

Treatment of Memory Disorders – I. Nonpharmacological and Non-interventional Therapies

Dr. Alain L. Fymat*

Professor, International Institute of Medicine & Science, California, USA.

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***Corresponding Author:** Dr. Alain L. Professor, International Institute of Medicine & Science, California, USA.

Abstract

Like the body, the brain requires certain nutrients to function smoothly. Even if it does not use a food directly, it benefits from a healthy circulatory system, pointing to the association with cardiovascular health.

Certain diets have specifically been created with the aim of promoting brain health and reducing the risk of dementia and other neurodegenerative diseases. I detail below these brain diet plans and the latest research on the way nutrition may affect dementia risks.

I will present the benefits of nutritional therapy and supplementation for memory, cognition improvement, and mental health in general. I will also review a number of complementary and alternative therapies and provide a detailed analysis of the ten most current medications for sleep therapy.

Abbreviations

AD: Alzheimer's disease; AD: Atkins' diet; AHA: American Heart Association; ATP: Adenosine triphosphate; BBB: Blood-brain barrier; CAT: Complementary and alternative therapies; CNS: Central nervous system; DHA: Docosahexaenoic acid; GI: Glycemic index; HSV: Herpes simplex virus; IBD: Inflammatory bowel disease; LDL: Low-density lipoproteins; LGIT: Low glycemic index treatment; MAD: Modified AD; MCT: Medium chain triglycerides; MOI: Monoamine oxidase inhibitors; NDD: Neurodegenerative diseases; NFT: Neurofibrillary tangles; PNS: Peripheral nervous system; PTSD: Post-traumatic stress disorder; TBI: Traumatic brain injury; VD: Vascular dementia.

Keywords

Complementary and alternative therapies; Creatine; Memory disorders; Nutritional therapy; Sleep therapy; Supplementation therapy.

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To function smoothly, the brain requires certain nutrients. If the diet is consistently insufficient or lacks in such nutrients, the risk of various types of dementia increases. The brain also benefits from a healthy circulatory system, so it would not be surprising if the best brain foods are also associated with cardiovascular health. There is clear evidence of the benefits of certain foods preferably to others. However, it is important to distinguish between the benefits of individual food items and those of diets utilizing some of them. Certain diets have specifically been devised for reducing the risk of certain neurodegenerative diseases, specifically dementia and its

Alzheimer's type. For this reason, Tables 1 and 2 below present respectively individual foods and diets.

Nutritional therapy for memory, cognition improvement, and mental health

The benefits of nutritional therapy and supplementation for memory, cognition improvement, and mental health in general are beginning to be better known, These and complementary and alternative therapies are analyzed here. Because of the importance of sleep, a detailed review of current medications for sleep therapy is also provided.

Nutrition in general

The following properties and health benefits of various food types are standard in the dietary and nutritional literature (Table 1). More will be said in the following sections regarding nutrition for brain health:

Food type	Examples	Properties	Health benefits
Avocados	o Avocado	o Antioxidants	<ul style="list-style-type: none"> o Memory improvement o Cholesterol lowering o Arthritis prevention o Skin protection
Beans	o Black beans o Chili beans	o Low-calorie, low-fat foods, healthy fiber, protein, beneficial minerals (iron and potassium)	<ul style="list-style-type: none"> o May lower dementia risk <u>DIETARY AIM:</u> o At least 3 servings/week
Berries	o Blueberries o Raspberries o Strawberries	<ul style="list-style-type: none"> o Anthocyanins (polyphenols) o Anti-inflammatory o Extract supplements show similar improvements o Strawberries are abundant with antioxidants 	<ul style="list-style-type: none"> o Better brain health o Neuroprotective of aging brains o Inflammation reduction o Short-term memory strengthening o Improves learning and other mental processes o DNA damage lessening o Cell communication improvement <u>DIETARY AIM:</u> o At least 2 servings/week. o Fresh berries are better
Dairy products	o Cheese o Milk o Yogurt <u>ALTERNATIVES:</u> o Orange juice (fortified)	Calcium	<ul style="list-style-type: none"> o Better bone health o Osteoporosis risk lowering o Cancer (colon) risk lowering

	<ul style="list-style-type: none"> o Rice o Soy drinks o Tofu 		<ul style="list-style-type: none"> o High-blood pressure lowering <u>DIETARY AIM:</u> 1,200[mg]/day
Fibers	<ul style="list-style-type: none"> o Fruits o Legumes o Nuts o Oatmeal o Veggies 	High fiber content	<ul style="list-style-type: none"> o Blood sugar lowering o Cholesterol levels lowering o Constipation easing o Weight controlling <u>DIETARY AIM:</u> o Men (50+): 30[g]/day o Women: 21[g]/day
Fish	<p>Fatty fish:</p> <ul style="list-style-type: none"> o Herring o Salmon o Trout (farmed) o Tuna <p><u>ALTERNATIVES:</u></p> <ul style="list-style-type: none"> o Algae o Chia seeds o Flaxseed o Walnuts 	<ul style="list-style-type: none"> o High in DHA (omega-3 fatty) acid o Low DHA linked to Alzheimer's disease (AD) 	<ul style="list-style-type: none"> o Touted as brain food o Brain enhancement o Memory enhancement o Learning improvement <u>DIETARY AIM:</u> o Once/day
Grains - Whole		<ul style="list-style-type: none"> o Retain more of their plant-based nutrients than refined grains 	<ul style="list-style-type: none"> o Improved odds against dementia <u>DIETARY AIM:</u> o At least 3 servings/ day
Lean protein	<ul style="list-style-type: none"> o Dairy products o Eggs o Meat (lean) 	Protein rich	<ul style="list-style-type: none"> o Muscle lessening of natural loss <u>DIETARY AIM:</u> o Avoid powdered protein
Nuts	Walnuts and most other nuts	<ul style="list-style-type: none"> o Soluble fibers o Healthy oils o Proteins o Vitamins 	<ul style="list-style-type: none"> o Walnuts singled out as brain food o Protection against Alzheimer's disease (AD) o Memory improvement o Potential protection from dementia and other neurodegenerative declines <u>DIETARY AIM:</u> o 5 servings/week
Oil	Olive (virgin)	o Phenols	<ul style="list-style-type: none"> o Anticancerous o Anti-inflammatory o Antimicrobial o Protection against Alzheimer's disease (AD) o Protects against other neural disorders (Parkinson's disease, spinal cord injury) <u>DIETARY AIM:</u> o Use for cooking
Poultry	<ul style="list-style-type: none"> o Chicken o Turkey 	o Preferred to red meat	<ul style="list-style-type: none"> o Maintains cognitive health <u>DIETARY AIM:</u> o Twice/week
Red- and orange-colored produce	<ul style="list-style-type: none"> o Bell peppers (red, orange) o Tomatoes o Watermelon 	Lycopene	<ul style="list-style-type: none"> o Cancer risk lowering o Stroke risk lowering

Spices	<ul style="list-style-type: none"> o Cinnamon o Garlic o Turmeric 	Antioxidants	<ul style="list-style-type: none"> o Cinnamon: Cholesterol and triglycerides lowering o Garlic: Blood vessels kept open o Turmeric: Depression, AD, and cancer protector <p><u>DIETARY AIM:</u></p> <ul style="list-style-type: none"> o Fresh or dried
Sweet potato	Sweet potato	o Beta carotene	<ul style="list-style-type: none"> o Beta carotene conversion to vitamin-A o Eyesight protection o Skin protection o Immune system strengthening o Brain changes lowered <p><u>DIETARY AIM:</u></p> <ul style="list-style-type: none"> o Use purple variety
Tree nuts	<ul style="list-style-type: none"> o Almonds o Cashews o Pecans o Pistachios o Walnuts o Other nuts 	o Anti-aging powers	<ul style="list-style-type: none"> o Aging brain protection <p><u>Delay or/and prevent:</u></p> <ul style="list-style-type: none"> o Age-related heart disease o Cancer (some types) o Diabetes type 2 o Nerve disease o Stroke
Vegetables	<p><u>CRUCIFEROUS:</u></p> <ul style="list-style-type: none"> o Broccoli o Brussel sprouts o Cauliflower 	Sulforaphane	<ul style="list-style-type: none"> o Immune booster o Cancer risk lowering
	<p><u>LEAFY GREENS:</u></p> <ul style="list-style-type: none"> o Bok choy o Broccoli o Collard greens o Kale o Mustard o Salads o Spinach o Swiss chard 	<ul style="list-style-type: none"> o Plenty of nutrients o Antioxidants o Rich in nitrates 	<ul style="list-style-type: none"> o Anti-cataract o Anti macular degeneration o Memory improvement o Cognition betterment o May lower dementia risk, cancer risks <p><u>DIETARY AIM:</u></p> <ul style="list-style-type: none"> o At least 6 servings/week
	<p><u>OTHERS:</u></p>	o Special phytochemicals	<ul style="list-style-type: none"> o May protect body in special ways o More vegetables for brain power <p><u>DIETARY AIM:</u></p> <ul style="list-style-type: none"> o At least 1 serving/day
Water	Water	Food for health	<ul style="list-style-type: none"> o Cushions joints <p><u>Helps control:</u></p> <ul style="list-style-type: none"> o Body temperature o Mood <p><u>DIETARY AIM:</u></p> <ul style="list-style-type: none"> 8 glasses/day
Whole grains	<ul style="list-style-type: none"> o Quinoa o Wheat berries o Whole-wheat bread o Whole-wheat couscous 	<ul style="list-style-type: none"> o Fibers o Vitamins: B-6, folate 	<ul style="list-style-type: none"> o Improves brain health o Cancer risk lowering o Diabetes risk lowering o Heart disease lowering risk

Wine	o Reds	o Polyphenols	<ul style="list-style-type: none"> o Protects aging memory decline o Boosts brain health o Aids in cognition regardless of dementia o May lower stroke risks <u>DIETARY AIM:</u> o 1 glass/day
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Table 1: General properties and health benefits of various food types

In brief, as per the above Table, good foods for memory improvement include especially: avocados, beans, blueberries, fish, whole grains, nuts, olive oil, poultry, tree nuts, dark leafy greens and other vegetables, and wine (red; in moderation).

Notes:

- Regarding blueberries consumption: In randomized, double-blind, placebo-controlled trials, researchers found that a daily dose of blueberries ameliorates brain health in that it improves executive function, strengthens short-term memory, and speeds up reaction times. However, they do not seem to ameliorate delayed recall. It appears that the blueberries’ anthocyanins (the blue pigments) are responsible for improving cerebral (and vascular) blood flow - the likely mechanisms behind healthy cognitive function. Anthocyanins are polyphenols, a family of plant-based compounds that are increasingly associated with health benefits. There are about 8,000 different types of polyphenols (some are also present in strawberries, raspberries, red grapes, purple vegetables, green tea, broccoli, pears, and spices like turmeric and cinnamon) that provide health benefits. They can also provide a brain boost, lower blood pressure, and contribute to better cardiovascular health.
- Mechanism behind the beneficial effects of polyphenols: It is not yet fully understood. One theory is that their metabolites may “act as

signaling molecules, acting through several cell-signaling pathways, modulating nitric oxide bioavailability and different enzymes”. However, while blueberries improve cerebral and vascular blood flow, they do not reduce arterial stiffness. It has also been hypothesized that polyphenols may act through enhancing the abundance of butyrate-producing beneficial bacteria and therefore the production of butyrate in the gut microbiota.

- Other foods linked to cognitive health: They are numerous (refer to Table 1) and include, for example, omega-3 fats (wild salmon and sardines), which are linked to better cognition because of their rich DHA (docosahexaenoic acid) content and potent anti-inflammatory properties. In addition, unsaturated fats may also help lower levels of beta-amyloid, a component in the development and progression of AD.

Diets

It is not my intent to dwell at length on the several diets available. I will, nonetheless, present in Table 2 the main available diets, including their particulars, neurological benefits, if any, and their side effects.

Diet	Principle	Application	Use(s)	Neurological benefits	Side effects
1. Atkins a. Original (AD)	<ul style="list-style-type: none"> o Similar to the classical ketogenic diet for adults o The classical “metabolic advantage” is false 	<ul style="list-style-type: none"> o Whole unprocessed food with low glycemic index (GI) o Low carb, high fat diet o No limit on calories & proteins 	For weight loss (questionable or false)	<ul style="list-style-type: none"> o Reduction of epileptic seizures in adults (some evidence) 	<ul style="list-style-type: none"> o Increased heart disease
b. Modified (MAD)	<ul style="list-style-type: none"> o Less strict regimen than the original Atkins' diet 	<ul style="list-style-type: none"> o Ketogenic ratio: 1:1 	<ul style="list-style-type: none"> o Not for weight loss o No initial fast o No hospital stay o No intensive dietitian support 		
2. Atlantic	<ul style="list-style-type: none"> o Same as the Mediterranean diet 	<ul style="list-style-type: none"> o More fish and seafood o More fresh greens 			
3. DASH	<ul style="list-style-type: none"> o To prevent/control hypertension 	<ul style="list-style-type: none"> o Rich in fruits, vegetables, whole grains, and low-fat dairy foods o Includes meat, fish, poultry, nuts, and beans o Limited in sugar-sweetened foods and beverages, red meat, and added fats 	<ul style="list-style-type: none"> o To reduce LDL, cholesterol, blood pressure, and heart disease risk 	<ul style="list-style-type: none"> o None reported o May have in direct benefits including in vascular dementia (VD) 	<ul style="list-style-type: none"> o None reported
4. Ketogenic a. Classic	<ul style="list-style-type: none"> o To burn fats, not carbs 	<ul style="list-style-type: none"> o High fat, adequate protein, low carb o Ketogenic ratio: (Fats to combined carbs + proteins): 4:1 	<ul style="list-style-type: none"> o Refractory pediatric epilepsy (no longer used) o Adult epilepsy with less strict diet (similar to MAD) o Other NDDs o Requires vitamins & minerals supplementation 	<ul style="list-style-type: none"> o Neuroprotective o Disease-modifying 	<ul style="list-style-type: none"> o Constipation o High cholesterol o Growth slowing o Acidosis o Possible kidney stones
b. (12/3) Variant	<ul style="list-style-type: none"> o 12 hours between dinner and breakfast o Last meal 3 hours before sleep 	<ul style="list-style-type: none"> o Same as classic ketogenic diet 	<ul style="list-style-type: none"> o Same as classic ketogenic diet 		
c. LGIT Variant	<ul style="list-style-type: none"> o Stable blood glucose level may be one of the mechanisms of action 	<ul style="list-style-type: none"> o ~ 60% of calories from fat o Allows more carbs than the classic ketogenic 	<ul style="list-style-type: none"> o No precise weighting of food o Initiated and maintained at outpatient clinics 		

	o Low GI carbs	or MAD	o No intensive dietitian support		
d. MCT Variant	o Ketogenic ratio: 1:1	o 50% of calories from coconut oil o 50% less overall fat than the classical ketogenic			
5. Mediterranean	o Traditional diet of Mediterranean basin	o Green veggies (specifically spinach, Swiss chard, and kale rich in nitrates) o High consumption of olive oil, legumes, unrefined cereals, fruits, vegetables o Moderate-to-high consumption of fish o Moderate consumption of dairy products o Moderate wine consumption o Low-consumption of non-fish meat products	Various rates of consumption of different foods	o Observational benefits o No clinical findings for individual foods o Better cognitive performance (unclear if causal) o Lower cognitive decline o Lower risk of Alzheimer's (AD) o Negative association with risk of progression from MCI to AD o Arteries dilation helped o Heart health diet optimization o Blood flow lowering o Vascular, heart	o None reported
6. MIND	o Combination of Mediterranean and DASH	o Emphasizes the intake of fresh fruits, vegetables, and legumes o Also includes recommendations for specific foods (such as: berries, leafy greens)	o Reduces cognitive decline	o Brain protective o More effective in reducing cognitive decline than either the DASH or Mediterranean diet alone o Lower risk of cognitive impairment (35%) o Protects from dementia (in one study: by up to 53% for people ages 58 to 98) o Validated through several studies o Causal relationship between diet and cognitive decline could not be	o None reported

				determined	
7. Paleo	<ul style="list-style-type: none"> o Eat only predominant foods presumed to have been available during the Paleolithic era o Assumes human digestion has remained unchanged 	<ul style="list-style-type: none"> o Includes fruits, vegetables, nuts, roots, meat o Excludes dairy products, grains, sugar, legumes, processed oils, salt, alcohol, coffee o Avoids processed foods o Avoids foods that humans began eating after the Neolithic revolution (transition from hunting-gathering to settled agriculture) 	<ul style="list-style-type: none"> o Improvements in body composition and metabolic effects o No evidence of help in weight loss except through its caloric restriction 		<ul style="list-style-type: none"> o Weakness o Diarrhea o Headaches o Nutritional deficiencies (such as inadequate calcium intake)
8. Caloric restriction (CR)	<ul style="list-style-type: none"> o Risk of dementia is associated with obesity o No clinical trials for human brain aging and NDDs (only minimal experiments) 	<ul style="list-style-type: none"> o Not specified 	<ul style="list-style-type: none"> o Weight loss o Improved health in general 	<ul style="list-style-type: none"> o Decreased incidence of AD and Parkinson's o May reduce disease risks o Improves longevity biomarkers o May increase lifespan o Improves mental health 	<ul style="list-style-type: none"> o None reported
9 Mimicking-Fasting	<ul style="list-style-type: none"> o A 5-day vegan diet with a composition such that the human body responds as it does to water-only fasting. 	<ul style="list-style-type: none"> o Focus on low-calorie, low-protein, and high-fat plant-based foods. 	<ul style="list-style-type: none"> o To potentially help slow down the growth of tumors, and make them more susceptible to chemotherapy in certain types of cancer (colorectal, breast therapy in people with hormone-receptor-positive cancer). 	<ul style="list-style-type: none"> o Treatment of multiple sclerosis (MS), cardiovascular disease, autoimmune diseases, inflammatory disease (IBD), skin issues, and Alzheimer's disease (AD). 	<ul style="list-style-type: none"> o Neither a 'stand-alone' solution nor a 'long-term alternative'. <u>Note:</u> The accumulation of the consequences of specific behavior or genetic predisposition cannot be reversed with one specific step.
10. Pescaterian	<ul style="list-style-type: none"> o Fish as a good source of lean protein, omega-3 fatty acids, and other nutrients. o Seafood is low in saturated fat and cholesterol. 	<ul style="list-style-type: none"> o Emphasis on fish, all types of seafood, shellfish, and squid, foods with more fiber, vitamins, and minerals. o Eggs and dairy. o Plant-based proteins (beans, lentils, and tofu). 	<ul style="list-style-type: none"> o Lower risk of heart disease, stroke, and some types of cancer. o Lesser risk of obesity and type 2 diabetes. 		<ul style="list-style-type: none"> o Low-quality seafood can be contaminated with pollutants (PCBs, dioxins), which can build up in the body and potentially cause health problems.

		<ul style="list-style-type: none"> o Fruits and vegetables (same as for vegans and vegetarians), also starchy vegetables (potatoes, corn, winter squash). o Variety of grains (rice, quinoa, oats). 			
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Keys: AD: Alzheimer's disease; AD: Atkins' diet; GI: Glycemic index; LDL: Low-density lipoproteins; LGIT: Low glycemic index treatment; MAD: Modified Atkins' diet; MCI: Mild cognitive impairment; MCT: Medium chain triglycerides; MS: Multiple sclerosis; IBD: Inflammatory bowel disease; VD: Vascular dementia.

Table 2: The main available diets, their particulars, benefits, and side effects

Thus, regarding the neurologic benefits of the several diets covered: The DASH diet may have benefits in vascular dementia; the Mediterranean diet may better cognitive health and lower the risk of AD; the MIND diet may be brain protective, lower the risk of cognitive impairment, and protect against the risk of dementia; the caloric restriction diet may decrease the risk of AD; and the fasting-mimicking diet may be beneficial in treatment of MS, auto-immune diseases, and AD.

Notes: According to the American Heart Association (AHA), a better cardiovascular and cognitive health is promoted by a diet rich in vegetables, fruits, whole grains, healthy proteins, minimally processed foods, and moderate oil and salt intake.

- The Mediterranean diet can help improve blood flow and vascular, heart, and cognitive function. It recommends:
 1. A high intake of vegetables, fruits, whole grains, beans, and legumes.
 2. Low-fat or fat-free dairy products, fish, poultry, non-tropical vegetable oils, and nuts.
 3. Limited added sugars, sugary beverages, sodium, highly processed foods, refined carbohydrates, saturated fats, and fatty or processed meats.

- The MIND diet breaks down the healthiest food types into 10 categories (not presented here).. The list also contains groups of five types of foods to stay away from to protect brain health. Along with these food groups, the diet suggests how much of each food should be consumed (or avoided). The diet recommends the following 10 foods:
 1. Whole grains: three or more servings a day.
 2. Green leafy vegetables (kale, collards, greens; spinach; lettuce/tossed salad): At least 6 servings/week.
 3. Other vegetables (green/red peppers, squash, cooked carrots, raw carrots, broccoli, celery, potatoes, peas or lima beans, tomatoes, tomato sauce, string beans, beets, corn, zucchini/summer squash/eggplant, coleslaw, potato salad): At least 1/day.
 4. Wine: 1 glass/day.
 5. Nuts: 5 servings/week.
 6. Beans and lentils: At least 3 servings/week.
 7. Berries: 2 or more servings/week.
 8. Non-fried poultry (like chicken or turkey): 2 times/week.
 9. Non-fried Fish: 1/week.
 10. Olive oil: Use it as the main cooking oil

The diet also discourages the following 5 foods:

1. Butter and stick margarine: More than a tablespoon daily.
2. Pastries and sweets: More than 5 servings/week.
3. Red meat and pork: More than 4 servings/week.
4. Cheese: More than 1 serving/week.

Fried or fast food (like French fries, chicken nuggets):
More than 1 serving/week.

Supplementation therapy for memory and mental health

The supplements considered include, creatine, vitamin B12, omega-3 fatty acids, and herbal remedies.

Brain creatine

In a 1999 research paper, it was shown that creatine (Cr) was also present in the human brain and that oral Cr intake increased brain Cr levels, suggesting that at least some Cr passed through the blood-brain barrier (BBB). Like muscle, human brain function is highly energy intensive. Therefore, it made sense that the brain would also use Cr as a supplemental energy source. In fact, research revealed that “creatine is so important to human brain function that the brain even synthesizes its own creatine”. Cr is most commonly known as a sports supplement to enhance physical performance. It is a powdery non-steroidal supplement sold in most health food stores and used by bodybuilders or weightlifters to increase strength and muscle size.

Although small amounts of Cr can be obtained directly from food (primarily, fish and beef), muscles also readily absorb Cr from oral supplementation because muscles can use Cr to create adenosine triphosphate (ATP), the life-enabling energy source vital to cellular and muscular function. Muscle cells containing more Cr can produce more energy for physical activities. Thousands of studies support the safety and efficacy of Cr for muscle function. New research indicates that Cr is also important to brain

function, affecting mood and cognition and early trials have suggested that Cr supplementation can improve stress resilience, depression, and brain functions such as memory.

Does Cr improve brain function? Given that it is a bioactive substance in the brain, and proven it improves muscle function, does Cr also improve brain function? If so, which brain functions and which people are most likely to benefit? After more two decades of Cr research, it now appears that:

- Cr supplementation moderately improves memory function in healthy adults. On average, improvements are larger for older adults and smaller for younger adults.
- Cr supplementation may be more beneficial for people experiencing acute/chronic stress or who consume smaller amounts of creatine through diet (e.g., vegans and vegetarians).
- There are higher depressive symptoms among people with lower Cr levels.
- Because anxiety, post-traumatic stress disorder (PTSD), and depression symptoms are associated with metabolic dysfunction and impaired energy levels in the brain - all mechanisms improved by Cr-supplementation can be beneficial. Further, initial human Cr interventional trials have reliably shown small to moderate symptom improvements for individuals with these mental health conditions.
- Animal studies and initial human trials likewise indicate potential benefits of Cr supplementation in people with mild traumatic brain injury (mTBI). Indeed, impaired metabolic function is a common side effect of TBI. This process could potentially be improved by higher Cr intake.
- However, at this point, the optimal dosing schedule (i.e., how much Cr? how often to take it? how long to take it?) for brain benefits remains unclear. Most brain Cr trials borrow

from protocols established for studies testing Cr for physical performance, where consistent regimens of 5 grams of creatine/day are consumed or "pre-loading" regimens of 10-20 grams of Cr/day for 1-2 weeks followed by a 5-gram/day "maintenance" dose are used. But, these doses for physical performance may not necessarily be the appropriate ones for brain function and performance. (Note: As with all health supplements, if considering creatine use, preference should be given to brands that submit to third-party testing to ensure product quality. There is also no scientific basis to use any form other than Cr monohydrate—the cheapest and most proven form of Cr.)

Vitamin B-12

If memory loss is due to vitamin B-12 deficiency, taking the vitamin through diet or nutritional supplement can help correct the condition.

Omega-3 fatty acids

Supplements of omega-3 fatty acids from plants or fish sources do not appear to benefit or harm people with mild to moderate AD, or improve other types of dementia.

Herbal remedies

Herbal remedies, including teas, do not seem to have any clinically-proven memory benefit.

Complementary and alternative therapies

A number of complementary and alternative therapies (CAT) are discussed below:

Aromatherapy and massage

There are unclear benefits.

Cannabinoids

They can relieve behavioral and psychological symptoms of dementia.

Cognitive behavioral therapy (CBT)

Dental hygiene

There is limited evidence linking poor oral health to cognitive decline. Poor oral hygiene can have adverse effects on speech and nutrition, causing general and cognitive health decline. Oral bacteria (*P. gingivalis*, *F. Nucleatum*; *P. intermedia*, *T. Forsythia*; *Treponema* spirochetes) and oral viruses have been observed in the brains of AD patients.

Notes:

- **Spirochetes:** These are neurotrophic in nature, meaning they act to destroy nerve tissue and create inflammation. Inflammatory pathogens are an indicator of AD. Bacteria related to gum disease have been found in the brains of AD individuals. They invade nerve tissue in the brain, increasing the permeability of the BBB and promoting the onset of AD among the elderly population (Fymat, 2018).
- **Herpes simplex virus (HSV):** Found in over 70% of the 50 and older population, it persists in the peripheral nervous system (PNS) and can be triggered by stress, illness or fatigue. High proportions of viral-associated proteins in amyloid-containing plaques or neurofibrillary tangles (NFTs) highly confirm the involvement of HSV-1 in AD pathology. HSV-1 produces the main components of NFTs, the primary marker of AD.

Digital puzzle gaming

Since aging has a negative impact on working memory,

are certain types of games connected with improvements in memory among younger and older adults? Certain experiments showed that adults who play strategy games show a greater working memory capacity compared to younger adults who play action games. This may be surprising because other experiments showed that action games have been associated with superior performance in various measures of attention, perception, and executive function.

For older people, puzzle games have the surprising ability to support mental capabilities to the extent that memory and concentration levels are the same as for 20 year-olds who had not played puzzle games. Older adults who play digital puzzle games may have a higher working memory capacity than older adults who play either other game types or do not play games at all. In addition, older adults who play digital puzzle games can ignore distractions better than other older adults. It seems that the strategy elements of the games (planning, problem solving, etc.) stimulate better memory and attention in older rather than younger people.

Sleep therapies

Sleep disturbances are common. An estimated 50–70 million people in the U.S. experience chronic sleep or wakefulness conditions, which are more common in females and older individuals. A range of medications can help people fall asleep, stay asleep, or both. Prescription sleep aids can often relieve insomnia for short periods. However, many of these medications carry

risks of side effects, misuse, and dependency. In addition, some sleep medications interact with other substances, including other medications, alcohol, and vitamin supplements. Several others are only for short-term use. This section reviews 10 of the best prescribed medications to help a person sleep. It also explores some non-medical solutions for sleep issues.

1. Doxepin (Silenor®): Doxepin is an immediate-release sleep aid tablet (dose: 3 and 6 [mg]), which may help a person fall asleep and stay asleep. People with insomnia use it for up to 3 months. It is not recommended for those taking monoamine oxidase inhibitors (MOI), a type of antidepressant, or people with glaucoma or urinary retention. It may cause side effects in some people, including: central nervous system (CNS) depression, where brain activity slows; worsening depression or suicidal thoughts; and unusual thinking patterns and behavior changes. If symptoms do not clear within 7–10 days, a doctor may need to rule out other possible causes of insomnia. (Note: Pregnant or nursing mothers should consult a doctor before using Silenor. Parents or caregivers should only give it to children or adolescents if directed by a medical professional.)

2. Estazolam (Prosomc®): Prescribed for the short-term treatment of insomnia (dose: 1-2 [mg]), it may help with falling and staying asleep. It has a risk of misuse and dependency and can cause some of the following reactions: Loss of coordination, dizziness, drowsiness, or hypokinesia (reduced range of movements).

Medication	Pros	Cons	Helps fall asleep?	Helps maintain sleep?	Risk of dependence or misuse	Side effects
Doxepin/ Silenor	May help fall and stay asleep	<ul style="list-style-type: none"> o May interact with other medications o May not be suitable for pregnant women 	Yes	Yes	Unlikely	<ul style="list-style-type: none"> o CNS depression o Mood or behavior changes o Suicidal thoughts
Estazolam/	o May help fall and	o Risk of	Yes	Yes	Yes	o Coordination lack

Prosomc	stay asleep	dependency or misuse				<ul style="list-style-type: none"> o Dizziness o Drowsiness o Movements reduced
Eszopiclone/Lunesta	<ul style="list-style-type: none"> o May help a person fall and stay asleep o Is generally safe 	<ul style="list-style-type: none"> o Can cause complex sleep behaviors (such as sleep-walking) 	Yes	Yes	Yes	<ul style="list-style-type: none"> o Anxiety o Dizziness o Headache o Taste unpleasantness o Viral infections
Ramelteon/Rozem	<ul style="list-style-type: none"> o Not a controlled substance o Little chance of causing dependency 	<ul style="list-style-type: none"> o Has the potential for adverse and allergic reactions 	Yes	No	Unlikely	<ul style="list-style-type: none"> o Dizziness o Drowsiness o Fatigue o Insomnia worsening
Suvorexant/Behsomra	<ul style="list-style-type: none"> o May help fall and stay asleep 	<ul style="list-style-type: none"> o Risk of dependency or misuse 	Yes	Yes	Yes	<ul style="list-style-type: none"> o Diarrhea o Dry mouth o Headache o Upper respiratory tract infection
Temazepam/Restoril	<ul style="list-style-type: none"> o Strong sedative effect may help with insomnia 	<ul style="list-style-type: none"> o Risk of dependency, withdrawal, and misuse 	Yes	Yes	Yes	<ul style="list-style-type: none"> o Anxiety o Depression o Headache o Fatigue o Nausea o Mouth dryness o Vertigo
Trazodone/Desyrel	<ul style="list-style-type: none"> o Low dose anti-depressant o May cause fewer side effects than traditional sleep medications 	<ul style="list-style-type: none"> o Can cause mental health side effects (suicidal ideation) 	Yes	Yes	Unlikely	<ul style="list-style-type: none"> o Drowsiness o Edema o Suicidal thoughts o Vision blurs o Weight loss
Triazolam/Halcion	<ul style="list-style-type: none"> o May help fall asleep 	<ul style="list-style-type: none"> o Only for short term use 	Yes	No	Yes	<ul style="list-style-type: none"> o Lack of coordination o Dizziness o Drowsiness o Lightheadedness
Zaleplon/Sonata	May help fall asleep	<ul style="list-style-type: none"> o Risk of dependency and adverse effects o Does not help maintain sleep 	Yes	No	Yes	<ul style="list-style-type: none"> o Abdominal pain o Headache o Weakness
Zolpidem (Ambient/Intermezzo/Zolptimist)	<ul style="list-style-type: none"> o May help fall and stay asleep 	<ul style="list-style-type: none"> o May cause complex sleep behaviors o Other adverse reactions 	Yes	Yes	Yes	<ul style="list-style-type: none"> o Dizziness o Headache o Sleepiness (next day)

Table 3: Benefits and risks of various sleep medications

3. Eszopiclone (Lunesta®): Lunesta (dose: 1 up to 3 [mg]) may help a person fall and stay asleep. It is a controlled substance with a tendency to lead to misuse and dependency. A person may also experience diminishing effects or increased tolerance to the medication over time. Though generally safe, its reported side effects include: Anxiety, dizziness, dry mouth, hallucinations, headache, rash, unpleasant mouth taste, and viral infections. In addition, it may cause a person to engage in complex sleep behaviors, such as sleep-walking or driving while asleep. Precautions before taking Lunesta include: Age: (older people should avoid taking higher doses); allergies (an allergic reaction can be caused in some people); liver function (people with reduced liver function should avoid taking Lunesta); mental health (Lunesta may worsen depression or suicidal thoughts); and safety (higher doses can impair a person's CNS even when awake, making driving and other complex tasks more dangerous). (Note: Pregnant or nursing mothers should consult a doctor before taking Lunesta.)

4. Ramelteon (Rozerem®): Unlike other medications, Rozerem (one size single dose not to be exceeded: 8 [mg]) may be prescribed for longer-term use to help a person fall asleep. It is not a controlled substance, has a low likelihood of misuse or dependency. However, it can still cause side effects such as: Allergic reactions in some people, dizziness, drowsiness, fatigue, and worsening insomnia. (Note: Use caution in taking this medication. Other groups may include people who may have had a past allergic reaction to the medication; have severe liver impairment; are taking the medication fluvoxamine; are pregnant.)

5. Suvorexant (Belsomra®): This medication (dose: 5-20 [mg]; higher doses could lead to more adverse reactions) may help a person fall asleep and maintain sleep. However, there is a risk of misusing it and developing dependency. Like other controlled substances, it can cause CNS impairments that can lead to trouble with driving and other activities. It can also cause:

Complex sleep behaviors; sleep paralysis; worsening suicidal thoughts or depression. Other potential side effects reported in clinical trials include: Cough, diarrhea, dizziness, unusual dreams, headache, dry mouth, or upper respiratory tract infection.

6. Temazepam (Restoril®): Temazepam (doses: 7.5 to 30 [mg]) is a benzodiazepine, which may cause dependency and addiction if a person misuses it. It is available by prescription for the short-term treatment of insomnia (typically, 7–10 days). It can cause a variety of side effects, which may include one or more of the following: Anxiety, confusion, depression, diarrhea, dizziness, drowsiness, dry mouth, fatigue, headache, nausea, nightmares, and vertigo. (Note: Pregnant or nursing mothers should not take Restoril).

7. Trazodone (Desyrel®): This medication (dose: typical starting 150 [mg] with a maximum [400 [mg] daily; typically 25-100 [mg] for sleep disturbances) modulates the neurotransmitter serotonin. It is typically used to treat major depressive disorder; however, it may be prescribed off-label to help a person fall asleep since one of its effects is drowsiness. Possible side effects include: Diarrhea, drowsiness, edema (body tissues contain too much fluid), fainting, fatigue, nasal congestion, increased suicide thoughts, blurred vision, or weight loss.

(Note: Alcohol consumption can increase the effects.)

8. Triazolam (Halcion®): Because the medication (dose: 0.25 and 0.50 [mg]) has the potential for dependency and misuse, it is not recommended as a long-term treatment for insomnia, typically for 7-10 days. Common side effects may include: Ataxia (or lack of muscle coordination), dizziness, drowsiness, lightheadedness. In some people. It can cause: CNS issues (anxiety, behavioral changes, and unusual thinking), dependency, worsening depression, worsening insomnia, complex sleep behaviors, issues with performing activities such as driving, or withdrawal symptoms when suddenly stopping taking it.

9. Zaleplon (Sonata®): This medicine (dose: 5-10 [mg]) may be useful for the short-term treatment of insomnia but, while it may help a person fall asleep, it does not help maintain sleep. It has some risk of dependency and a high likelihood of misuse. Side effects include: Diarrhea, difficulty concentrating, dizziness, drowsiness, and less commonly: hallucinations, memory loss, and mood changes.

10. Zolpidem (Ambien®, Intermezzo®, and Zolpimist®): This sleep medication (dose: not exceeding 12.5 [mg]) may help with falling asleep and maintaining sleep maintenance. It may be prescribed for short-term insomnia relief but may cause complex sleep behaviors. It can also lead to anaphylactic reactions, CNS depression, worsening depression, and withdrawal effects. Common side effects may include: Dizziness, headache, next-day sleepiness.

(Note: It is not recommend during pregnancy.)

Table 3 compares the benefits and risks of these several sleep medications.

Tweaking memories

Can replacing bad memories with good ones or even erasing certain memories improve mental health? Researchers are exploring ways to manipulate memories to discover novel methods to treat PTSD, depression, and AD. National Geographic is actually conducting public events that feature thought-provoking presentations by today's leading explorers, scientists, photographers, and performing artists.

Lifestyle changes

Such lifestyle changes include:

- Relaxation techniques.

- Engaging in healthy sleep habits (sleeping in a cool, dark room, and avoiding distractions and large meals before bed).

- Increased physical exercise.

Conclusions and take-aways

- To function smoothly, the brain requires certain nutrients. If the diet is consistently insufficient or lacks in such nutrients, the risk of various types of dementia increases. There is clear evidence of the benefits of certain foods preferably to others.

- The benefits of nutritional therapy and supplementation for memory, cognition improvement, and mental health in general are beginning to be better known.

- The brain also benefits from a healthy circulatory system, so it would not be surprising if the best brain foods are also associated with cardiovascular health.

- Certain diets have specifically been devised for reducing the risk of certain neurodegenerative diseases, specifically dementia and its Alzheimer's type.

- The mechanism behind the beneficial effects of polyphenols is not yet fully understood.

- A better cardiovascular and cognitive health is promoted by the Mediterranean diet, which can help dilate the arteries, and improve blood flow and vascular, heart, and cognitive function.

- Creatine supplementation moderately improves memory function in healthy adults, may be

more beneficial for people experiencing acute/chronic stress or who consume smaller amounts of creatine through diet, ameliorate depressive symptoms, and moderately improve mental health conditions and mild traumatic brain injury.

- If memory loss is due to vitamin B-12 deficiency, taking the vitamin through diet or nutritional supplement can help correct the condition.
- Researchers are exploring ways to manipulate memories to discover novel methods to treat post-traumatic stress disorder (PTSD), depression, and Alzheimer's disease.
- Digital puzzle strategic gaming improves working memory more for older adults than for younger adults who play action games.
- For older people, puzzle games have the surprising ability to support mental capabilities to the extent that memory and concentration levels are the same as for 20 year-olds who had not played puzzle games.
- The ten best prescribed medications to help a person sleep have been critically discussed.
- Lifestyle changes are also recommended for better mental health.

Sidebar 1 and 2 respectively provide more details on Cr and caring for mental health.

Sidebar 1 – Creatine

A brief history

In 1832: Michel Eugène Chevreuil isolated and first identified creatine (Cr) from the basified water-extract of

skeletal muscle.

In 1912: Otto Folin and Willey Glover Denis found evidence that ingesting Cr can dramatically boost the Cr content of the muscle.

In the 1920s: Consumption of large amounts of Cr did not result in its excretion, pointing to the ability of the body to store Cr which, in turn, suggested its use as a dietary supplement.

In 1927: Phosphocreatine (PCr, creatine phosphate) is discovered.

In 1928: Cr is shown to exist in equilibrium with creatinine.

In the late 1920s: After finding that the intramuscular stores of Cr can be increased by ingesting Cr in larger than normal amounts, and having discovered PCr, scientists determined that Cr, naturally formed in vertebrates, is a key player in the metabolism of skeletal muscle.

In the 1960s: Creatine kinase (CrK) is shown to phosphorylate ADP using PCr to generate ATP. It follows that ATP, not PCr is directly consumed in muscle contraction. CK uses Cr to "buffer" the ATP/ADP ratio.

Since the early twentieth century: Cr's influence on physical performance has been well documented.

In 1992: Following the 1992 Olympics in Barcelona, an August 7, 1992 article in The Times reported that Linford Christie, the gold medal winner at 100 meters, had used Cr before the Olympics. (Christie was found guilty of doping later in his career.) Further, an article in Bodybuilding Monthly named Sally Gunnell, the gold medalist in the 400-meter hurdles, as another Cr user. Still further, The Times also noted that 100-meter hurdler Colin Jackson began taking Cr before the

Olympics.

In 1993: Cr supplements designed for strength enhancement became commercially available when a company called Experimental and Applied Sciences (EAS) introduced the compound to the sports nutrition market under the name Phosphagen. Research performed thereafter demonstrated that the consumption of high glycemic carbohydrates in conjunction with Cr increases Cr muscle stores.

Metabolic role

Cr is a naturally occurring non-protein compound and the primary constituent of PCr, which is used to regenerate ATP within the cell. 95% of the human body's total Cr and PCr stores are found in skeletal muscle, while the remainder is distributed in the blood, brain, testes, and other tissues.

Cr is not an essential nutrient. It is an amino acid derivative, naturally produced in the human body from the amino acids glycine and arginine and subsequently methylated. Cr itself can be phosphorylated and used as an energy buffer in skeletal muscles and the brain. A cyclic form of Cr, called creatinine, exists in equilibrium with its tautomer and with Cr.

Phosphocreatine systems

Cr is transported through the blood and taken up by tissues with high energy demands, such as the brain and skeletal muscle, through an active transport system. Cr has the ability to increase muscle stores of PCr, potentially increasing the muscle's ability to resynthesize ATP from ADP to meet increased energy demands.

Cr supplementation appears to increase the number of myonuclei that satellite cells will 'donate' to damaged muscle fibers, which increases the potential for growth of those fibers.

Genetic deficiencies

Genetic deficiencies in the Cr biosynthetic pathway lead to various severe neurological defects. Clinically, there are three distinct disorders of Cr metabolism. Deficiencies in the two synthesis enzymes are inherited in an autosomal recessive manner. A third defect, Cr transporter defect, is caused by mutations in SLC6A8 and inherited in a X-linked manner. This condition is related to the transport of Cr into the brain.

(Note for vegetarians: Some studies suggest that total muscle Cr is significantly lower in vegetarians than non-vegetarians, probably due to an omnivorous diet being the primary source of Cr. Supplementation is needed to raise the concentration of Cr in the muscles of lacto-ovo vegetarians and vegans up to non-vegetarian levels as they have lower Cr concentrations in muscle and blood, but not brain.)

Pharmacokinetics

Most of the research to-date on Cr has predominantly focused on its pharmacological properties and not into its pharmacokinetics. Studies have not established pharmacokinetic parameters for clinical usage of Cr such as volume of distribution, clearance, bioavailability, mean residence time, absorption rate, and half life. A clear pharmacokinetic profile would need to be established prior to optimal clinical dosing.

Dosing

- Loading phase: Approximately 0.3 g/kg/day divided into 4 equally-spaced intervals has been suggested since Cr needs may vary based on body weight. Also, taking a lower dose of 3 grams a day for 28 days can increase total muscle Cr storage to the same amount as the rapid loading dose of 20 g/day for 6 days. However, a 28-day loading phase does not allow for ergogenic benefits of Cr

supplementation to be realized until fully saturated muscle storage. Supplementing Cr with carbohydrates or carbohydrates and protein has been shown to augment Cr retention. Higher doses for longer periods of time are being studied to offset CR synthesis deficiencies and mitigating diseases.

- Maintenance phase: After the 5–7 day loading phase, muscle Cr stores are fully saturated and supplementation only needs to cover the amount of Cr broken down per day. This maintenance dose was originally reported to be around 2–3 g/day (or 0.03 g/kg/day), however, some studies have suggested 3–5 g/day maintenance dose to maintain saturated muscle Cr.

Absorption

Endogenous serum or plasma Cr concentrations in healthy adults are normally in a range of 2–12 mg/L. A single 5 gram (5000 mg) oral dose in healthy adults results in a peak plasma Cr level of approximately 120 mg/L at 1–2 hours post-ingestion. Cr has a fairly short elimination half-life, averaging just less than 3 hours, so to maintain an elevated plasma level it would be necessary to take small oral doses every 3–6 hours throughout the day.

Clearance

It has been shown that once supplementation of Cr stops, muscle Cr stores return to baseline in 4–6 weeks.

Exercise and sport

Cr supplements are marketed in ethyl ester, gluconate, monohydrate, and nitrate forms. For sporting performance, they are considered safe for short-term use

but there is a lack of safety data for long term use. Cr monohydrate might help with energy availability for high-intensity anaerobic exercise, but has no significant effect on aerobic endurance.

Research on cognitive performance

Cr is reported to have a beneficial effect on brain function and cognitive processing, although the evidence is difficult to interpret systematically and the appropriate dosing is unknown. The greatest effect appears to be in individuals who are stressed (due, for instance, to sleep deprivation) or cognitive impairment.

A 2018 systematic review found that *"generally, there was evidence that short term memory and intelligence/reasoning may be improved by creatine administration", whereas for other cognitive domains "the results were conflicting"*. Another 2023 review initially found evidence of improved memory function. However, it was later determined that faulty statistics led to the statistical significance and after fixing the "double counting", the effect was only significant in older adults.

Some mitochondrial diseases

Parkinson's disease (PD)

Cr's impact on mitochondrial function has led to research on its efficacy and safety for slowing PD. As of 2014, the evidence did not provide a reliable foundation for treatment decisions, due to risk of bias, small sample sizes, and the short duration of trials.

A National Institutes of Health (NIH) study suggests that caffeine interacts with Cr to increase the rate of progression of PD.

Huntington's disease (HD)

Several primary studies have been completed but no systematic review on HD has been completed yet.

Adverse effects of supplementation

Side effects include:

- Weight gain (within the first week of the supplement schedule), likely attributable to greater water retention due to the increased muscle Cr concentrations by means of osmosis.
- Potential muscle cramps / strains / pulls.
- Upset stomach.
- Diarrhea.
- Dizziness.

- Making sleep a priority.
- Trying a relaxing activity (wellness programs or apps, which may incorporate meditation, muscle relaxation, or breathing exercises).
- Setting goals and priorities.
- Practicing gratitude.
- Focusing on positivity.
- Staying connected.

Sidebar 2 – Caring for mental health

Mental health includes emotional, psychological, and social well-being. It affects how we think, feel, act, make choices, and relate to others. Mental health is more than the absence of a mental illness—it is essential to overall health and quality of life. Self-care can play a role in maintaining mental health and help support treatment and recovery.

About self-care

Self-care means taking the time to do things that help live well and improve both physical health and mental health. Although it is not a cure for mental illnesses, understanding what causes or triggers mild symptoms and what coping techniques work can help manage mental health. When it comes to mental health, self-care can help manage stress, lower risk of illness, and increase energy. Even small acts of self-care in daily life can have a big impact such as:

- Getting regular exercise.
- Eating healthy, regular meals, and staying hydrated.

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