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# Natural Therapies to Preserve and Enhance Cognition and Memory

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**F**or many patients, one of the most disturbing prospects of aging is the possibility of a decreasing ability to recall desired memories and comprehend new information and stimuli. This is understandably a very real concern considering that as much as 7 percent of the population more than 65 years old has overt Alzheimer's disease and that prevalence of the disease doubles every five years of age thereafter.<sup>1</sup> It is safe to estimate that less-severe mental deterioration is substantially more prevalent. This article explores some of the simplest interventions such as modest dietary changes and botanical and supplemental interventions. Essential to maintaining cognitive ability is adhering to a long-term health maintenance plan that can be sustained over the course of a lifetime; thus, a simple and high-compliance preventive approach is of paramount importance.

## Wise Dietary Choices

The most crucial consideration when devising a comprehensive health intervention is understanding how to prevent or slow the degenerative process best. Without question, dietary factors constitute the single most important preventive focus. In one prospective study, 586 participants without clinical symptoms of dementia, age 55 or older, had their diets assessed at the beginning of the study and were screened for symptoms of dementia an average of 2 years later.<sup>2</sup> After adjusting for other factors, such as age, gender, and education, subjects with

the highest total fat intake had a significantly elevated relative risk (RR) of dementia (RR = 2.4 [1.1–5.2]). Other dietary factors associated with an increased risk of dementia were a high intake of saturated fat (RR = 1.9 [0.9–4.0]) and cholesterol (RR = 1.7 [0.9–3.2]). An encouraging finding was that a high intake of fish was associated with a significantly lower risk of dementia in general (RR = 0.4 [0.2–0.91]) and was particularly associated with a lower risk of the dementia of Alzheimer's disease (RR = 0.3 [0.1–0.9]). Several other epidemiologic studies produced similar findings.<sup>3,4</sup>

Current research supports a free-radical-based theory of cognitive decline that is supported by data suggesting that foods that are rich in antioxidants, such as strawberries and spinach, and supplemental vitamin E, retards the age-related onset of cognitive deficits.<sup>5</sup> It is also noteworthy that, in individuals 65 and older (a population facing an ever-increasing risk of dementia), higher beta-carotene and vitamin C levels have been shown to correlate with enhanced memory performance.<sup>6</sup> Thus, following a diet rich in whole foods and emphasizing fresh fruits and vegetables provides the low fat and antioxidant abundance protection essential for sustained cognitive function and overall enhanced longevity.

It should also be noted that some clinicians believe that following a low-calorie diet that provides a wide array of fresh fruits and vegetables can lessen oxidative damage to the central nervous system thus slowing cognitive decline. This area of research shows some promise; yet, as with all dietary modifications, finding the appropriate balance between therapeutic goals and sustained wellness can be challenging.

## Supportive Botanical Medicines

### *Ginkgo*

If additional interventions to maintain cognition become warranted, one of the first considerations, and by far most popular one, is ginkgo (*Ginkgo biloba*). It is by way of various mechanisms of action, perhaps most notably inhibition of lipid peroxidation, that ginkgo may help to preserve, and to some extent restore, healthy cognition. Extracts of ginkgo have been shown to act as free-radical scavengers, preventing induced lipid peroxidation of neural tissue under several experimental conditions.<sup>7,8</sup> A review of the literature also suggests that additional actions, such as a relaxing effect on vascular walls, inhibition of platelet-activating factor, enhancement of microcirculation, and stimulation of neurotransmitters,<sup>9</sup> could all contribute to ginkgo being a multifaceted therapeutic agent for patients with dementia (see box entitled *How Ginkgo biloba Supports Cognition*).

It would be remiss, however, not to acknowledge that, while many trials show benefit with the use of ginkgo,<sup>10,11</sup> there are notable exceptions. A 24-week trial failed to show any benefit of ginkgo for more than 200 elderly subjects with dementia.<sup>12</sup> Such results stand in sharp contrast to those of other trials, such as a year-long study of more than 300 subjects with dementia who received only 120 mg of an extract of this herb and that manifested stabilized or even improved cognitive performance for 6 months to a year during the study.<sup>13</sup> In such situations, when data from peer-reviewed sources seem to disagree, it is important to remember that many factors may combine to skew the data of one, or even several studies, in a particular direction. A recent review of the ginkgo literature points out that discrepancies between results of one study and

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### Dietary and Botanical Strategies for Supporting Healthy Cognition

#### Dietary considerations

- Total fat intake limited, especially saturated fat
- Cholesterol intake should be controlled
- At least 2–3 servings of fish per week
- 4–5 daily servings of foods that are rich in antioxidants, especially fresh fruits and vegetables

#### Botanical supports

- Quality extract of *Ginkgo biloba*,<sup>a</sup> 240 mg/day, if taken alone or 120 mg/day if taken with 200 mg/day of *Panax ginseng*
- Huperzine A, 200 µg, bid

<sup>a</sup>Use of ginkgo should be stopped prior to surgery to prevent bleeding. Patients should tell physicians about taking ginkgo for this reason.

another may be the result of factors such as the study population used, the outcome measures utilized, the duration of treatment, and the dosing regimen of the subjects.<sup>14</sup> Generally, the literature seems to support the benefit of ginkgo extract for subjects with dementia. Also, equally important is that, clinically, ginkgo has repeatedly demonstrated itself to be an effective and safe intervention.

In addition to senior subjects with dementia, however, there is also evidence that ginkgo extract may enhance memory for those who are younger. In a smaller study of 20 subjects, volunteers were given 120 mg, 240 mg, or 360 mg of *Ginkgo biloba* extract or a placebo. A series of computerized tests was then done to assess speed and accuracy of attention and speed and quality of memory. The most striking change was a dose-dependent improvement in the speed of attention that was apparent at both 240 mg and 360 mg after 2.5 hours and was still present after 6 hours. While this was a small study, it is encouraging that the botanical was effective enough to produce a dose-dependent response.

### How *Ginkgo biloba* Supports Cognition

- Inhibition of free-radical damage to lipid neural tissue
- Inhibition of platelet-activating factor
- Relaxation of vascular walls
- Increase in local blood flow
- Increase in neurotransmitter activity

#### Ginseng

Another botanical that may be helpful for cognitive support, in combination with ginkgo, is ginseng (*Panax ginseng*). The biologic effects of the various constituents of ginseng are complex: While one of its phytochemicals shows affinity for the nicotinic-acid receptor,<sup>16</sup> a receptor for which reduced stimulation is associated with cognitive decline, another of its phytochemicals block this receptor.<sup>17</sup> However, in both animal and clinical research, a combination of ginseng with ginkgo seems to hold promise. In rats, for example, a ginkgo/ginseng combination was shown to enhance the learning ability of both older and younger rats.<sup>18</sup> A recent double-blind, placebo-controlled trial of more than 250 human subjects over a 14-week period has been reported. In this study subjects' cognition/memory were assessed every 4 weeks using a number of standard scales and questionnaires. Overall, there was significant improvement (mean 7.5 percent) in subjects who received the botanical combination (120 mg per day of ginkgo and 200 mg per day of ginseng), including gains in working and long-term memory.<sup>19</sup>

#### Club Moss

One of the chemicals found in a rare club moss (*Huperzia serrata*), Huperzine A, has been studied in China for its effects on memory, cognition, and behavior in patients with Alzheimer's disease. In both preliminary<sup>20</sup> and double-blind research<sup>21</sup> Huperzine A raises hopes that, with further research and validation, this chemical may soon be of more widespread and significant help to patients who are suffering from dementia.

### Key Nutrients and Supplements

The box entitled Supplements for Cognitive Support summarizes recommended dosages for the nutrients discussed below. It is assumed that the practitioner will draw upon personal experience and familiarity with the individual nutrients in planning treatment. Regular consumption of 1–2 of the nutrients could help to prevent loss of mental function, whereas 3–4 nutrients might be more appropriate to slow loss that has already begun, and 3–5 nutrients might be needed to address substantial loss.

#### Acetyl-L-Carnitine

One nutritional supplement that has been studied extensively for the treatment of dementia is acetyl-L-carnitine, which is believed to be a precursor for the synthesis of acetylcholine. In one double-blind study, typical of other similar trials, half of 60 subjects with mild dementia were treated with 2 g per day of acetyl-L-carnitine and half received placebo for 3 months. When subjects were assessed, using scales of behavior, memory, attention, and verbal fluency, there was significant improvement in the group receiving the acetyl-L-carnitine.<sup>22</sup> Several other studies also suggest positive findings, indicating that acetyl-L-carnitine may be helpful in slowing the progression of Alzheimer's disease and in improving cognitive function in patients with this disorder.<sup>23,24</sup>

Enthusiasm for acetyl-L-carnitine may be tempered somewhat, however, by several year-long trials showing less-promising results. In the first of these trials, with more than 350 patients completing treatment consisting of 3 g per day of acetyl-L-carnitine for 1 year, a trend was seen toward a slower progression of Alzheimer's disease symptoms. However, the trend was only seen in subjects who were under 65, while older subjects who were given acetyl-L-carnitine might actually have experienced a more rapid progression of their symptoms.<sup>25</sup> In an additional study of several hundred subjects under 65 with onset of Alzheimer's disease, treat-

## One potentially emerging biomarker for risk of Alzheimer's disease could be blood levels of homocysteine.

ment with 3 g per day of acetyl-L-carnitine for 1 year, again, did not slow decline.<sup>26</sup> While it is difficult to understand completely why some studies show positive results and others do not, it may be that, for early-onset cases of Alzheimer's dementia, a short-term treatment protocol might offer some slowing of the progressing dementia. If there is even some improvement clinically, such a course seems justified within the context of the progressing and debilitating dementia of Alzheimer's disease.

### *Phosphatidylserine*

Phosphatidylserine (PS) is a glycerophospholipid that is an important component of cell membranes. While some work suggests that 300 mg of PS in divided doses might help to improve cognition in dementia of Alzheimer's type,<sup>27</sup> other work seems to be less encouraging.<sup>28</sup> In this context, perhaps one of the most important studies is one in which subjects who took supplemental PS were assessed by several techniques, including neuropsychologic testing, monitoring their cerebral metabolism of glucose, and measuring electroencephalograms over the course of 6 months. While improvements were noted during the study, it is interesting that the improvement was most noticeable at 8 and 16 weeks and that the improvement faded toward the end of the 6-month study. Thus, it may be important to bear in mind that this therapy might offer only short-term instead of long-term benefit for patients with Alzheimer's dementia.

What is noteworthy is that the variance seen among studies of PS could have been caused, in part, by the origin of the PS. The original studies used animal-tissue derivatives, which have a very different fatty-acid composition than PS from soy, which is used more typically by many clinicians and researchers today. An important concern about using animal-derived PS in the current research and clinical environment is the risk of exposing patient populations to prion-infected material.

### Supplements for Cognitive Support

Supplement	Dosing
Acetyl-L-carnitine	1 g tid <sup>a</sup>
Phosphatidylserine	200 mg, bid
Mixed vitamin E	800–1200 IU per day, under close supervision
Vitamin C with bioflavonoids	1000–2000 mg per day
Vitamin B complex	100 mg bid
Methylcobalamin	2000 µg per day sublingually
Folic acid <sup>b</sup>	800 µg per day orally
Lyprinol	210 mg, 2–3 times per day

IU = international units; <sup>a</sup>It is advisable to limit use to patients who are under 65 years old; <sup>b</sup>Because folic acid can mask the symptoms of vitamin B<sub>12</sub> deficiency, it should always be taken with vitamin B<sub>12</sub>.

### *Vitamin B<sub>12</sub> and Folic Acid*

One potentially emerging biomarker for risk of Alzheimer's disease could be blood levels of homocysteine. In a study of 164 patients with clinical diagnoses of dementia of Alzheimer's type and 108 controls, the patients with Alzheimer's disease had significantly higher levels of total homocysteine and significantly lower levels of serum vitamin B<sub>12</sub> and folate compared to controls.<sup>29</sup> In addition, a follow-up for 3 years of the subjects with Alzheimer's disease showed a correlation between the progression of the disease measured radiographically and the level of homocysteine seen at the beginning of the study. Such research may underscore the importance of maintaining a healthy vasculature throughout the whole body. Indeed, as we learn more about the involvement of vascular health as it relates to dementia, we may begin to see that cardiovascular disease and dementia are varying manifestations of the same underlying, and treatable, deficiencies and imbalances. The same supplemental vitamin B<sub>12</sub> and folic acid that may curb the chronic inflammation of cardiovascular disease associated with increased homocysteine, may help to support and protect the cerebral vasculature of patients with dementia who also tend to suffer from homocysteinemia.

### **Other Considerations**

Also essential to prevent the progression of deterioration of neuronal tissues and vasculature is the consumption of sufficient antioxidants, and supportive nutrients, and the avoidance of free-radical sources. Well-proven antioxidant nutrients, such as vitamin C and vitamin E, should be given strong consideration. In addition, vitamin E has an antiplatelet aggregation effect assisting in optimal cerebral blood flow and the prevention of occlusive strokes and impedance of optimal blood flow. General support for nervous-system function including optimal cognition also depends upon sufficient levels of the each of the B vitamins to support neurotransmitter production and function.

Finally, as conventional approaches to prevention of dementia have continued to focus on the use of anti-inflammatory agents such as COX-2 inhibitors, the practitioner may find that eicosapentaenoic acid from fish oil and lyprinol which is derived from green-lipped mussels (*Perna canaliculus*), are helpful as adjunctive therapies.

### **Closing Thoughts**

As with degenerative disorders, the causes of decreasing cognitive prowess and dementia are certainly multifactorial.

## In the context of already existing dementia, botanical medicines may prove to be some of the most effective treatment options available.

When focusing on the dementia of Alzheimer's disease specifically, epidemiologic evidence highlights as probable risk factors a diet high in total fat, saturated fat, and cholesterol, and suggests that an increased consumption of fish is associated with a decreased risk. In the context of already existing dementia, botanical medicines, such as *Ginkgo biloba* and *Panax ginseng*, especially when combined, may prove to be some of the most effective treatment options available. In particular, *Ginkgo biloba*'s many synergistic actions, such as inhibiting lipid peroxidation, improving microcirculation, and stimulating neurotransmission, speak to this plant's ability to tonify neural tissue. While as yet inconsistent, there is sufficient positive literature on several nutrients, namely acetyl-L-carnitine and PS to justify their use, at least over a short time period as a trial. As further research allows us a more clear and broad understanding of dementia, we may find that a combined approach of wise dietary choices and botanical and nutritional interventions increases our chances greatly of maintaining and even increasing cognition and memory throughout the lives of our patients. □

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