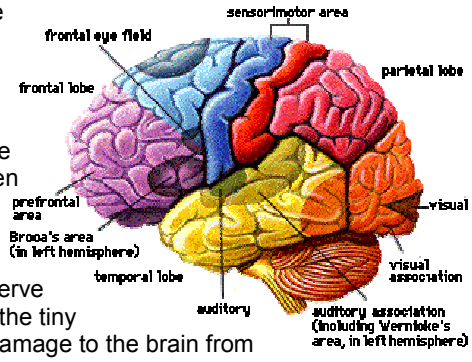
Phosphatidylserine: The Remarkable Brain Cell Nutrient



Phosphatidylserine (PS) is a naturally-occurring phospholipid that is found in all cells of the body, with particularly high concentrations in the brain. PS is an essential cell membrane building-block for nerve cells. Of all the body's organs, the brain, without question, performs the most complex and most energy-demanding functions. Healthy nerve cell membranes are essential to generate optimum energy and to produce, package and release numerous chemical neurotransmitters in their proper amount and balance. Cell membranes are also the sites where nerve cells react to these neurotransmitters and where neurotransmitters are then recycled for later use for clearance from the brain.

The site where nerve cells perform most of their specialized functions is on or within their membranes. These membranes are composed mainly of phospholipids and proteins.

Among the causes of memory decline and other cognitive impairment are: (1) the death of nerve cells, or (2) the decreased density of their interconnected networks due to loss of dendrites, the tiny filaments which connect one nerve cell to another. These changes may be due to aging or damage to the brain from such insults as alcohol consumption, cigarette smoking, toxic chemicals, chronic emotional stress, stroke, trauma or hypoglycemia.

Supplementation of the diet with PS has been proven to slow, halt, or in many cases, even reverse cognitive degeneration due to age-related cognitive decline (ARCD) [2, 3, 9] and dementing illnesses like Alzheimer's disease.[1,4, 6, 7, 8, 10] PS has been scientifically established to be among the most effective substances to consistently result in dramatic cognitive improvements and enhancements of other higher brain functions. Until recently, however, PS was available in the U.S. only as a very minor constituent of lecithin. Now, new technology has made it possible to greatly enhance the PS content of lecithin, making phosphatidylserine readily available in effective amounts for the first time.

Structure and Biochemistry of PS

The PS molecule has a "head," a middle piece, and two tail groups. The head piece consists of serine and phosphate, the middle piece is derived from glycerol, and the tails are fatty acids. PS is extremely bioavailable and crosses the blood-brain barrier with ease. Once in the brain, the PS molecule as a unit merges smoothly into the nerve cell membrane where it is available to facilitate cell-level energetics and homeostasis, as well as enhance neurotransmitter production, release, and action. PS also serves as a precursor reservoir for the related phospholipids, phosphatidylethanolamine (PE) and phosphatidylcholine (PC).

As a unique phospholipid constituent of all known cell membranes, PS helps to ensure membrane integrity (in conjunction with the other phospholipids: PE, PC and phosphatidylinositol [PI]). This demarcates the "living" cell interior from the "nonliving" outer environment. This demarcation is absolutely necessary for life to exist. PS also helps support the functions of a number of membrane proteins. A list of these membrane proteins reads like a "Who's Who" of important proteins for the cell: Na/K ATPase; Ca ATPase; Mg ATPase (for ion transport); protein kinase C; adenylate cyclase (for processing signals that reach the cell from the environment); NADPH-cytochrome C reductase (for mitochondrial energy production); proteins that mediate the release of transmitters via secretory vesicles; and receptors for NMDA and other transmitters. PS also serves as a reservoir for fatty acids which are the sources of messenger molecules which carry signals from the cell membrane to the surroundings (the prostanoids or "prostaglandins").

PS occurs in all tissues of the body. In addition to its many nerve cell functions, it is also known to be involved in red cell recycling, bone matrix formation, testicular function, generation and regulation of the heartbeat, and hormone secretion by the adrenal glands.

Clinical Findings of Memory Improvement

Findings from many controlled clinical trials indicate that PS consistently ameliorates memory loss and other cognitive decline related to aging (many of these findings have been cited and described in Smart Drugs IIThe Next Gen-eration).5 In 14 double-blind clinical trials [1-4, 6-11, 14-16,18] conducted with subjects aged 50 and older, PS benefited all degrees of cognitive impairment. In one U.S. trial by Crook, et al (1991) on subjects with age-related cognitive decline (ARCD),[3] PS reversed the decline of name-face acquisition skills by a statistical 12 years, i.e., from average scores attained by 64 year-old subjects, to average scores attained by 52 year-olds. This is a reduction in "cognitive biological age" of 12 years!

In double-blind trials conducted with more severely afflicted subjects, PS brought about statistically and clinically significant improvements in measures of recall, learning, concentration, adaptability, mood and sociability. In other double-blind trials, PS improved neuro-physiological measures such as EEG (electroencephalogram) and reflexes (as judged by flicker-fusion response time).[17]

In another human trial conducted with young male volunters, PS significantly improved EEG alpha rhythm (which often declines with aging and memory loss).[17] In older subjects with severe cognitive impairment, PS dramatically enhanced brain glucose consumption (assessed via positron emission tomographic [PET] imaging) and partially restored the 24-hour rhythm of TSH (thyroid-stimulating hormone) secretion in aged men.19 Also, in elderly subjects, PS enhanced the hypothalamic-pituitary-adrenal (HPA) stress-coping axis, as assessed by the dexamethasone suppression test.[13]

PS as a Cortisol Blocker

PS also ameliorated elevations of stress hormones (ACTH and cortisol) associated with strenuous exercise in young men.[12,13] This is an extremely important finding, as age-related increases in the cortisol/DHEA ratio (due to both prolonged elevated cortisol levels due to stress and/or aging and decreased DHEA levels due to aging) are a significant biomarker of aging. This changing ratio reflects the toxic effects on the body of prolonged relative "hypercortisolemia" (elevated blood levels of cortisol). These effects can ultimately manifest as the "Cushingoid" appearance of many people over the age of 50. Consequently, the cortisol-blocking effects of phosphatidylserine may have profound effects on delaying many adverse effects of aging.

Double-Blind Studies Determine the Right Dose

The dosing strategy for PS has been elucidated from more than 40 clinical studies (many of them double-blind) with over 2,000

subjects in Europe and the USA during the past two decades. Clinically effective oral intakes ranged from 200 to 800 mg per day, taken in divided doses with meals. Most of the trials were conducted at 300 mg per day but for subjects with motor impairment, higher doses may be necessary.

A Proven Track Record of Safety

The incidence of side effects from PS is very low. This is best illustrated by the largest double-blind trial (Cenacchi and others, 1993), [2] in which one subject (of 494) dropped out because of an adverse PS effect, as compared with seven dropouts from the placebo group.

After some 20 years of clinical use, PS has exhibited no known negative interactions with drug therapies. In the Cenacchi, et al. trial cited above, [2] the subjects were elderly (65-93 years) and were allowed to continue on their prescribed drug regimens for the full six months of the trial. Of the 494 subjects who began the trial, 425 completed it. Other dropouts were due to deaths or other reasons not related to PS. Over the full six months, no adverse interactions were noted between

PS and the assortment of drugs that were being taken by this typically elderly population (diuretics, anti-thrombotics, anti-diabetogenics, anti-arrhythmics, anti-hypertensives, anti-inflammatories, anti-acids, anti-ulcers, mucolytics, insulin, calcitonin, and calcium channel blockers).

PS has an extremely favorable benefit-to-risk profile, which stands to reason since it is a major intrinsic constituent of all human cells. Lecithin, the plant extract source of PS, is rated GRAS (Generally Recognized As Safe). Human subjects have safely tolerated up to 800 mg of PS per day. PS has safely been administered to dogs at 70 gm per day for one year, without any toxicity or adverse effects. Furthermore, no clinical blood abnormalities have ever been seen after long-term intake. Toxicological assessments indicate that PS is neither mutagenic nor carcinogenic; it is not teratogenic in animals, and there are no indications it would be unsafe during human pregnancy.

Contraindications for the use of **PS** include soy allergy, known intolerance to lecithin preparations, and rare cases of antiphospholipid autoimmune syndromes. PS has infrequently caused gastro-intestinal upset and can cause insomnia if taken in a large dose (600 mg) just before going to bed.

Over Two Decades of Studies Validate the Efficacy of PS

PS has been studied exhaustively for over twenty years. During this time, it has demonstrated in study after study that it has a significant effect on enhancing memory and other brain functions in both normal and cognitively impaired individuals. These studies confirm that PS is a highly effective agent for enhancing brain function, with a remarkable safety profile. Whether the impaired mental function is linked to aging, toxic or traumatic damage, cerebral insufficiency, or nonspecific causes; diverse measures of brain performance indicate that PS is rarely, if ever, surpassed for its clinical benefits to the brain as a whole.

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Phosphatidyl choline is available in gel caps of 100 mg per capsule, and as, AdrenaCalm, a microsomal cream, which delivers higher blood levels of PS than is possible orally.

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