of L-Phenylalanine or L-Tyrosine (empty stomach in the morning)
 - 50 mg./day of P-5-P (empty stomach in the morning)
 - Supplement iron as indicated by testing.

Enhance Acetylcholine - 1

- Phosphatidylserine:
 - A structural component of a neuron's membrane
 - Enhances acetylcholine release
 - Calms stress pathways in the brain, reducing cortisol
 - Many studies show decreased cognitive decline with aging
 - 100 - 300 mg./day

Enhance Acetylcholine - 2

- Alpha GPC (glycerylphosphorylcholine) stimulates manufacture of new acetylcholine by providing a supply of choline for neurons.
- Stimulates release of GABA
- Benefits shown for memory, stroke, Alzheimer's, and vascular dementia
- Try 300 - 600 mg. (by prescription in Europe)

Enhance Acetylcholine - 3

- Huperzine A is extracted from Chinese club moss. It helps prevent breakdown of acetylcholine.
- Some studies have shown effectiveness with Alzheimer's disease; one study showed improved memory in adolescents.
- 50 - 200 mg./day. Start slow. Although studies say no side effects, I have seen them.

Broad Neurotransmitter Increase

- When fatigue is an issue, even chronic fatigue, a complete amino acid blend can be very useful.
 - Taken on an empty stomach, it temporarily but strongly boosts amino acids levels.
 - The theory is that it primes the pump and gets the body and brain going.
- Use a free amino acid balanced blend.
 - Take on an empty stomach, 30 minutes before food in the morning.
 - 3 - 10 grams
 - Can modify with amino acid testing (from integrative practitioners).
 - Make sure vitamin and mineral co-factors are present.⁶⁰

Bonus #6 Increase Glutathione

- Increase glutathione, perhaps the most important anti-oxidant in the brain.
 - Lipoic acid: 100 - 600 mg. per day.
 - Consider R-Lipoic form.
 - Consider time-release lipoic acid.
 - NAC (N-Acetyl-Cysteine)
 - Most important building block of glutathione
 - May benefit the GABA/Glutamic Acid ratio
 - May be hard to tolerate on the digestive system
 - Try 500 - 2000 mg. per day on an empty stomach.
 - Oral glutathione is not well absorbed.

Bonus #7: Hormones

- Check thyroid if fatigue is a factor.
 - TSH should ideally be under 2.00, but certainly under 3.00.
- Estrogen does many good things for the brain:
 - Improves mood
 - Supports memory
 - Helps prevent dementia
- Menopausal women should test estrogen levels and consider supplementation.
 - Always bioidentical
 - Always transdermal -- patch, cream, or spray

Bonus #7: Hormones

- Various studies of bio-identical estradiol showed a decreased dementia risk of 20% – 40%.
- Stanford imaging study showed that bio-identical estradiol – not Premarin – protected areas of the brain that decline with approaching Alzheimer’s disease.
- WHI study found that Premarin with Provera (a stupid form of “progesterone”) increased risk of breast cancer. Estrogen alone did not do this, even Premarin. Over time, estrogen alone decreased risk by 23%!

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