



ONNA LO MD
Reclaim Joy, Vitality, Balance



Guide to Understanding
Cognitive Decline
and What to Do About It

from the Work and Recommendations of Dr. Bredesen

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Understanding What is Causing Your Symptoms

Type 1 Inflammation	Chronic inflammation, whether due to infections or poor diet or other factors, is the key contributor to Type 1 Alzheimer's disease.
Type 1.5 Glycotoxicity	Sugar toxicity causes both inflammation and insulin resistance, and therefore contributes to both type 1 and type 2 Alzheimer's disease.
Type 2 Trophic Loss	Reduction in hormonal, vitamin, nutrient, or growth factor support drives Type 2 Alzheimer's disease.
Type 3 Toxicity	Some toxins are "dementogens" - in other words, they cause dementia. Examples are some metals such as mercury, and mycotoxins (toxins produced by specific molds).
Type 4 Vasculature	Vascular damage and poor blood flow are important contributors to Type 4 Alzheimer's disease.

Understanding the 6 Types of Alzheimer's Disease

Type 1: Inflammatory

This type is associated with inflammatory markers such as hs-CRP, and the inflammation may be due to infections or suboptimal diet or other factors. Risk for Type 1 is increased by ApoE4, chronic infections, trans fats, and other factors.

Type 1.5 Glycotoxic

Type 1.5 has features of both type 1 (inflammatory) and type 2 (atrophic). In this type, chronically high glucose levels damage multiple proteins, cells, and tissues, leading to inflammation and auto-antibodies, thus increasing risk for type 1. Meanwhile, the responding high insulin levels cause insulin resistance, reducing the trophic effects of insulin and increasing risk for type 2. Risk for type 1.5 is increased by ApoE4 and by type 2

Type 2 Atrophic

This type is associated with reduction (especially rapid reduction) in trophic support such as estradiol, testosterone, insulin, vitamin D, and neurotrophins. Risk for type 2 is increased by ApoE4, early hysterectomy/ oophorectomy without hormone replacement, low vitamin D levels, and in some cases menopause /andropause. It is important to rule out sleep apnea, as well.

3 Toxic

Type 3 is quite different than types 1, 1.5, and 2, and often presents with features other than (or in addition to) memory loss, such as depression, problems calculating, organizing, following instructions, or finding words. Type 3 is associated with exposure to toxins (dementogens) such as mercury, high copper levels, anesthetics, mycotoxins (toxins produced by molds), or tick-related toxins (e.g., from Lyme disease). Risk for type 3 is not increased (and may be decreased) by ApoE4.

Type 4 Vascular

We used to think of vascular disease as being unrelated to Alzheimer's disease, but over the past several years it has become clear that vascular abnormalities contribute importantly to Alzheimer's disease. In type 4, chronic vascular disease (which may be associated with high homocysteine or vascular amyloid or breach of the blood-brain barrier, among other contributors) is associated with the development of Alzheimer's disease.

Type 5 Traumatic

When the brain is traumatized, for example due to an auto accident, the amyloid associated with Alzheimer's disease is produced as a response. Trauma is thus a risk factor for Alzheimer's disease. In many cases, the amyloid is removed, and thus chronic traumatic encephalopathy (CTE, which occurs in football players among others, and was featured in the film *Concussion*) typically lacks amyloid, but is related to Alzheimer's disease in featuring neurofibrillary tangles made of the tau protein.

Where Do I Start? What Actions can I Take?

Step 1: Achieve Mild Ketosis

0.5 to 4mM beta-hydroxybutyrate by ketone meter. Ketosis has several mechanisms to enhance cognitive function. The instructions for how to do this are included in your overall program, and combine the use of MCT oil, fasting at least 12 hours between dinner and breakfast/brunch, following the "Ketoflex 12/3" diet outlined in this report, exercising 4-6 times per week, and minimizing stress. Your physician and health coach can guide you to optimize your ketosis, which in turn will support your optimal brain function

Step 2: Resolve Ongoing Inflammation, and Prevent New Inflammation

Chronic inflammation is a critical contributor to Alzheimer's disease, and your genetic and biochemical profile is compatible with that finding. Preventing inflammation is important, but first the ongoing chronic inflammation must be resolved. Specialized pro-resolving mediators (SPM) are used for this purpose, followed by inhibitors of new inflammation, such as curcumin and specific anti-inflammatory nutrients. These are included in the synaptic support section of your program.

Step 3: Enhance Methylation to Reduce Homocysteine

Homocysteine is an important contributor to Alzheimer's disease and vascular inflammation, and reducing your homocysteine is one of the key goals of your program. This is accomplished with the synaptic support items listed in your program.

Step 4: Optimize Hormonal Support for Your Brain

Your profile indicates that optimal hormonal support will be key for cognition, and therefore it is recommended that you consult your physician about the ideal hormonal support.

Step 5: Optimize Vitamin D Level

Vitamin D affects hundreds of genes, and plays a role in numerous processes, including brain function. Therefore, optimizing vitamin D levels (and vitamin K2, which should be taken with vitamin D) is critical as part of an overall program to prevent or reverse cognitive decline

Step 6: Minimize Exposure to Dementogens

There are many contributors to cognitive decline—just as we are exposed to many carcinogens, we are also exposed to dementogens, such as specific toxic metals, mycotoxins (toxins produced by mold species), and some medications, among others. Proton pump inhibitors (PPIs), often taken for reflux (GERD, or gastroesophageal reflux disorder), may reduce our absorption of critical nutrients for brain function, such as zinc

and vitamin B12. Statins may reduce cholesterol, which is critical for brain structure, too far. Anesthetic agents, some antidepressants, some antihistamines, benzodiazepines, some pain killers (like opiates), and anticonvulsants (seizure drugs), are all drugs that affect cognition and can contribute to reduced cognitive ability.

Your Suggested Plan: Nutrition

1. **Fast for at least 12 hours between the end of dinner and the beginning of breakfast.** This allows autophagy to occur, which helps your brain to destroy aggregated proteins and other unwanted accumulated molecules. It is best to break the fast with water with some lemon, as a detoxifying drink.
2. **Fast for at least 3 hours prior to going to bed.** This helps to prevent insulin from inhibiting melatonin and growth hormone, and thus improves sleep and immune function.
3. It is key to **minimize simple carbohydrates** (sugar, sweet treats, bread (white and brown), white rice, white potatoes (OK to eat sweet potatoes and other colored potatoes in small quantities), soft drinks (both regular and diet, since diet alter microbiome), alcohol, candy, cakes, processed foods, and anything else with simple carbohydrates. The goal is to change from carbohydrate metabolism to lipid metabolism.

Carbohydrates, processed foods and sugar stimulate the production of insulin in the body, and create insulin resistance. They also lower the ability of the body to destroy and excrete toxins, such as mycotoxins and divalent metals like mercury.

4. Make most of your diet from items that have a **glycemic index lower than 35**. For a list of glycemic indices for food, see:

<https://www.health.harvard.edu/diseases-and-conditions/glycemic-index-and-glycemic-load-for-100-foods>

5. **Vegetables should be the largest part of the diet**, especially non-starchy ones. Include both uncooked (salads) and cooked. Include as many colors as possible.
6. **Avoid fruit juices, but eat fruits** (which include the fiber) or smoothies with fruit, but do not make the smoothies too sweet –best with some vegetables.
7. **Avoid gluten and dairy to the extent possible.** It is recommended that you get Cyrex Arrays 2, 3, and 20 to help guide you: Array 2 is to determine if you have leaky gut; Array 3 is to determine if you have gluten sensitivity; and Array 20 is to determine whether you have a leaky blood-brain barrier.
8. **Reduce blood sugar** by including fiber, both soluble and insoluble.

9. **Reduce toxins** by including cilantro, cruciferous vegetables (e.g., broccoli, cauliflower, brussels sprouts).

10. **Include good fats** such as avocado, nuts, olive oil, seeds, etc.

11. **Avoid processed foods**, and instead eat whole foods.

12. **Meat is a condiment, not a main course.** If you eat it, fine, but don't eat too much (2 or 3 ounces, 1-5 nights per week), and eat pastured chicken or grass-fed beef. Fish is fine if wild caught, best to avoid high-mercury fish such as tuna, swordfish, and shark (fish with large mouths and long lifespans are worst). "SMASH" fish are best (salmon, mackerel, anchovies, sardines, and herring).

13. **Emphasize foods with high nutrient density**, such as kale and romaine lettuce. Each day, try to eat at least 3 helpings of:

Dark leafy greens, such as kale, collards, spinach, or chard. Colored vegetables or fruits, such as berries, carrots, or beets. Sulfur-rich vegetables, such as cabbage, broccoli, cauliflower, or asparagus. Include aromatic herbs such as cilantro, parsley, basil, or mint.

14. **Be aware of the "dirty dozen and clean 15" foods.** The Dirty Dozen are foods highest in pesticides, and therefore important to buy as organic:

The Clean 15 are foods that are not sprayed as heavily, and therefore relatively safe to buy conventionally (non-organically):

CLEAN FIFTEEN <i>Lowest In Pesticides</i>	DIRTY DOZEN <i>Buy These Organic</i>
BEST	WORST
1 Onions	1 Celery
2 Avocado	2 Peaches
3 Sweet Corn	3 Strawberries
4 Pineapple	4 Apples
5 Mangos	5 Blueberries
6 Sweet Peas	6 Nectarines
7 Asparagus	7 Bell Peppers
8 Kiwi	8 Spinach
9 Cabbage	9 Cherries
10 Eggplant	10 Kale/Collard Greens
11 Cantaloupe	11 Potatoes
12 Watermelon	12 Grapes (<i>Imported</i>)
13 Grapefruit	
14 Sweet Potato	
15 Honeydew Melon	

See: www.fullyraw.com/dirty-dozen-clean-15

15. For grains, legumes, nuts, and seeds, it is helpful to **remove the lectins and phytates** by soaking prior to cooking.

16. **Incorporate pro-biotics and pre-biotics**, after determining that you do not have a leaky gut (Cyrex 2). Pro-biotics help to optimize your microbiome, the bacterial population in your gut. Pro-biotic foods include fermented foods such as sauerkraut, kimchi, kombucha, dairy-free yogurt, tempeh, miso, kefir, and coconut water. Pre-biotics help to support the bacteria of the microbiome. Pre-biotic foods include jicama, chicory, Jerusalem artichoke, and others.

Your Suggested Plan: Brain & Body Work

Exercise

5-6 times per week for 30-60 minutes, raising heart rate and including both cardiovascular and strength training. Exercise increases brain-derived neurotrophic factor (BDNF), which has important anti-Alzheimer's effects. It also helps to improve oxygenation, improve sleep, reduce overall stress, reduce fat and associated adipokines, improve insulin sensitivity, and improve overall brain and body physiology in numerous ways. Exercise is one of the best ways to prevent cognitive decline, and is an important part of the protocol to reverse cognitive decline.

Sleep

Sleep has multiple mechanisms to reduce cognitive decline: for example, it induces melatonin, which reduces the amyloid-beta associated with Alzheimer's disease; it is critical to memory consolidation; and it alters cellular anatomy to foster the removal of abnormal and toxic species from the brain. Thus sleep has multiple mechanisms to support the reversal of cognitive decline.

Most people have a sleep debt, due to chronic lack of optimal sleep, both in quantity and quality. It is crucial to ensure that you do not have sleep apnea, and, if you do, to treat it, whether by CPAP, oral device, altering sleeping position, or other methods. It is helpful to use melatonin at bedtime, and a physiological dose is 0.5mg, which can be taken by mouth or sublingually, depending on formulation. Some take higher doses, up to 20mg, and it is a relatively benign supplement, so you can adjust your dose: if the dose is too high, you may notice that you awaken after about three hours of heavy sleep, and you may feel sluggish the next morning; if the dose is right, you should notice increased dreaming, and awaken feeling refreshed. Melatonin has many effects, among them reducing amyloid-beta, reducing reactive oxygen species, and tumor suppression.

If you find that you are awakening in the middle of the night and ruminating, unable to return to sleep, you may find that Tryptophan (500mg) or 5-hydroxytryptophan (100 mg) helps to prevent this. Please discuss this with your practitioner, especially if you are on an SSRI (selective serotonin reuptake inhibitor) for depression, or a related SNRI (serotonin and norepinephrine reuptake inhibitor).

In order to optimize cognition, try to get as close to 8 hours of sleep each night as possible. It is best to go to bed before midnight, although some people find that their circadian rhythms do not allow this. It is also best to make sure that the room is as dark as possible (many people like to use a blindfold for this purpose), as quiet as possible, and is free of EMFs. Try to wind down in the evening instead of exercising or working right up until bedtime.

Reduce Stress

Stress is one of the most important contributors to cognitive decline, and stress-related molecules such as cortisol and corticotropin releasing factor receptor 1 are mediators of neural cell death and cognitive decline. Therefore, an important part of the overall program is to reduce stress-related effects, and there are many ways to do this, so please choose the ones that you enjoy: some people choose meditation, and indeed meditation has a positive effect on cognition; others love music, or walks in the park, or yoga, or visiting museums, lovemaking, or many other things (or all of those things). The Neural Agility recording, designed for brain neurophysiology, is "meditation on steroids," and many enjoy that. This should be done 5 times per week, in the evenings, for 30 minutes, relaxed and lying down with the lights down. Finding joy and relaxation in life is very important to reduce the brain-damaging stress that many of us feel in our busy lives.

Mental Exercise

Use Posit or Dakim or Lumosity, or learn a new language, or do Sudoku, or crossword puzzles, etc. The key is to do these in the presence of improved biochemistry. Do not do to exhaustion; typical is 40-60 minutes for 4 or 5 times each week. Make it a point to stay mentally active. In essence, you need to "use it or lose it."

Auditory Physiology

"Meditation on steroids." Use with headphones (you can play from your iPod or computer) in the evening, 5 times per week, for 30 minutes – lie on back, darken room, relax. These specialized tones can affect the release of powerful brain chemicals that can regulate mood, improve sleep, and reduce aggression as well as depression.

<http://www.fariastechnique.com/music-for-interhemispheric-synchronization>

Hygiene

Dr. Kenneth Seaton from Australia spent his career studying the relationship between hygiene, inflammation, and cognition. One of the measures he used to gauge inflammation was the albumin-to-globulin (A/G) ratio. Albumin is an important protein to remove amyloid, and to carry many other molecules (including drugs and hormones) in the blood. When inflammation occurs, whether from bacteria or fungi or viruses or other microbes or dietary inflammagens like trans fats or simple carbohydrates, the globulin fraction (from which antibodies are derived) increases at the expense of the albumin fraction, reducing the A/G ratio. This is associated with reduced cognition. Hygiene, and the maintenance of intact barriers (gut lining, blood-brain barrier, oral, nasal, integumentary (skin, nails, hair), etc.), play a key role in optimizing the A/G ratio. Oral hygiene, with electric toothbrush, floss, and water-pressure flosser, is important, especially since oral microbes have been

identified repeatedly in the brain in Alzheimer's disease. Some like to use nasal washes, as well. Evaluation for MARCoNS (multiple antibiotic resistant coagulase-negative Staphylococcus) is helpful, especially in anyone with type 3 (toxic) Alzheimer's disease. Ensuring good nail and skin hygiene can be helpful, as well.

Exercise, sleep, reduced stress, and optimal brain stimulation are powerful methods to alter the plasticity network, enhancing the ability to form new memories. These modalities increase trophic factors such as BDNF (brain-derived neurotrophic factor), decrease damaging agents such as cortisol, and help to reduce the burden of aggregated and damaged proteins as well as toxins

Recommended Reading

The Toxin Solution by Dr. Joseph Pizzorno
The End of Alzheimer's by Dr. Dale Bredesen
The Plant Paradox by Dr. Steven Gundry
The Brain That Changes Itself by Norman Doidge, M.D.
Fat Chance by Robert H. Lustig, M.D., M.S.L.
The China Study by T. Colin Cambell, PhD & Thomas M. Campbell
Disease Delusion by Jeffrey Bland
Dr. Gundry's Diet Evolution by Steven R. Gundry, M.D., F.A.C.S., F.A.C.C.
Eat to Live by Joel Fuhrman, M.D.
Superimmunity by Joel Fuhrman, M.D.
The End of Dieting by Joel Fuhrman, M.D.
Grain Brain by David Perlmutter M.D
Brainmaker by David Perlmutter M.D
Hormone Cure by Sara Gottfried, M.D.
Omnivore's Dilemma, In Defense of Food, Food Rules by Michael Pollan
Prevent and Reverse Heart Disease by Caldwell B. Esselstyn, Jr., M.D.
The Prime by Kulreet Chaudhary, M.D.
Salt, Sugar and Fat by Michael Moss
The Spectrum by Dean Ornish, M.D.
The UltraMind Solution by Mark Hyman, M.D.
The Blood Sugar Solution by Mark Hyman, M.D.
Eat Fat, Get Thin by Mark Hyman, M.D.
The Wahls Protocol by Terry Wahls, M.D.
What Your Doctor May Not Tell You About Heart Disease by Mark Houston, M.D., M.S.

Your Suggested Plan: Personalized Synaptic Support

- 5000 IU vitamin D each day plus 100mcg vitamin K2 per day
- Alpha-lipoic acid 100mg
- Ashwagandha 500mg twice per day with meals
- Bacopa 250mg twice per day with meals
- Berberine 400mg po tid
- (400mg orally 3x/day)
- Check basal body temperature or Thyroflex
- Cinnamon ¼ tsp each day
- Citicoline 250mg twice per day
- CoQ 100-300mg as ubiquinol
- Curcumin 1g twice per day. To optimize absorption, take this on empty stomach or with good fats (such as avocado or nuts or olive oil)
- Gotu kola 500mg, once or twice per day
- Hericium erinaceus 500mg po bid
- Magnesium threonate 2 grams each day. This is 3 pills, with a total of 144mg of magnesium.
- Manganese 10mg
- MCT oil (Start at one teaspoon and work up to one teaspoon three times per day over 2 weeks, in order to avoid diarrhea.)
- Methyl-B12 1mg
- Methyl-folate 2mg
- Mixed tocopherols and tocotrienols, 400 IU
- N-acetylcysteine 500mg
- Nicotinamide riboside 100mg
- Omega 3: 1g DHA and EPA
- P5P (pyridoxal 5-phosphate) 50mg
- PQQ 10mg
- Pro-biotics and pre-biotics after bone broth (for gut healing) or colostrum x 4 weeks (if Cyrex 2 is negative, can skip the healing phase)
- Repeat homocysteine in 3 months, and if still > 7, add trimethylglycine 500mg.
- Resveratrol 100mg
- Talk with practitioner about thyroid (Armour or NP Thyroid or Westroid or Naturethroid) 60mg
- Thiamine 50mg per day
- Vitamin C 1 g twice per day
- Zinc picolinate 50mg