MEMORY MEDICATIONS GERALD ENTE, M.D. AUGUST, 2024

Memory boosters, brain enhancers, smart drugs, cognition enhancers are some of the names for a new group of legal drugs called **Nootropics**, a word first coined in 1972, but new to me, which are surging into a multi-billion dollar industry based on almost no science. Nootropics include drugs used for specific brain diseases like Alzheimer's, Narcolepsy, Attention Deficit Disorder and sleeplessness. **We shall only talk about the OTC drugs that claim to improve brain function.** These supplements are being devoured by student teens to forgetful elders. These drugs seek to improve memory, enhance focus and clarity, increase mental energy, problem solving skills, shorten reaction time, protect brain health and reduce cognitive decline and brain fog. We shall discuss what they are, what they claim to do, the evidence pros and con, and the side effects as well as their benefits. To do this, we must start with the effects of aging on our memory.

Aging may affect our brain physically in lots of different ways including loss and shrinkage of cells, loss of brain liquids (neurotransmitters), and wearing down of myelin sheaths (the coverings of nerve cells). We become aware of the problem when we notice more frequent brain fog, memory lapses and "senior moments". Overall, these changes diminish our memory, make it more difficult to bring in new information and to retrieve old information. Deep **sleep** becomes more problematic and difficult as we grow older. Surprisingly, this adversely affects memory function because the storage of new data occurs during this deep sleep. So, we misplace things and can't find them; we temporarily or permanently forget names or other words; we become slow in the uptake of information that we are sure we know; and we are not as good at multi-tasking as we were. The process of aging affects every part of our bodies. Here we are discussing a**ged-related memory loss**, not any of the pathological diseases like Dementia, Alzheimer's Disease, etc.

Certain chemical compounds have been proven to somehow enhance brain function and increase brain neurotransmitters by various methods. They are:

1. Vitamins and supplements, such as B-complex, vitamins C, D, and E, magnesium, zinc, choline (alpha GPC) and fish oil (omega-3-fatty acids—to be discussed below) are vital nutrients for healthy neuronal (nervous system including brain) cells. Many nootropics contain various combinations of these. They are known to nourish and protect the brain.

2. **Ginkgo Biloba** from the world's oldest tree species, the Chinese ginkgo tree has been used for thousands of years to cure many ailments including memory loss (its main selling point). The medical literature includes many studies with conflicting results as to its efficacy for use to improve memory. It does increase cerebral blood flow.

3. There are 3 types of fish oil, omega-3-fatty acids: EPA and DHA mostly abundant in fatty fish like salmon, mackerel, herring, sardines, rainbow trout and

anchovies- and ALA (not from fish) found in some leafy green vegetables like spinach kale, watercress and Brussel sprouts, some vegetable oils like canola and soybean, and nuts and seeds like walnuts, sunflower seeds, sesame and flaxseeds. Our bodies convert ALA into EPA and DHA, but do this poorly, so that the best way to get high amounts of omega 3s is by eating fatty fish. (This also works better than taking supplements.)

4. **Bacopa Monnieri**, a traditional Indian herbal medication (also known as brahmi) is said to increase memory, focus and clarity, because it is known to enhance the branching of nerve cells (dendrites) and boost levels of acetylcholine choline. Although it is usually well tolerated it can cause belly pain, bloating and/or diarrhea.

5.**Lion's mane** adaptogenic (healing herb) mushroom complex combined with BioPerine (a black pepper derivative which increases absorption) is said to reduce memory loss.

6.**Phosphatidylserine** supports neuroplasticity (the ability of the brain to reorganize), enhances learning and formation of memory.

7. **Green Tea does** provide significant antioxidant protection from free radical damage. (Many negative bodily effects and processes).

8. **Caffeine**, a natural stimulant that has been shown to improve thinking skills and improve access to brain neurotransmitters like acetylcholine. (Be extremely cautious with caffeine powder which is deadly because 1 teaspoon equals 28 cups of coffee.)

9. **L-theanine**, found in green and black tea as well as mushrooms, is an amino acid that counteracts caffeine's jitteriness problem and combined with caffeine improves multi-tasking abilities, mental performance and focus.

10. **Theobromine**, a natural stimulant found in cocoa bean and **chocolate** which aids alertness. Animal studies show that this increases blood flow to the brain which enhances brain function, but this has not yet been shown in humans.

11. **Creatine monohydrate,** common in body and muscle building supplements, has been found to improve reasoning skills and short-term memory because it increases levels of ATP (AdenosineTriPhosphate) which increases cellular energy.

12. Choline alpha GPC/ Choline CDP, 2 forms of choline, which is a precursor to acetylcholine which is a neurotransmitter needed for brain function.

13. **Huperzine A**, an ancient herbal medication from mushrooms increases bioavailable levels of acetylcholine

14. **Rhodiola Rosea**, a healing staple herb used in ancient Egypt and by age-old Native Americans for improving brain function.

15.Hericium Erinaceus, a mushroom used by Buddhist monks to increase focus and alertness during meditation enhances the manufacture of acetylcholine and aids in the production of nerve growth factor (NGF), which is a protein that is involved in maintaining and regenerating neurons (nerve cells).

16. **Ashwagandha,** a traditional Indian (Ayurvedic) root extract medication has recently been shown to improve brain function.

17. **Probiotics** and **Prebiotics** are both involved with Gastrointestinal health. Probiotics are good bacteria, viruses and fungi which help in all gut functions. Prebiotics are non-digestible fibers from fruits, vegetables and grains which feed the probiotics. There is a strong gut-brain connection which improves brain function. There are certain **diets** which have shown strong evidence for improving brain function. They are **DASH diet**, **Mediterranean diet and the MIND diet**. Fish is the main protein staple of these diets. There have been many fruitless studies to determine which of the specifics of these diets have the greatest responsibility for these good results. The **DASH diet**, originally designed for people with high blood pressure, limits foods high in sugar, salt and saturated fats. The **Mediterranean diet** modeled after typical Mediterranean foods features mainly fish and plant foods with some poultry, eggs and healthy oils. The **MIND diet** takes elements of both these other diets which are known to boost brain health, such as green leafy vegetables, berries, fish, whole grains, olive oil, beans and poultry. Nutrients found in foods are more easily absorbed by the body than those in pills or capsules.

Twenty five percent of all adults over 50 take a supplement to improve their brain health although there is no scientific proof that any of them work. One reason for this is that more than 50% of adults over 60 are worried about their memory loss. The problem is that the **F.D.A. does not regulate any drug unless** it is said to cure or improve a specific disease like Dementia. All these nootropic drugs are nonspecific aiming to help brain function. Another way the F.D.A. might get involved is if there were an unusual number of deaths or serious side effects (hospitalizations). Fortunately or unfortunately, this has not happened. So this over-the-counter and on-line industry continues to thrive without product testing or ingredient accuracy.

To be truly effective a Nootropic drug should contain high quality, clinically-tested ingredients put together in proper proportions and the final combination must be tested against a placebo by an independent third-party testing facility. This has not been done yet. The **placebo effect** says that is you are confident that this is going to work, because you were told by your "expert", or it cost you a lot of money, then the odds are that it will work.

If we wish to try any one of the nootropics, experts tell us that the **desired effects are slow to occur.** The placebo effect may occur within days. Research shows that the process requires 3 months for full efficacy. During the first month we may experience fewer senior moments, seem less forgetful and more focused. During the second month we may notice our short-term memory (what happened yesterday) is sharper and recall is faster. After the third month, If the medication worked, we have reached peak cognition, memory, concentration, focus, alertness and confidence.

Now let us discuss some of the chosen TOP 5 NOOTROPICS by various groups:

PREVAGEN, made by Quincy Bioscience, is made from a protein called Apoaequorin and vitamin D, the unique compound as advertised heavily on TV that comes from a certain jellyfish. Other ingredients are white rice flour, sugar, acetic acid and magnesium stearate. This is said "to improve cognitive function in some people who are cognitively normal or mildly impaired". This result is based on a computer-assessed clinical study conducted by the manufacturer. This has been extensively tested for safety, toxicity and allergenicity. Some studies question the effectiveness of Prevagen as a memory booster. From my scientific medical background, I find it difficult to believe that after ingesting this whole protein, which the hydrochloric acid in our stomachs break down to peptides and amino acids, can somehow line up correctly to help memory any more than any other ingested protein. Prevagen also contains sugar, soy and dairy. It is the "subject of FTC lawsuits and an FDA case about potential side effects".

NEURIVA, made by Schiff Pharma, contains vitamin B6, B12, folic acid, Cognivive (a non-caffeine Alpinia galanga extract [a Ginger family plant used as an herb in Unani {Thai} medicine and as a spice in Arab and Asian cooking]) and Neurofactor (a natural patented extract made from Premium Coffee arabica coffee cherries).

Shroom IQ - Brain Gummies, made by Shroom IQ, contains "10 brain boosting mushrooms known for their cognitive enhancing properties", phosphatidyl serine, Rhodiola Rosea, and Hericium Erinaceus. It is vegan-friendly, non-GMO, gluten-free, allergen free and has no artificial colors or additives or side effects. It comes in sachets They claim that "this is made with clinically tested ingredients" but there is no proof that this fulfills its promise.

Lion's 'Mane Adaptogenic) **Mushroom complex** combined with BioPerine, made by Pattern Wellness, contains certain whole mushroom compounds including polysaccharides, erinacines, hericerines, alkaloids, steroids, and lactones.

BEN CARSON'S NEURO BOOST IQ, made by Neuro Boost IQ, contains Ginkgo, Bacopa, Siberian ginseng, alpha-lipoic extract and phosphatidyl serine. Made for adults, this comes in unflavored capsules and there is no data as proof.

RESEARCH VERIFIED MEMORY BOOSTER, made by Research Verified LLC, contains Vit B-X, B complex, Amino-X, Amino complex, BioPerine and caffeine with "all the useful ingredients of the highest quality", "in the correct proportions" and is 100% safe. It is monitored and has a 365-day risk-free 100% money back guarantee.

MOMENTOUS BRAIN DRIVE, made by Momentous, contains the B vitamins and Bacopa tyrosine, acetyl L-carnitine, BioPerine and "High absorption Lion's Mane complex. Has no guarantees. It is GMO and gluten free.

AGELESS BRAIN, made by Pure Health, contains Bacopa, GABA, caffeine, Camu, Cat's Claw extract, Cinnamon bark, Pau d'Arco, cacao powder, Dragon's Blood resin extract vitamins B 3 (niacin) and 6, Huperzine A, Alpha GPC and phosphadityl-serine but does not give the proportions of the ingredients. It is GMO and gluten free, vegan and has mixed reviews on Amazon.

SYNAPTIC XR COGNITIVE ENHANCER, made by Wholesale Health Club, contains Bacopa, Rhodiola, lutein, bilberry leaf, vitamins B6 and B12, Ginkgo, zeaxanthin, green tea extract, cinnamon, AGP choline, and Holy Basil. It is caffeine, sugar, gluten and dairy free. Its ingredients are clinically tested and proven safe. **NEURO TECH IQ, made** by Wholesale Health Club, contains Bacopa Ginkgo, Ginseng, Ashwagandha, caffeine, Huperzine A, vitamins B3 and C, green tea, and Taurine. It is gluten, dairy and soy free. It has ingredients that may cause allergies but are all tested.

Noobru Advantage, made by Noobru, contains 11 brain enhancing ingredients including vitamin B5, B6, phosphatidyl serine, Alpha GPC, L-theanine, Huperzine A, choline bitartrate, BioPerine, tyrosine, Ashwagandha, and sulbutiamine. It also contains caffeine and gelatin (not good for vegans). It comes in a well absorbed strawberry flavored powder.

SuperHealth Lion's Mane, made by SuperHealth Labs (around for 20 years), contains Lion's Mane mushroom extract, fish, soy and needs 4 tablets daily.

DYNAMIC BRAIN, made by Stonehenge, contains vitamin B5, B6, Bacopa Monnieri, Huperzine A, etc. It has fish and soy but is free of gluten and dairy.

Alpha Brain, made by Onnit, contains L-theanine, L-Tyrosine, Alpha-GPC, Huperzia Serrata, B vitamins, etc. It is gluten and caffeine free.

According to the Mayo Clinic and most other medical experts, aside from memory medications which may work or may not, there are **7 recommendations known to improve and sharpen our memory.**

- 1. Be physically active, which increases blood flow to our brain and the rest of body.
- 2. Stay mentally active with reading, puzzles, hobbies, volunteering, etc.
- 3. Spend time with others, which helps prevent depression and stress.

4. Stay organized. Clutter and disarray feed into forgetfulness. Make to-do lists. Write down appointments. Keep wallets, keys, eyeglasses in the same place.

5. Sleep well. Not enough sleep, disturbed sleep, or restless sleep are linked to memory loss. As adults we require 7-9 hours' sleep nightly on a regular basis.

6. Eat a healthy diet. Eat a variety of fruits, multi-colored vegetables, and whole grains. Eat low-fat proteins like fish and poultry without skin and beans. Be careful with alcohol, which definitely has negative effects on the brain.

7. Attend to our chronic health problems. Visit our health care providers and heed their expert advice.

As we reach our mature years and our brains age, the thought of boosting our brain power certainly is appealing and popping a pill seems to be an easy solution. The multiple combinations manufactured in these commercial products have not been adequately tested for efficacy. Many of them have been tested for ingredient safety so they should not be considered "snake oil" but they are expensive, do not make us more intelligent nor prevent Dementia or Alzheimer's Disease and appear to perform their nootropic effects only while they are in our bodies. So, I suggest "caveat emptor" Let the buyer beware.