Cognitive Function

Learning, memory and reasoning are all important aspects of brain function that fall under the general heading of cognitive function. While they are taken for granted on a daily basis, failings in these areas are often the first signs of degeneration associated with aging and/or disease. Interrelated changes in brain chemistry and cellular function underlie the cognitive dysfunction associated with neurodegenerative conditions.

There are several neurodegenerative conditions that affect cognitive function, including Parkinson's disease and Huntington's disease, which are among the degenerative brain disorders. Parkinson's symptoms can include dementia, memory loss, impaired coordination and confusion. It affects more than 1.5 million Americans, according to the American Parkinson Disease Foundation. Huntington's disease is a genetic disorder with early symptoms including cognitive failings, with progression to diminished memory and concentration and loss of motor control; it afflicts approximately 250,000 Americans, according to the Huntington's Disease Society of America.

The general term dementia covers several forms, including multi-infarct dementia and subcortical dementia, and is also a symptom of other degenerative conditions such as Alzheimer's disease. Multi-infarct dementia, known as vascular dementia, is characterized by confusion, loss of memory and heightened emotion, and is a common cause of dementia in the elderly.

However, the best-known condition of cognitive dysfunction is Alzheimer's disease, which afflicts more than 4.5 million Americans, according to the Alzheimer's Association. Dementia is one of the symptoms of this condition, which is characterized by the formation of protein deposits (amyloid plaques) and tangled bundles of fibers (neurofibrillary tangles) composed of misplaced proteins in the brain. As neurons are destroyed, the amount of neurotransmitters is significantly diminished, affecting the ability of the brain cells to communicate. The most affected neurotransmitter is acetylcholine; the newest class of drugs for Alzheimer's disease aims to enhance the secretion of, or prolong the life of, acetylcholine in the brain.(1)

The aging of the population increasingly concerns health professionals about the potential costs associated with incidence of conditions like Alzheimer's. Researchers from the Jean Mayer Human Nutrition Research Center on Aging at Tufts University in Boston noted within the next 50 years, approximately 30 percent of the population will be aged 65 or older, with 18 million Americans over age 75 afflicted by Alzheimer's.(2) "Unless some means is found to reduce these age-related decrements in neuronal function, health care costs will continue to rise exponentially," they wrote, adding it is critical to examine the role of dietary compounds in alleviating certain disorders.

Some research supports this idea. A review from the University of Aberdeen pointed out the brain has some neuroprotective and neurorestorative adaptive mechanisms to respond to accumulating damage caused by oxidative stress and inflammation in the brain.(3) They suggest adequate intake of antioxidant micronutrients and anti-inflammatory macronutrients, as well as nutrients to reduce homocysteine concentrations, could enhance the body's defenses against brain aging. Similarly, French researchers suggest important nutritional factors for brain health include the omega-3 fatty acids to support cellular function and B vitamins for the synthesis of neurotransmitters.(4)

The Homocysteine Connection

Mounting evidence suggests high levels of serum homocysteine are associated with declining cognitive function and dementia.(5) Two Italian studies investigated the link between homocysteinemia and cognitive dysfunction, including dementia and Alzheimer's disease. In the first, researchers found homocysteine levels were significantly higher in the 40 patients with Alzheimer's and vascular dementia compared to the 42 control subjects; serum folate and vitamin B12 levels were lower in the Alzheimer's and dementia patients as well.(6) The second study examined 62 healthy and cognitively normal subjects between the ages of 65 and 91, and found increased homocysteine levels correlated to poorer performance in language abilities that would be affected by dementia states.(7) In contrast, a U.S. study in 679 elderly subjects without dementia at baseline found no association between high homocysteine levels and development of dementia or loss of memory over time.(8)

The possible link between homocysteinemia and dementia led researchers at the Jean Mayer Center to suggest researchers investigate the hypothesis that **folate** supplementation could reduce the risk of neuropsychiatric dysfunction.(9) A *Cochrane Database System Review* from 2003 explored the issue of folic acid with or without **vitamin B12** for cognition and dementia.(10) The review included four randomized, controlled trials, which the study authors noted showed no benefit on cognition in healthy or demented people, regardless of inclusion of B12; however, they suggested more studies are needed to determine the value of folic acid in cognitive function. Similar results were reported by researchers from King's College London, who included six studies in their review and found the evidence did not support a correlation between folate and B12 supplementation and cognitive function.(11)

However, recent studies have suggested a link between folate deficiency and dementia onset. Researchers from the Geriatric Division and Department of Metabolic Diseases in Mendrisio, Switzerland, investigated the relations of mild cognitive impairment, Alzheimer's and vascular dementia with serum levels of homocysteine, folate and B12.(12) The study included 228 patients, consisting of 55 nondemented controls, 81 mildly cognitively impaired subjects, and 92 demented subjects. Hyperhomocysteinemia was significantly associated with dementia and Alzheimer's, as was low folate status, leading the researchers to suggest folate deficiency may precede the onset of dementia. Similarly, Belgian researchers found significant negative correlations between levels of serum B12 and folate and degree of cognitive deterioration in 180 patients with Alzheimer's and/or vascular dementia.(13)

Adding to the discussion is the fact that many older adults are deficient in B12 and folate, often due to the presence of atrophic gastritis, which afflicts up to half of elderly subjects and decreases the body's ability to digest and absorb these B vitamins, according to German researchers.(14) They added beyond the homocysteine issue, the B vitamins are critical for the transmethylation of neurotransmitters; therefore, deficiencies further the progressive breakdown in neural communications.

Additional studies have investigated the roles of B12 and **vitamin B6** in cognition, both alone and in combination with other B vitamins. Two *Cochrane* reviews on B12 and B6 for cognition failed to find significant evidence suggesting the vitamins could benefit cognitive function in demented or healthy older individuals.(15,16) However, there have been some recent studies investigating the impact of

the B vitamins on cognitive function and homocysteine levels. Australian researchers assessed dietary intake of folate, B12 and B6 in 1,183 men and women, and found higher intakes of B12 and B6 were positively related to memory function, while higher intakes of folate and B6 were positively associated with better memory function in women.(17) And in an open-label, eight-week pilot study, Alzheimer's patients who received a combination of folic acid, B12 and B6 had significantly reduced fasting and post-methionine-loading homocysteine levels; the researchers plan to assess the impact of supplementation on rate of cognitive decline in a later study.(18)

Oxidative Stress

A great deal more investigation in the dementia field has surrounded the role of oxidative stress on the etiology of dementia, Alzheimer's disease and other neurological pathologies. Researchers from the University of California, San Diego, noted oxidative damage is present within every class of biomolecule in the brains of Alzheimer's patients, and such injury may develop secondary to the excessive oxidative stress posed by beta-amyloid-induced free radicals, mitochondrial abnormalities, inflammation and altered endogenous antioxidant systems.(19) They noted, "Treatment with antioxidants is a promising approach for slowing disease progression to the extent that oxidative damage may be responsible for the cognitive and functional decline observed in Alzheimer's." Another review, out of the University of Catania, Italy, noted oxidative stress and disturbed cellular metabolism appear to feed on one another in a cycle that, together with chronic inflammation associated with brain injury, furthers progression of cognitive dysfunction.(20)

Population studies appear to support the role of antioxidants in prevention of brain dysfunction. Data from the Rotterdam Study, a cohort of 5,395 participants, associated higher intakes of **vitamin C** and **vitamin E** with a lower risk of Alzheimer's disease.(21) German researchers found patients with Alzheimer's or vascular dementia had significantly lower plasma levels of both water-soluble and lipid-soluble antioxidants compared to controls.(22) And another study, conducted by the Rush Institute for Healthy Aging in Chicago, involved 815 community-dwelling residents over age 65, who were free of Alzheimer's at baseline and were followed for almost four years.(23) The researchers found higher intake of vitamin E from food was associated with a reduced risk of Alzheimer's disease, particularly among individuals without APOE epsilon 4 allele, a gene linked to Alzheimer's onset.

Further research has investigated supplemental use of antioxidants on brain function. In a study from the University of Washington, Seattle, researchers assessed cognitive function in 2,082 subjects three and seven years from baseline, focusing on the 10 percent of subjects who reported taking an antioxidant supplement at baseline.(24) Antioxidant users had a 34-percent lower risk of developing cognitive impairment compared to non-users, and a 29-percent lower risk of experiencing cognitive decline. In another study, researchers from Johns Hopkins University in Baltimore examined data from the Cache County, Utah, population study (n=4,740) and found combined use of vitamins C and E was associated with reduced prevalence and incidence of Alzheimer's.(25)

Differing results were reported in two studies using data from the Honolulu-Asia Aging Study, which involved 3,385 Japanese-American men. A 2000 study from the University of Hawaii found a significantly protective effect of vitamins C and E against onset of vascular dementia and mixed dementia; the supplements also benefited cognitive test performance among subjects without dementia.(26) But a 2004 study from the National Institute on Aging in Bethesda, Md., found intakes of antioxidants at midlife were not associated with the risk of dementia;(27) and, a study in 980 elderly

subjects conducted by the Taub Institute for Research on Alzheimer's Disease and the Aging Brain, New York, found no relationship between supplemental intake of vitamins C or E and risk of Alzheimer's disease.(28)

However, Spanish researchers reported the effect of vitamin E, for example, has shown considerable variations in studies, with positive results shown when vitamin E acted as an antioxidant according to blood markers of oxidative stress.(29) Another review noted the efficacy of vitamin E (tocopherol) supplements may differ depending on the form of the vitamin used.(30)

In fact, some research has found the use of the **tocotrienol** vitamin E isomers may be more potent at protecting the brain. Alpha-tocotrienol (as Tocomin® from Carotech Inc.) was reported in cell studies to be more potent than alpha-tocopherol in protecting neurons from glutamate-induced toxicity.(31) Another study in pregnant rats found supplementation with tocotrienols (as Tocomin) was bioavailable to both mother and fetal brains, indicating the ability to cross the blood-brain barrier.(32) These findings have led the National Institute of Neurological Disorders and Stroke (NINDS) to grant more than $1 million for a study on how alpha-tocotrienol (from Tocomin) protects against inducible neuronal cell death.

There are many antioxidants being investigated for their role in brain function. **Alpha-lipoic acid** and **N-acetylcysteine** (NAC) were studied in combination for their ability to reverse cognitive defects in a mouse model of neurodegenerative disease.(33) The combination of antioxidants was found to improve cognition in aged mice as well as reverse all three indices of oxidative stress. On its own, alpha-lipoic acid was found in an animal model of neurodegeneration to significantly reduce the level of cognitive impairment compared to mice that did not receive the antioxidant prior to induction of brain degeneration.(34) However, a cell study found that only the reduced form of the compound, **dihydrolipoic acid**, was able to protect against Abeta and iron/hydrogen peroxide-meditated toxicity.(35) In that study, alpha-lipoic acid instead potentiated the oxidative stress, suggesting the state of the antioxidant is critical to its function in neurodegenerative conditions.

One important category of antioxidants in the brain health area is the **flavonoids**. These water-soluble compounds found in fruits and vegetables appear to have a variety of mechanisms of action in neuroprotection, including protecting against oxidative stress, influencing gene expression and preventing apoptosis.(36) Cellular studies suggest flavonoids increase intracellular levels of the endogenous antioxidant glutathione, directly lower levels of radical oxygen species (ROS) and prevent the influx of Ca(2+), which leads to neuronal death, even with high levels of ROS present.(37) French researchers found in a cohort of 1,367 elderly subjects that intake of antioxidant flavonoids halved the risk of incident dementia.(38)

There are many sources of flavonoids. **Naringenin**, a major flavanone from citrus, was found in a studies from Cornell University in Geneva, N.Y., to prevent generation of Abeta-induced ROS in neurons and prevent neurodegeneration in mice in response to scopolamine injection.(39) **French maritime pine bark extract** (as Pycnogenol® from Natural Health Sciences) was found in a cell study at Loma Linda University, Calif., to suppress the generation of ROS in neurons exposed to Abeta (25-35), as well as prevent apoptosis and DNA fragmentation.(40) And the bioflavonoid **quercetin**, found in apples, onions and other fruits, was found in an Indian mouse study to reverse cognitive defects in aged mice.(41)

A rich source of the **polyphenol** class of flavonoids is **red wine**. A cell culture study in Japan examined the impact of different wine-related polyphenols, including myricetin and quercetin, and found they dose-dependently destabilized preformed beta-amyloid fibrils.(42) Researchers at McGill University in Verdun, Quebec, found red wine flavonoids and **resveratrol** protected hippocampal cells against oxidative toxicity.(43) Further research on resveratrol found it was able to attenuate beta-amyloid-induced cytotoxicity and apoptosis,(44) as well as prevent in rats streptozotocin-induced cognitive impairment associated with oxidative stress.(45)

One of the most common dietary sources of flavonoids is **tea**. The catechins in green tea, including **epigallocatechin gallate** (EGCG) appear to impact cognitive function through not only antioxidant activity, but also by chelating iron, activating survival genes and cell signaling pathways, and by regulating mitochondrial function.(46) In vitro studies in Korea found EGCG elevated survival of hippocampal cells exposed to amyloid beta protein, and decreased levels of ROS.(47) And researchers from the University of Shizuoka, Japan, found long-term intake of green tea catechins in mice prevented cerebral atrophy and cognitive dysfunction associated with aging.(48) In addition, the study found catechin intake prevented oxidative DNA damage during the early stages of brain atrophy.

Soy is another dietary source of flavonoids, primarily as **isoflavones**. Scientists from Brigham Young University in Provo, Utah, conducted a review of studies on soy isoflavones' impact on aspects of brain structure and function, and discovered a protective effect of isoflavones against brain and neural disorders, particularly in women.(49) Animal studies have found administration of soy isoflavones to male rats increased activity of choline acetyltransferase in the brain, reducing age-related neuron loss and cognitive decline.(50) Use of the isoflavone **genistein** protected Abeta-induced neuron death in cell cultures without causing proliferation of uterine endometrial cells, which may be linked to uterine cancer in women.(51)

Such findings have led researchers to conduct intervention studies using isoflavone diets and supplements. Researchers at the University of California, San Diego, examined the effect of 110 mg/d of supplemental soy isoflavones (as Healthy Woman Soy Menopause Supplement from McNeil-PPC Inc.) or placebo on 56 postmenopausal women over six months.(52) The women in the treatment group performed better on cognitive tests compared with their own baseline scores and compared with the placebo group, with verbal memory particularly enhanced. British researchers also found in a double blind, parallel study that administration of a supplement with 60 mg/d of soy isoflavones significantly improved cognitive function in postmenopausal women.(53) However, a double blind trial in The Netherlands involving 175 healthy postmenopausal women who received 25.6 g/d of soy protein (delivering 99 mg/d of isoflavones) or placebo found no differences in cognitive function between the groups after one year.(54)

Cellular Dysfunction

Beyond oxidative stress, there are many compounds that appear to act on the cellular level to prevent cellular dysfunction that can lead to degenerative disease. A great deal of attention has been paid to the role of **essential fatty acids** (EFAs) in the brain. In particular, research suggests **omega-3** EFAs, especially those of marine source that deliver preformed long-chain EFAs, maintain cerebral structure and cellular membrane health.(55) Neuronal cell membrane phospholipid composition reflects fat

intake from the diet, with **omega-6** EFAs having a higher inflammatory potential and propensity to autoperoxidation.(56,57)

Population studies have investigated the relationship between fat intake and risk of impaired cognitive function. For example, researchers from the Julius Center for Health Sciences and Primary Care in Utrecht, the Netherlands, examined the association of fish intake (a rich source of long-chain omega-3 EFAs) and cognitive function in 1,613 subjects over age 45.(58) Intake of fish and of marine omega-3s (**eicosapentaenoic acid**, EPA, and **docosahexaenoic acid**, DHA) was inversely related to the risk of overall impaired cognitive function, while higher dietary cholesterol intake increased the risk of impaired memory. Another Dutch study, using data from the Rotterdam cohort, found no relation between intake of omega-3s or cholesterol with onset of dementia.(59)

In contrast, researchers from the Rush Institute examined data from 815 patients, initially free of Alzheimer's, who were followed for 2.3 years; participants who ate fish once or more per week had a 60-percent lower risk of Alzheimer's onset compared to those who rarely or never ate fish.(60) The study also found a positive association between total intake of omega-3 EFAs and reduced risk of Alzheimer's. And a study in Ireland measured serum EPA and DHA levels in 148 subjects with dementia and 45 control subjects, and found the demented subjects had significantly lower EPA and DHA levels compared to control values.(61) Serum DHA levels were progressively reduced with severity of clinical dementia.

Another aspect of preventing neurodegenerative diseases relates to the importance of maintaining neuronal function and production of the neurotransmitters, including acetylcholine (ACh). Decreases in levels of ACh in cerebrospinal fluid have been found in patients with Alzheimer's disease as well as those suffering vascular dementia, suggesting ACh is a critical neurotransmitter for memory.(62) This theory is buoyed by animal studies showing implants of ACh-releasing cells into the brains of aged rats with cognitive defects enhances cognitive performance and memory.(63)

The question for human health becomes how to naturally increase ACh release and/or prevent the degeneration of neuronal cells that produce ACh. An Italian research review noted treatment with pharmaceutical ACh inhibitors, as well as use of some natural cholinergenic precursors, appears to favorably affect cognitive function in demented individuals.(64) **Lecithin** is a major dietary source of choline, which has led to the suggestion that it may enhance the brain's production of ACh and reduce the progression of dementia. A *Cochrane* review, however, examined 12 randomized trials involving patients with Alzheimer's, Parkinson's or other memory problems and found no clinical benefit of supplementation.(65)

Instead of whole lecithin, research has turned to different compounds that may be beneficial individually. In a review from the University of Camerino, Italy, researchers noted phospholipids involved in choline biosynthetic pathways, including **phosphatidylserine** (PS) and **CDP-choline**, have been shown to enhance ACh availability and release, and provide a modest improvement of cognitive dysfunction.(66) A clinical trial in the Netherlands substantiated the safety of 300 mg/d or 600 mg/d of soy-sourced PS in elderly humans.(67) Its efficacy has been a subject of more investigation. Researchers from the Yakult Central Institute for Microbiological Research in Tokyo found oral administration of soy PS to aged male rats improved performance on the water maze test, suggesting enhanced cognitive function.(68) Contrasting results were found in two human clinical studies. While a 12-week study in 15 healthy, memory-impaired elderly found 300 mg/d of soy PS

improved cognitive function,(69) a 12-week study in 120 elderly subjects with memory impairment found no impact on cognitive function by either 300 mg/d or 600 mg/d of soy PS.(70)

More positive results have been reported for CDP-choline (cytidinediphosphocholine or citicoline). A *Cochrane* review noted it is a frequently prescribed drug for cognitive impairment in several European countries and, after reviewing seven studies, concluded it has significant beneficial effects on memory function and behavior.(71) Another review, from the American Institute for Biosocial and Medical Research Inc. in Puyallup, Wash., noted citicoline appears to serve as a choline donor in the metabolic pathways for ACh and neuronal phospholipids, and easily crosses the blood-brain barrier.(72) Animal studies have shown administration of citicoline protects against degeneration of spatial memory retention,(73) restores hippocampal acetylcholinesterase activities(74) and positively affects memory while maintaining hippocampal cell structure.(75) An unpublished animal study funded by Kyowa Hakko (supplier of Cognizin® citicoline) found mice given a diet of 2-percent citicoline for four weeks exhibited enhanced memory compared to control mice.

Clinical studies have investigated the impact of citicoline on dementia progression. A study from Brown Medical School in Providence, R.I., involved 30 patients with vascular dementia who received either 500 mg/tid or placebo for 12 weeks.(76) Both groups showed significant declines in neuropsychological performance at the end of the study, suggesting administration to patients already meeting criteria for vascular dementia may not be effective. However, reviewers have noted citicoline appears most effective on memory and behavioral outcomes in patients with memory deficit, positioning the ingredient for possible use in conditions such as mild cognitive impairment.(77)

As neurodegenerative conditions also appear linked to cellular dysfunction, there has been study into the possible role of **L-carnitine** and its ester **acetyl-L-carnitine** (ALCAR), which are critical cofactors for mitochondrial oxidation of fatty acids and may also possess neuromodulatory properties.(78) ALCAR appears to modulate both phospholipid metabolism and transmission of several neurotransmitters.(79)

Cellular and animal studies have sought to further elucidate ALCAR's action in the brain. A study at the University of California, Berkeley, involved administration to old rats of ALCAR and/or alpha-lipoic acid in drinking water; supplementation with both substances individually and the combination improved spatial and temporal memory.(80) The compounds also reduced the extent of oxidized RNA and reversed age-associated mitochondrial structural decay. In vitro, ALCAR was found to attenuate oxidative stress and ATP depletion in neuronal cells exposed to Abeta.(81) And when researchers at the Tokyo Metropolitan Institute of Gerontology gave 100 mg/kg of ALCAR to aged rats for three months, the rats' learning capacity and cholinergic synaptic function were enhanced.(82)

In humans, studies are less conclusive. A *Cochrane* review included 11 clinical trials and found no benefit of ALCAR on dementia or advanced Alzheimer's.(83) In contrast, a meta-analysis from Imperial College London explored the impact of ALCAR on mild cognitive impairment and early Alzheimer's and found a significant advantage for ALCAR compared to placebo.(84) ALCAR may also be useful in conjunction with pharmaceutical treatment, as Italian researchers found 2 g/d of ALCAR increased the response rate of patients on acetylcholinesterase inhibiting drugs by up to 50 percent.(85)

Another substance with benefits at the mitochondrial level is **coenzyme Q10** (CoQ10). A review from Cornell University reported there is increasing evidence that mitochondrial dysfunction and oxidative damage contributes to beta-amyloid deposition in Alzheimer's, and CoQ10 may have efficacy in preventing these activities.(86) Another review from the University of North Dakota, Grand Forks, noted CoQ10 appears to attenuate the loss of dopaminergic neurons, which characterizes Parkinson's disease.(87) And a comparison of serum CoQ10 levels in patients with Huntington's disease found untreated patients had significantly lower levels of CoQ10, suggesting supplementation could reduce impaired mitochondrial function in the condition.(88)

CoQ10 also functions as an antioxidant, which can benefit neurodegenerative diseases characterized by oxidative stress. Researchers from the University of Windsor, Ontario, noted a link has been established between exposure to the herbicide paraquat and neurodegenerative diseases; their in vitro study found CoQ10 prevented the generation of ROS by neuronal mitochondria as well as the collapse of mitochondrial membranes.(89) The researchers concluded CoQ10 could possibly prevent and help treat neurodegenerative diseases caused by environmental toxins.

Enhancing blood flow is another mode of action considered beneficial to enhancing cognitive function. A review from the University of New Mexico, Albuquerque, noted the compound **vinpocetine** from **vincamine** (*Vinca minor*) increases blood circulation and metabolism in the brain.(90) The researchers added animal studies show vinpocetine can reduce the loss of neurons associated with decreased blood flow, while trials in adults with memory problems related to poor circulation or dementia show vinpocetine produces significant improvements in cognitive function tests. A 2003 *Cochrane* review concluded vinpocetine treatment at 30 mg/d and 60 mg/d had moderate benefits for patients with cognitive decline and/or dementia, though the findings are inconclusive.(91) Part of vinpocetine's benefit may also come through antioxidant mechanisms, as an in vitro study in Portugal found vinpocetine prevented generation of ROS in PC12 cells after Abeta exposure.(92)

Another compound studied for its circulatory–and antioxidant–benefits in brain health is **Ginkgo biloba**. Researchers from the University of Oxford, England, who wrote a review from the *Cochrane Database System* noted a standardized extract (EGb761 from the Willmar Schwabe Group) is widely prescribed in Europe for cognitive issues including memory and concentration problems, confusion and anxiety.(93) Further, their research review revealed ginkgo supplementation benefited cognition, activities of daily living and measures of mood and emotional function. They concluded there is "promising evidence of improvement in cognition and function associated with ginkgo." Another meta-analysis using the *Cochrane* findings found ginkgo was as effective as cholinesterase inhibitors in patients with dementia.(94)

Clinical studies on EGb 761 have investigated its effects in both demented and healthy elderly populations. Researchers from the Acute Unit for Alzheimer's Patients in Toulouse, France, recently released data on a study in women over age 75 comparing 69 women with Alzheimer's dementia to 345 women with normal cognitive function.(95) Fewer women who developed Alzheimer's dementia had been prescribed EGb 761, suggesting treatment reduced the risk of disease onset. Contrarily, another study in 214 patients with dementia found no effect of treatment with EGb 761 (240 mg/d or 160 mg/d) on any outcome measures compared to placebo.(96) Another study investigated the effect of EGb 761 in Alzheimer's disease depending on baseline severity of the condition.(97) The researchers from New York University Medical Center found a favorable treatment effect on cognitive performance and social functioning; however, the effect was more pronounced in patients with mild

impairment, while those with more severe dementia experienced more of a stabilization of the condition.

Similarly, studies in older individuals with no history of dementia or neurocognitive impairments have shown more positive results. Researchers from Liberty University in Lynchburg, Va., found cognitively intact participants taking 180 mg/d of EGb 761 (n=131) had significantly greater improvement on cognitive tests compared to participants taking placebo (n=131).(98) And in a study from Ludwig-Maximilians-Universitat Munchen, Germany, subjects between the ages of 50 and 65 with no age-related cognitive impairment who received 240 mg/d of EGb 761 (n=34) for four weeks had statistically significant improvements in mental health and quality of life scores.(99)

Ginkgo has also been studied together with ***Bacopa monniera***, a traditional Ayurvedic botanical. A study at the Central Drug Research Institute in Lucknow, India, compared the effects of three different extracts of bacopa and three of ginkgo for seven days after induction of dementia in mice.(100) Both compounds showed a dose-dependent inhibitory effect on ACh activity, suggesting usefulness in treating dementia. In contrast, researchers at Swinburne University in Victoria, Australia, looked at the activity of a ginkgo/bacopa combination (as Ginkgo Brahmi from Blackmores) in 85 healthy human adults and found no impact on cognitive function.(101)

On its own, bacopa has been studied for its impact on memory as well as its ability to moderate stress, which can cause ROS generation. A study at the University of Wollongong, Australia, in 76 healthy adults found bacopa extract enhanced retention of new information both during supplementation and up to six weeks after.(102) Another Australian study found administration of 300 mg/d of bacopa improved the speed of visual information processing and memory function.(103) Finally, Indian researchers investigated the impact of bacopa extract on stress levels in rats, and found treatment with bacopa prior to exposure to stress significantly reduced increases in ulcer index, plasma glucose and adrenal gland weight, suggesting bacopa possesses strong adaptogenic activity.(104)

As countries around the world face increasing economic pressures with aging populations, the ability of nutraceutical compounds to alleviate some of the health care economic burden associated with neurodegenerative diseases is increasingly critical. Consumers who turn to preventive care as they age are likely to find a growing stable of nutritional ingredients to support cognitive function.

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