

LE Magazine May 2000

## COVER STORY

**Enhancing Cognitive Function**

Keeping your memory in tip top shape

by Ivy Greenwell

First, the bad news: Doctors have confirmed that aging-related mental decline is faster and more profound than originally believed. A new British study of people over age 74 shows there is undeniable evidence of a steep mental decline. The director of the study, Dr. Carol Brayne of the Institute of Public Health in Cambridge, U.K. stated: "Although we would prefer that aging not necessarily be accompanied by cognitive decline, these data suggest that for the vast majority of (elderly) populations, it is."

The good news is the exciting finding that the brain can generate new neurons. After decades of believing that neurons can only be lost with age, scientists at Princeton have recently demonstrated that new nerve cells are indeed being created in the brains of monkeys. The new neurons are formed deep in the brain near the ventricles, then migrate to various areas, including the prefrontal cortex, regarded as the seat of "higher cognitive functions." The implication of this discovery is that neurons (brain cells) can at least be partly replaced. The old dogma held that the brain inevitably shrinks and progressively atrophies as we age. Now this dismal view can be discarded in favor of a new search for ways to help the brain regenerate and preserve its youthful powers. If the synthesis of new neurons takes place in human brains as well, and everyone thinks it does, there is great hope for reversing brain damage and preserving good cognitive function well into old age. The new discovery also points to the importance of providing the brain with the right nutrients, so that the new cells can be easily formed. It would appear that neuronal regeneration is facilitated when there is an abundance of cell membrane building blocks such as phosphatidyl choline and phosphatidyl serine. Considering that nerve growth factors are under hormonal control, adequate sex-steroid hormone replacement is also an important consideration. Age-related cognitive decline becomes noticeable in middle age, when people typically start complaining that their memory isn't as good as it used to be. Past the age of 50 or so, mental fitness, like physical fitness, has to be consciously worked at. Raising the declining levels of neurotransmitters is one challenge. The other is to maintain efficient neural cell membranes with optimal fluidity.

**Why we need choline**

The brain has a voracious appetite for choline. There are two main reasons for the brain's huge need for this nutrient: choline is required for synthesis of the key neurotransmitter acetylcholine, and it is used for the building and maintenance of brain cell membranes. Acetylcholine is vital for thought, memory and sleep, and is also involved in the control of movements. Not surprisingly, the production of acetylcholine decreases with age, resulting in poor memory, diminished learning ability and cognitive decline in general. In Alzheimer's disease, the levels of acetylcholine are abnormally low. It is the cholinergic neurons that show the most degeneration as Alzheimer's disease progresses. When the brain does not receive sufficient choline to manufacture acetylcholine, it may resort to extracting choline out of the nerve cell membranes. This is called auto-cannibalism. While in the short run this process provides a supply of choline to produce enough acetylcholine to keep memory and other brain functions going, in the long run the nerve cells become badly damaged as neural cell membranes grow rigid and increasingly dysfunctional. Choline is also important for the building of healthy cell membranes. As phosphatidyl choline, it constitutes one third of the cell membrane phospholipids. Phosphatidyl choline also serves as the substrate, an enzyme that activates the formation of other signaling neurochemicals.



## Choline and sleep



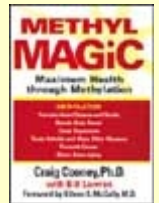
One of the lesser-known functions of acetylcholine is helping to maintain sleep. Acetylcholine controls the amount of sensory input. It strengthens the so-called stimulus barrier, making it possible to sleep through minor noises and other disturbances. As we age, we tend to become "light sleepers," easily roused from sleep. Menopausal women, who experience a sudden drop in acetylcholine levels due to estrogen withdrawal, often complain about having suddenly become "light sleepers." The same stimulus barrier also helps us concentrate and solve problems. Too little acetylcholine makes us distracted and irritable as too many unimportant stimuli bombard us, in essence preventing us from thinking.

Menopausal women who are not on hormone replacement also tend to complain about the dryness of their mucous membranes, which leads to problems such as nosebleeds. Again, it is acetylcholine that keeps the mucous membranes moist. The bladder too is under cholinergic control.

## Choline helps facilitate youthful methylation

The role of choline in methylation probably explains the finding that choline-deficient diets are associated with an increased rate of cancer in animal studies. Dr. Craig Cooney, an expert in the field of methylation, suggests that choline may in fact turn out to be important in the treatment of cancer. He points out that besides being a methyl donor, choline function as a "key component in the 'cellular switchboard' that regulates the chemical signaling system in the membranes of our cells." It is desirable to take folic acid concurrently with choline; it seems that if more folic acid is available, less choline is used up for methylation, and can thus be used by the nervous system. Thus, methylating agents have a choline-sparing action. Particularly as we grow older and our absorption and the uptake of choline by the nervous system are likely to decline, we simply can't afford to "waste" choline on methylation while our cell membranes deteriorate.

A statement in Dr. Craig Cooney's book, *Methyl Magic*, suggests that taking your choline supplement with coffee may increase the release of acetylcholine. "Research with rats shows that a combination of caffeine and choline releases much more acetylcholine than choline alone," Cooney states. This is probably due to the fact that caffeine competes with adenosine, an inhibitor of acetylcholine synthesis.



## Protection against high cholesterol

Choline is also an enormously important nutrient because it helps prevent the buildup of cholesterol. It synergizes with inositol in its function as a lipotropic—a compound that emulsifies fat, keeping it in liquid suspension. As long as cholesterol is emulsified, it is not likely to settle on artery walls or in the gallbladder. In addition, phosphatidyl choline actually helps transport cholesterol and fats so they can be used by the body, or else excreted. If you are watching your cholesterol, you may also be engaging in a serious exercise program. But beware: strenuous exercise such as marathon running may seriously lower the levels of choline. A study of the Boston marathon runners found as much as a 40% decrease in some runners. The reason for this might be the need for choline in the metabolism of fats, which is increased during exercise.

## Fetal development

Several fascinating recent studies found that when pregnant rats were supplemented with choline (four to seven times the amount present in the standard rat chow) during the last half of pregnancy, their offspring showed lifelong improved learning capacity, attentiveness and memory. Furthermore, the rats born to choline supplemented mothers did not show the decline in memory with aging that was apparent in control rats. The extra choline during fetal development apparently produced a more efficient nervous system and ensured superior brain health for the rest of the animals' lives. Thus, there is reason to think that prenatal choline supplementation results in enhanced attention, faster and more persistent learning, and improved cognitive function in general across the life span. If these exciting findings apply to humans as well, the implications of prenatal choline supplementation for human cognitive performance and continued brain health in old age are staggering. Newborns continue to require large amounts of choline for development. Normally choline is supplied in mother's milk. However, it is worth repeating that the amount of choline in breast milk correlates with dietary consumption of choline. A nursing mother who doesn't consume choline-rich foods runs the risk of depriving her child of the higher choline levels that would ensure optimal brain development, and also of becoming choline-deficient herself.

## How much do you need?

It has been suggested that especially the elderly should supplement with 1-3 g of choline a day, along with methylating agents such as vitamins B12, B6 and folic acid. Dr. Cooney suggests increasing one's choline supplementation as one gets older. While 250 mg might be sufficient for a young person (though possibly not for a pregnant or nursing woman), as we get older we should move to 500 mg, then 750 mg, until we reach 1500 to 3000 mg a day in old age.

It appears that supplementation with choline may increase acetylcholine synthesis by promoting increased neuronal activity. Otherwise, the extra choline is probably used for other purposes, mainly the crucial task of building and maintaining brain cell membranes. Choline supplementation has also been shown to increase the density of certain cholinergic receptors.

Do note: if you have never taken choline supplements before, do not start with a large dose, particularly if you are still relatively young. To do so might make you feel hyperactive or anxious. It is best to increase your intake gradually, Dr. Cooney suggests. It is also recommended that you concurrently take other methylating agents, such as folic acid. Dr. Cooney states that the fishy smell sometimes associated with ingestion of large doses of choline disappears if you take 800 mcg of folic acid with your choline.

#### Where to get it

Stroke victims have shown improvement when supplementing with glyceryl-phosphorylcholine. In rat studies, tissue examination showed that the administration of glyceryl-phosphorylcholine was able to help repair damaged neurons. A large dose of glyceryl-phosphorylcholine was also found to help prevent a drug-induced drop in acetylcholine levels. Clinical trials with glyceryl-phosphorylcholine in Alzheimer's patients showed that 1200 mg/day of glyceryl-phosphorylcholine produced a greater improvement on most cognitive and behavioral measures than 1500 mg/day of acetyl-L-carnitine. Glyceryl-phosphorylcholine has also been compared with CDP-choline (cytidine diphosphocholine), and has been found to produce superior results in patients with vascular dementia. Another study found much higher plasma choline levels after injections of glyceryl-phosphorylcholine than CDP-choline. Glyceryl-phosphorylcholine appears to be the best choline donor in the brain. Studies using glyceryl-phosphorylcholine as a choline donor found typical multiple benefits. Besides the expected improvements in memory and learning in older animals, glyceryl-phosphorylcholine prevented the age-related loss of certain cholinergic receptors, as well as the age-related loss of neural tissue in the cerebellum. A combined administration of growth hormone-releasing hormone (GHRH) and glyceryl-phosphorylcholine produced a greater release of growth hormone than GHRH alone. The potentiating effect of glyceryl-phosphorylcholine on growth hormone release was more pronounced in older subjects. It is interesting to note that a quart of cow milk contains about 250 mg of glyceryl-phosphorylcholine and 50 mg of phosphatidyl-ethanolamine. Since newborn mammals have a tremendous need for choline, it is not surprising that milk should contain compounds that are the most efficient choline donors. In order for oral glyceryl-phosphorylcholine to increase the levels of acetylcholine, several other co-factors are involved such as pantothenic acid (vitamin B5) and methylation-enhancing nutrients such as folic acid, B12 and TMG.

#### Maintaining brain cell membrane integrity

Phosphatidylethanolamine is part of the cell membrane, together with compounds such as phosphatidyl choline, phosphatidyl inositol and phosphatidyl serine. The individual properties of these various phospholipids and their metabolites are now under intense investigation. We know that phosphatidyl- ethanolamine is deficient in the neurons of the victims of Alzheimer's disease. These patients are also deficient in other phospholipids. But one need not be diagnosed with a degenerative brain disorder in order to become gradually deficient in phospholipids, including phosphatidyl- ethanolamine. The aging process decreases the levels of phospholipids in cell membranes throughout the body, with particularly disastrous consequences for the brain. Because of the brain's enormous need for choline, some phosphatidylethanolamine in neural membranes may be methylated as needed to provide choline.

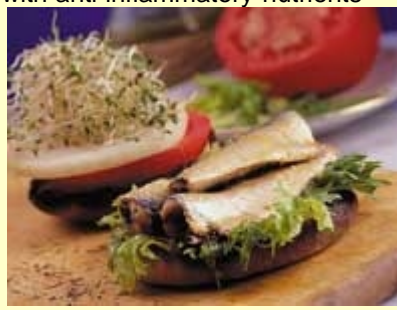
#### Dietary Sources



It is estimated that the average American consumes 500 - 1000 mg of choline from food. Health-conscious people, however, are likely to avoid the richest sources of choline, such as eggs, meat and organ meats.

If you are interested in increasing your intake of choline from the diet, let us suggest that you substantially increase your consumption of fish. Fish is correctly known as "brain food," since it supplies a lot of choline (fish lecithin is a particularly rich source of choline) and nucleic acids, which provide building blocks for the synthesis of new cells. Cold-water fish is also the richest source of the much-needed omega-3 fatty acids, with their anti-inflammatory and antidepressant properties. If you are interested in protecting your brain function from the ravages of aging, daily consumption of fish is one of the best dietary changes you can make. Note that the fish-eating Japanese have an enviably low incidence of Alzheimer's disease in spite of enjoying the longest life expectancy in the world. This argues against the mainstream belief that simply living long enough inevitably leads to Alzheimer's disease.

An adequate supply of choline, combined with anti-inflammatory nutrients such as omega-3 fatty acids, may significantly lower the risk of developing this tragic degenerative disorder.



### Increasing neurotransmitter receptors

Phosphatidylserine (PS) is a phospholipid that is part of every cell membrane in the body. It is especially abundant in brain cells. One special function of phosphatidylserine is to keep neuronal membranes flexible. Adequate PS levels in cell membranes also enables the free flow of nutrients into the cells and facilitates the removal of metabolic waste products. Improved membrane function also means improved energy production. Furthermore, PS facilitates the release of neurotransmitters, including acetylcholine and dopamine. Thus, PS is vital for neuronal communication. It has been shown that PS can increase the number of neurotransmitter receptors back to youthful levels. In one mouse study, supplementation with PS was found to increase the density of NMDA receptors in the forebrain by 25%. PS also increased the binding of glutamate and glycine to the NMDA receptors. This improvement in receptor density and function naturally leads to improved neural communication as the neural signal gets stronger and can be transmitted with greater speed. This in turn results in improved cognitive function, as shown by better memory and learning, the typical outcome of studies on PS. In the most famous human study, the researchers gave 300 mg of PS a day for 12 weeks to 149 subjects over 50. Various memory and learning tests were administered before and after. The results showed that PS managed to raise cognitive performance to the levels typical for as much as 12 years younger. In other words, it is possible that supplementation with PS may be able to reverse over a decade's worth of cognitive decline. The most dramatic improvement was seen in subjects with the greatest degree of initial memory impairment. In addition, in one study, aged animals supplemented with PS actually performed better than young animals. A fascinating study found that Parkinson's patients with a slowed EEG showed accelerated EEG in response to PS. These dramatic results are probably due to better function of neural membranes, increased density of neurotransmitter receptors, and higher levels of acetylcholine and dopamine, as well as to enhanced glucose metabolism. Holistic clinicians such as Dr. Khalsa are thrilled with the improvements they see in older patients who start taking PS: better memory, more mental alertness and clarity, more energy and zest, a brighter mood.

### Sources of glyceryl- phosphorylcholine

Milk contains free glyceryl-phosphorylcholine and glycerophosphoryl ethanolamine, which also acts as a choline donor, since it can be methylated to glyceryl-phosphorylcholine. Other choline-rich foods, such as lecithin, provide bound forms of glyceryl-phosphorylcholine and glycerophosphoryl-ethanolamine that are not readily utilized by the body. Lecithin is about 8% glyceryl-phosphorylcholine and glycerophosphoryl ethanolamine. Pure glyceryl-phosphorylcholine powder, on the other hand, is very stable (no fatty acids) and water-soluble. It is a much more efficient donor of choline than lecithin. At present, glyceryl-phosphorylcholine is manufactured by an Italian firm that uses a special patented process to extract it from soybean lecithin. It is sold as a drug in Europe to treat various forms of senility. For the first time, glyceryl-phosphorylcholine is being offered in the United States as a dietary supplement.



Another study showed that supplementation with PS increased the beneficial alpha brain waves by up to 20%. Interestingly, there is a decline in the alpha-range brain waves as we age; PS may be able to prevent this senescent pattern. By enhancing the release of neurotransmitters and the number of receptors, improving energy production, and keeping neural cell membranes flexible, PS helps the brain preserve youthful levels of functioning. One of the most important anti-aging supplements, PS optimizes neural communication and helps prevent cortisol-related brain damage. Together with other nutrients that improve neural membrane fluidity, and thus the efficiency of neurotransmitter receptors, PS also appears to be an effective antidepressant. Finally, phosphatidyl serine treatment has been shown to produce significant clinical improvement in early stages of dementia. Doses as large as 300 - 500 mg may be needed.

Phosphatidyl serine is widely present in foods, but only in trace amounts. It is not possible to obtain enough PS from the diet; the body has to synthesize it, and apparently does it less and less efficiently as we age. Fortunately, the effectiveness of PS supplementation has been widely documented. Please note: if you take phosphatidylserine (PS) supplements, you should also take antioxidants to protect PS from free radicals.

A critical cofactor needed to produce acetylcholine

Pantothenic acid, also known as vitamin B5, is a little-publicized key nutrient for neuroprotection. Pantothenic acid is converted in our bodies into pantethine, which in turn serves as a substrate for the synthesis of Coenzyme A (CoA). CoA improves brain function by promoting the synthesis of acetylcholine. Metabolites of CoA enhance brain metabolism and energy production through its essential role in the Krebs cycle. The more energy brain cells have, the better they can function in signal transmission, as well as repair themselves and defend against free radicals. Another indirect contribution of pantothenic acid to brain health stems from the fact that CoA improves the metabolism of the heart muscle and lowers serum lipids, thus improving blood flow to the brain. Yet another benefit of pantothenic acid is the increased formation of acetylcholine in the intestines. This intestinal acetylcholine enhances peristalsis (rhythmic intestinal motion), thus preventing constipation and facilitating elimination. Faster peristalsis also means less complete digestion of food, helping prevent obesity.

An increased susceptibility to infections, fatigue and decreased ability to cope with stress could indicate a deficiency of pantothenic acid. This important B vitamin has been shown to help in wound healing, arthritis, building immune antibodies and lowering the toxicity of many antibiotics. Like many other cardioprotective and energy-enhancing compounds, pantothenic acid also appears to protect against cancer. It even helps remove lipofuscin, the ugly brown pigment in "age spots." More importantly, though, is the fact that the brain uses pantothenic acid to transform choline into acetylcholine.

### Ancillary benefits of PS

One interesting study showed that PS (phosphatidylserine) reduces the activation of the pituitary-adrenal axis and the production of stress hormones. Excess cortisol, our main stress hormone, is known to be neurotoxic; it is also known to increase with age. Intense exercise also results in considerable release of cortisol. An important part of the anti-aging effect of PS may be due to this lowering of stress hormones.

Some athletes and body builders also take PS to alleviate the catabolic effects of high cortisol. It is too bad that most people who are under intense stress are aware neither of the brain damage that stress causes, nor of the protective properties of PS.

Continuation of: Enhancing Cognitive Function

[Back to the Magazine Forum](#)

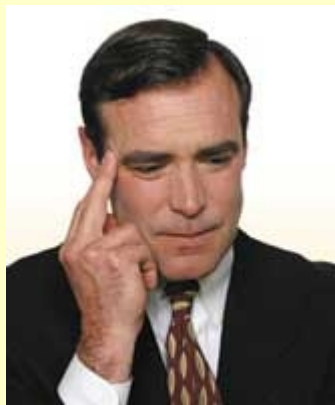
## COVER STORY

Continuation of: Enhancing Cognitive Function

"Viagra" for the brain

First introduced 22 years ago in Hungary for the treatment of vascular dementia—a disorder resulting from insufficient blood flow to the brain tissue—vinpocetine has gradually gained popularity as a European "smart drug." Recently it has become available in the United States. It is a promising neuroprotective supplement and cognitive booster. It is interesting that vinpocetine has a similar mechanism of action as Viagra. Both are known to be effective phosphodiesterase inhibitors. That is, they work to enhance blood flow by inhibiting an enzyme in the phosphodiesterase family. Not surprisingly, the main benefit of vinpocetine is an improvement in cerebral blood flow. More blood reaching the brain cells means better oxygenation, nutrition and waste removal—all of which adds up to more youthful brain function.

Vinpocetine has also been found to improve the transport of glucose (both uptake and release) across the blood-brain barrier. Low cellular energy production is perhaps the primary factor underlying all aging-related brain degeneration. In addition, vinpocetine has been shown to increase the firing rate of certain types of noradrenergic neurons, which could explain one mechanism of its action as a cognitive booster. The enhancement of blood flow and energy production means that vinpocetine is particularly recommended for people whose cognitive dysfunction stems chiefly from insufficient blood flow to the brain. Vinpocetine also shows promise in helping prevent damage to vision, especially dry macular degeneration. Vinpocetine likewise appears to improve blood flow to the inner ear, thus protecting hearing. Interestingly, vinpocetine has likewise been found to counteract space motion sickness. It can also partly protect against the damage resulting from excess glutamate and other excitotoxins. A new neuroprotective property of vinpocetine has just been discovered: it can lower the production of inflammatory cytokines. Together with other phosphodiesterase inhibitors, vinpocetine has been shown to lower the production by the microglia of a major inflammatory compound known as tumor necrosis factor-alpha (TNF-alpha). Some alternative clinicians believe that if we could truly control inflammation, we could prevent Alzheimer's disease. This view is based on the proven effectiveness of anti-inflammatories such as ibuprofen in lowering the risk of Alzheimer's disease. The problem with commonly used pharmaceutical anti-inflammatories is their side effects. Vinpocetine and other natural anti-inflammatories (fish oil, vitamin E, estrogens, many antioxidants including bilberry extract and green tea catechins) appear to be a nontoxic alternative. Vinpocetine is an alkaloid, in the same family as caffeine and nicotine, both known to be very effective cognitive enhancers. Nicotine increases the release of acetylcholine and dopamine, and improves both short-term recall and long-term potentiation. But while caffeine and nicotine each have well-known drawbacks, vinpocetine appears to be safe and non-addictive. It would not be surprising if vinpocetine shared nicotine's protective benefits against Alzheimer's disease and Parkinson's disease, without the problem of addiction. An interesting side benefit of vinpocetine is that it has also been found to protect against both gastric and cerebral damage induced by alcohol, against kidney problems caused by renal vasoconstriction, and against retinal damage caused by the hepatitis B virus.



### Enhancing Short-Term Memory

Another natural memory enhancer, Huperzine A—an extract from the Chinese club moss—appears to maintain higher acetylcholine levels by inhibiting acetylcholinesterase, the enzyme that breaks down acetylcholine. While it appears to be a promising adjuvant agent in the treatment of Alzheimer's disease, it is still too early to say whether it is desirable for people who have only minor memory deficit. Huperzine A is a great short-term memory booster that can be taken in doses of 50 mcg to 100 mcg first thing in the morning for special situations where maximum cognitive function is required. While Huperzine A appears to be safe for special situations, daily use could cause a neurotransmitter imbalance that could lead to undesirable complications such as acetylcholine overload. Huperzine A should not be taken more than a few

times a week at the most.

Hormone of memory and good cheer

Pregnenolone was discovered during the 1930s and was extensively studied at first, particularly in connection with job performance

and as a therapy for arthritis. Then it faded into oblivion as other hormones, notably synthetic forms of cortisone, became more trendy, not to mention lucrative for the drug industry. Now we are witnessing a revival of interest in pregnenolone-after 60 years, it's gaining popularity alongside DHEA. Pregnenolone functions largely as a pro-hormone. Produced primarily in the adrenals, it is also the primary precursor of all the steroid hormones, the first hormone to be formed from cholesterol, the raw material for all steroids. The levels of pregnenolone go down with aging. By the time we are 75, we have only 40% of the pregnenolone we had when we were 35. Besides aging, stress, disease, hypothyroidism, exposure to toxins and depression all result in low pregnenolone levels. Patients suffering from depression have been found to have pregnenolone levels less than half those found in nondepressed persons. These decreased levels of pregnenolone have been found in both unipolar and bipolar depression (the manic-depressive disorder). In job-performance studies, subjects reported better mood when taking pregnenolone. Like estrogen and DHEA, pregnenolone seems to have a pleasantly stimulatory effect on the brain, making one feel sharp without that wired, jittery feeling that may come from too much caffeine, for instance.

While many people know that DHEA and its sulfate, DHEA-S, are very abundant in the brain, few know that the brain levels of pregnenolone and pregnenolone sulfate are 10 times as high as those of DHEA. Pregnenolone could be called our primary neurosteroid. It is produced not only in the adrenals, but also in the brain-a finding first reported by the famous French steroid researcher, Dr. Etienne-Emile Baulieu. The peripheral nervous system can also manufacture pregnenolone, possibly for the purpose of maintaining the myelin sheath. Pregnenolone is somewhat like ginseng. It improves energy, endurance and ability to cope with stress. Studies using factory workers, college students and airline pilots all found that pregnenolone effectively counteracts fatigue. When you are under stress, pregnenolone gives you an extra edge. When you are relaxed, however, you tend not to feel much difference. This may be particularly true of younger people. The elderly, who are more seriously deficient, seem to appreciate pregnenolone's extra energy boost more keenly. In the 1940s, it was established that pregnenolone facilitates learning and helps us perform any task in which memory is involved. But pregnenolone's chief claim to fame is the fact that this pre-hormone has been found to be the most effective memory booster yet discovered in animal studies. It has been shown to increase the release of acetylcholine and to modulate NMDA (aspartate/glutamate) receptors in a way that suggests that pregnenolone stimulates central cholinergic communication. It also seems to modulate enzyme activity, calcium-ion flow through cell membranes, protein turnover and other complex reactions involved in memory function. Together with DHEA, pregnenolone also synchronizes the firing of the neurons. A decline in pregnenolone thus makes all mental function more difficult. There is some anecdotal evidence suggesting that pregnenolone may be especially effective in elderly women as a restorer of energy and mental clarity, and as an antidepressant. Even a small amount of supplemental pregnenolone may affect the quality of sleep. Most studies find that pregnenolone, like DHEA, increases the amount of REM sleep, which appears to play a role in the formation of memory. Like progesterone, pregnenolone is also important for repairing the brain and the spinal cord in case of injury. Pregnenolone is a precursor to progesterone in the body. Caution: Men diagnosed with prostate cancer are advised to avoid pregnenolone because of the possibility of conversion into androgens.

### The effects of deficiency

One area that we are barely beginning to investigate is pregnenolone's influence on various enzymes. One of the enzyme groups stimulated by pregnenolone is the cytochrome P-450 enzyme system, an important defense against various toxins and carcinogens. Thus, by helping the liver detoxify carcinogens, pregnenolone helps protect against cancer. Like many other steroids, pregnenolone also appears to modulate the immune response. Low levels of pregnenolone in aged individuals correlate with depression, cognitive decline and increased rate of cancer. Similarly, when cholesterol is excessively lowered, and thus the synthesis of pregnenolone is hampered, we see depression, cognitive impairment and more cancer.

Pregnenolone levels in premenopausal women have been found to be the highest during the luteal (progesterone) phase of the menstrual cycle. PMS sufferers have reported relief from their symptoms when they use pregnenolone. Since PMS is largely an inflammatory disorder, this action may be due to pregnenolone's anti-inflammatory effects. The overall hormone balancing effect may also be involved, particularly the conversion into progesterone.

At the same time, like DHEA and progesterone, pregnenolone seems to protect against the destructive consequences of elevated cortisol, such as weakening of the immune system. Cortisol levels increase with aging, while pregnenolone levels diminish. Probably the older one gets, the more crucial it is to take both DHEA and pregnenolone to correct this imbalance between the pro-oxidant, neurotoxic stress hormones and the beneficial steroids.

It is possible that pregnenolone's anti-inflammatory effects help protect against Alzheimer's disease, which has a marked inflammatory component.



### Brain boosters

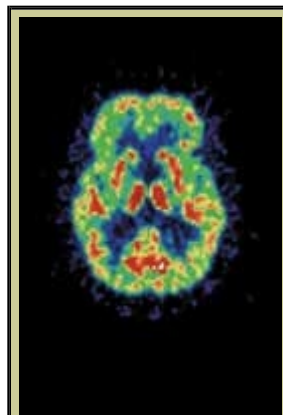
There are a variety of other supplements that may enhance your brain longevity program. Among these is alpha lipoic acid, which is both an antioxidant and a metabolic enhancer and has emerged as a new star. It is joined by neuroprotective energy-enhancers: acetyl-L-carnitine and coQ10. The nervous system also needs the benefits of antioxidants and anti-inflammatories such as vitamin

E, shown not only to protect the membranes but also to restore damaged neurotransmitter receptors, and fish oil. After all, fish eating has been documented to correlate with a dramatic lower risk of Alzheimer's disease. Neuroprotective regimens should also include the catechins in green tea extract, and/or the proanthocyanidins in grape seed extract and similar compounds in bilberry extract. High-potency ginkgo is also highly recommended. In addition to being a documented cognitive enhancer, it has recently been found to extend life span in rats. Improvement in Alzheimer's disease patients has been noted with doses of 240 mg and higher.

Getting enough sleep and rest is extremely important. We must also take measures to reduce cortisol, which has neurotoxic effects. Meditation and stress reduction are effective measures, as are supplements such as DHEA, pregnenolone, and KH3. Chronic stress, today the daily condition of millions, causes an increase in free radicals (both oxygen and nitric oxide-based) and inflammatory cytokines. Fortunately most of the compounds mentioned here are both excellent antioxidants and anti-inflammatories; vitamin E and green tea catechins are stellar examples. Finally, vitamin C is extremely important for the brain. Besides functioning as an antioxidant, it also enhances the synthesis of key neurotransmitters, including acetylcholine and dopamine. Niacin (B3) also helps manufacture neurotransmitters, including the calming GABA. Interestingly, yet another B vitamin, thiamin (vitamin B1) has turned out to be a potent antioxidant, helping other antioxidants such as vitamin E to destroy free radicals.

### Conclusion

Remember: unless you slow down your aging, aging is going to slow you down. It will make you increasingly physically and mentally disabled, sluggish, forgetful and depressed, ultimately making life not seem worth living. Fortunately, you can fight back with lifestyle, the right diet and the right supplements.



Alpha lipoic acid has emerged as a new star in brain

boosting, in addition to the neuroprotective energy-enhancers such as acetyl-L-carnitine and CoQ10.

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