

Brain Teasers

BY DAVID SCHARDT

Popping Pills for Better Memory

Antioxidants

“There’s good reason to think that oxidative stress is deleterious to the aging brain,” says Victor Henderson, professor of neurology at Stanford University in Palo Alto, California. Oxidative stress creates rogue molecules called free radicals, which can damage brain cells.

“But this doesn’t necessarily mean that taking antioxidants will slow down or reverse some of the harmful effects,” Henderson cautions. It would take clinical studies to show that, he says, “and so far the published results for antioxidants are disappointing.”

For example, in a study published last December, roughly 3,200 healthy middle-aged and older U.S. women who took 600 IU of vitamin E every other day for four years scored no better on thinking and memory tests than a similar group of women who took a placebo.¹

That’s consistent with the results of two earlier studies that looked at cocktails of antioxidants.

In one, from the United Kingdom, roughly 10,000 men and women aged 40 to 80 with heart disease or diabetes took a daily combination of vitamin E (600 IU), vitamin C (250 mg), and beta-carotene (33,000 IU). After five years, they were just as likely to show mental decline as 10,000 similar people who took a placebo.²

And 1,000 U.S. men and women in their 70s who took 400 IU of vitamin E, 500 mg of vitamin C, and 25,000 IU of beta-carotene every day for more than six years scored no differently on concentration and memory tests than a comparable group who took a placebo.³

There’s no convincing evidence for other antioxidants, either:

■ **Lipoic acid.** Lipoic acid, which is found naturally in the body, functions as both a fat-soluble and a water-soluble antioxidant.



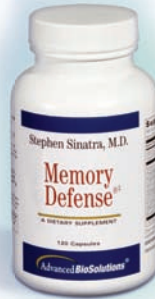
Julian Whitaker has one. So do Susan Lark, Stephen Sinatra, Marcus Laux, and other well-known alternative medicine doctors. Ditto for chiropractor David Williams. And Amway and Shaklee. Even *Prevention* magazine has its own.

Memory pills sell...for as much as \$70 a month. And this isn’t your grandmother’s ginkgo. With so much competition today, companies are scouring warehouse shelves for ingredients that will make their brain-boosting pills stand out.

All that’s missing, in most cases, is hard evidence that the stuff works. Here’s the research behind some of the most popular ingredients in memory supplements.

Alternative medicine cardiologist Stephen Sinatra puts 50 mg of it in his Memory Defense pills to “protect against free radicals before they can even reach your brain,” according to his Web site.

But no good studies have looked at whether lipoic acid can help protect the brains of healthy people. In fact, the *only* study of lipoic acid and cognition showed that it didn’t help HIV-infected patients who had dementia.⁴



■ **Bacopa.** *Bacopa monnieri* is an Asian plant used in traditional Indian medicine as a “brain tonic,” according to the *Alternative Medicine Review*. Shaklee adds a bacopa extract to its Memory Optimizer pills because the herb “improves memory and the ability to learn new information,” according to the company.

That doesn’t jibe with results from the only three well-designed studies of bacopa, which were all conducted in Australia.

In one, 23 adolescents and young adults who took 300 mg of bacopa every day for three months scored higher on learning and memory tests than similar people who took a placebo.⁵ But that finding would have been chalked up to chance if the researchers hadn’t been unusually lenient in defining what was “statistically significant.”

And in the other two studies, 300 mg a day of bacopa for four to six weeks did little or nothing for the minds of 80 middle-aged and older adults.^{6,7}

Neurotransmitters

Neurotransmitters are chemical messengers that relay signals from one nerve cell to another. Beef up neurotransmitters that are involved in memory, like acetylcholine, and perhaps you can ward off mental decline.

■ **Choline.** While you can’t take acetylcholine pills, you *can* take supplements that contain its major building block. Choline “helps your body to make a superior brain substance called acetylcholine,” says *Prevention* magazine, which puts 100 mg of choline in its Memory Support pills.

But choline supplements have failed just about every test of whether they boost memory or thinking. Maybe that’s because the choline never gets to where it’s needed.

“We’ve found that, beginning in middle age, people seem to lose their ability to transport choline from the blood into the brain,” says Bruce Cohen, director of the molecular pharmacology laboratory at McLean Hospital in Belmont, Massachusetts.

“Maybe by taking enormous amounts it’s possible to force choline in,” he adds. “But we didn’t see it with even three grams or more.” (Three grams, or 3,000 milligrams, is 30 times more choline than *Prevention* puts in Memory Support.)



■ **DMAE.** If the choline you take doesn't make it into your brain, something that your body converts into choline probably won't do you any good either. That hasn't stopped some supplement makers from adding DMAE (dimethylaminoethanol) to their memory formulations.

"Your body uses DMAE to create choline," says alternative women's health physician Susan Lark on her Web site. Lark includes DMAE in her Memory Answer pills. "While research on DMAE is in its infancy," she notes, "I feel very strongly that women need a high amount of it."

"Infancy" is giving DMAE far too much credit. We couldn't find a single study that looked at DMAE's impact on memory or powers of concentration in healthy adults. And DMAE has failed nearly every test of its usefulness in neurological diseases like Alzheimer's and Huntington's chorea.

■ **Huperzine A.** If you can't boost levels of acetylcholine in your brain, how about trying to keep more of it around for longer?



Drugs called cholinesterase inhibitors—Tacrine and Aricept—delay the breakdown of acetylcholine. They've been approved by the Food and Drug Administration for treatment of Alzheimer's disease, though their effects are modest.

But Tacrine and Aricept are available only by prescription. Not so huperzine A, a cholinesterase inhibitor that's derived from the Chinese herb *Huperzia serrata*.

For example, naturopathic physician Marcus Laux puts 50 micrograms (mcg) of huperzine A in his BioAdapt Memory Formula. It's "good for your brain," he says on his Web site.

Maybe. Maybe not. Huperzine A pills have never been tested on memory or other brain functions in healthy adults.

"There have been no controlled clinical trials outside China assessing its toxicity and efficacy," says Dana Belongia of Georgetown University in Washington, D.C. (The Chinese studies were almost exclusively in people with Alzheimer's or other dementias.)



"Huperzine A is a highly potent compound," cautions The Natural Pharmacist, a series of reviews of dietary supplement research. (You can access it through Web sites like iherb.com.) "We recommend using it only under a doctor's supervision."

■ **Phosphatidylserine (PS).** PS is a fat-like substance in brain cell membranes that helps the cells transmit and receive electrical signals. Cardiologist Stephen Sinatra puts 100 mg of PS in his Memory Defense pills because it "keeps your cell membranes fluid and flexible and helps to maintain healthy memory-related pathways."

Two decades ago, a few studies showed that PS might help some people with dementia or with serious memory problems. In that pre-mad-cow-disease world, PS was extracted from cow brains. Today, soybeans provide PS.

But the only good study of soy PS, published six years ago, came up empty. Researchers in the Netherlands gave 300 mg or 600 mg a day to 120 men and women aged 58 and older who were suffering from a greater than typical memory decline for their age. After 12 weeks, the volunteers didn't perform any better on memory tests than similar people who took a placebo.⁸

In 2004, the FDA concluded that there is "little scientific evidence" that PS can reduce "the risk of cognitive dysfunction in the elderly."

Three to Forget

Which of today's "brain-booster" pills will join these three supplements, which we described in September 2001 ("Memory Pills—Mostly Forgettable")?

■ **Cognita.** It "represents...the best available science," General Nutrition Centers said when it introduced Cognita in 2001. But that science failed to materialize. GNC never published the study that it told us it was conducting in 2001. Instead, the company quietly stopped selling Cognita in 2003.

■ **Focus Factor.** "Dramatically improve your focus, concentration and memory, and eliminate mental fatigue in one month or less," promised Texas chiropractor Kyl Smith. But Smith never published the clinical trial that he said would back up his ads.

In 2004, the U.S. Federal Trade Commission fined Smith \$60,000 for making "false or misleading" advertising claims. (The "consumers" who endorsed Focus Factor

in his infomercials turned out to be Smith's attorney, employees of the public relations firm he hired to promote Focus Factor, and distributors of the supplement.)

Focus Factor is now sold by a Portland, Maine, company that advertises it simply as support for "healthy brain function"—a claim that requires no evidence.

■ **Senior Moment.** Manufacturer Nutramax never had any proof for what it called "the next generation in memory enhancement."

In 2002, the Council of Better Business Bureaus' National Advertising Division recommended that Senior Moment's advertising claims "be substantially modified or discontinued." And in 2004, the Federal Trade Commission prohibited Nutramax from claiming that Senior Moment could "prevent or reverse the effects of memory loss."

Nutramax no longer sells Senior Moment.

B Vitamins

"High levels of homocysteine in the blood have been linked in some studies to poor cognition," says Stanford University's Victor Henderson. Three B vitamins—B-6, B-12, and folic acid—can lower homocysteine levels. Could they also improve memory and other brain function?

Marcus Laux thinks so. He adds B-12 (200 mcg) and folic acid (400 mcg) to his BioAdapt Memory Formula because "more and more research is emerging linking homocysteine levels and brain health," as his Web site claims.

"That's the kind of intervention that makes good sense," says Henderson. "But not everything that makes good sense actually turns out to work."

Through the end of 2006, 18 trials had tested vitamin B-6, vitamin B-12, folic acid, or a combination of the three on memory and learning in people who took them for up to two years.

Test Yourself

Only one of the 18 found any benefit. And that was a small study of 16 cognitively impaired people in Italy who took a megadose of 15,000 mcg of folic acid every day for two months.⁹ (The recommended daily intake of folic acid is 400 mcg.)

In a 2007 study, 400 Dutch men and women aged 50 to 70 who took 800 mcg of folic acid every day for three years scored better on tests of memory and information processing than 400 similar people who took a placebo.¹⁰

"But the study isn't relevant to people in the United States," says Martha Morris of the Rush Institute for Healthy Aging in Chicago.

"The Dutch researchers targeted volunteers who were lacking in folate when they entered the study," she notes. "But in the United States, the grain supply is fortified with folic acid and folate insufficiency is rare." (In the Netherlands, flour and cereals aren't fortified with folic acid.)

"So it is very misleading to make a broad statement about how this study shows that folic acid can help your brain."

Blood Boosters

If you can increase the flow of blood through your brain, will it make you smarter or less forgetful?

"I don't think that's been demonstrated," says Victor Henderson. "In fact, in healthy people, brain tissue that's being used efficiently in the performance of a cognitive task actually requires less blood. So something that increases blood flow without showing at the same time a cognitive benefit doesn't mean very much."

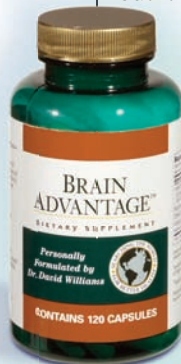
That hasn't stopped supplement makers from adding blood-flow-boosting ingredients to their memory pills:

■ **Ginkgo biloba.** Naturopathic physician Marcus Laux recommends ginkgo "to enhance circulation, which is critical when it comes to your brain getting the oxygen and nutrients it needs."

Chiropractor David Williams adds ginkgo to his Brain Advantage pills because it "improves a variety of brain functions, including memory, attention, recognition tasks, reaction time, and short-term memory."

Yet "studies of ginkgo in healthy people haven't been that encouraging," says Henderson. In six of the seven trials that tested ginkgo in healthy middle-aged and older adults over the past five years, the herb did little or nothing.

The most recent: Australian researchers gave 80 men and



How do researchers measure whether a person's memory or capacity to absorb new information is declining as they age?

They administer tests that measure how well and how quickly the person can manipulate and retain information. Then they wait—six months, a year, or more—and give the same person the same tests.

Here are two examples of the kinds of tests that were used in a recent study of hormone replacement therapy and brain aging in women aged 65 and older.¹

Verbal Fluency

You have one minute to say aloud the names of as many animals as you can, and one more minute to say aloud all the words you can think of that begin with the letters F, S, and A.

How'd you do? See how you compare to these results from 1,300 healthy Canadian volunteers.

Age	Number of F/S/A Words	Number of Animal Words
16-19	39	22
20-29	41	20
30-39	43	22
40-49	44	21
50-59	42	20
60-69	39	18
70-79	35	16
80-89	29	14
90-95	28	13

Source: *Arch. Clin. Neuropsychology* 14: 167, 1999.

women aged 55 to 79 either 120 mg of ginkgo or a placebo every day for three months.¹¹ The ginkgo takers scored better on one of 14 tests of brain function, a result the researchers said "may not be reliable." (When only one out of many tests yields promising results, researchers suspect that it may be due to chance.)

■ **Vinpocetine.** Vinpocetine is sold in Europe as a drug for treating dementia, but it's available as a supplement in the United States.

Alternative medicine physician Julian Whitaker adds vinpocetine to his Memory Essentials pills "for healthy oxygen flow, nutrient supply, and energy production in the brain," according to his Web site.

Yet no published studies have looked at whether a daily dose

California Verbal Learning Test

Someone reads you a list of 16 nouns that are drawn from four different categories—fruits, tools, clothing, and spices, for example. You try to immediately recall as many of the 16 as possible. The test is repeated four more times. The entire test (all five attempts) typically takes 15 to 30 minutes.

Example: Have someone read you this list (*don't peek at it first*): drill, plums, vest, parsley, grapes, paprika, sweater, wrench, chives, tangerines, chisel, jacket, nutmeg, apricots, pliers, slacks.

How'd you do? If you could remember all 16 words five successive times, you'd have a perfect score of 80 (16 x 5). Here's the average score of a group of 210 well-educated people living in the Midwest.

Age	Score	
	Men	Women
59	45	52
62	45	51
65	43	50
68	43	49
71	41	47
74	41	47
77	40	46
80	38	44
86	37	43

Source: *J. Clin. Exp. Neuropsychology* 19: 220, 1997.

¹ *Clinical Trials* 1: 440, 2004.



of vinpocetine can help healthy adults' brains keep humming along normally.

Maybe Whitaker was thinking of the handful of preliminary studies, conducted more than 15 years ago, in which vinpocetine seemed to help some patients suffering from stroke or Alzheimer's disease.

¹ *Arch. Intern. Med.* 166: 2462, 2006.

² *Lancet* 360: 7, 2002.

³ *Neurology* 63: 1705, 2004.

⁴ *Neurology* 50: 645, 1998.

⁵ *Psychopharmacology* 156: 481, 2001.

⁶ *Neuropsychopharmacology* 27: 279, 2002.

⁷ *Hum. Psychopharmacol.* 19: 91, 2004.

⁸ *Nutr. Neurosci.* 4: 121, 2001.

⁹ *Arch. Gerontol. Geriatr.* 26: 1, 1997.

¹⁰ *Lancet* 369: 208, 2007.

¹¹ *Hum. Psychopharmacol.* 21: 27, 2006.