Science-based, Targeted Nutritional Support for Optimal Nerve Function
The nervous system is an intricate network comprised of 47 miles of nerve fibers, each of which communicates with as many as 1,000 other nerves. As people age, the central and peripheral nervous systems undergo natural changes, including loss and/or atrophy of nerve cells and slower nerve conduction, which can affect the senses, reflexes, and cognitive processes. The ability of peripheral nerves to repair themselves also occurs more slowly and less completely in older people, making them more vulnerable to nerve injury or disease.

Nutrition plays a significant role in nerve health, and recent research has demonstrated the potential impact of nutritional factors and individual micronutrients on the central and peripheral nervous systems. Studies show that measures of brain electrophysiology and behavior are sensitive to even brief periods of nutritional inadequacy. While a healthy, balanced diet goes a long way toward keeping the nervous system functioning at optimal capacity, older adults may be more vulnerable to nutrient deficiencies and may benefit from supplementation targeted at maintaining nerve health.

**Risk Factors for Nutrient Insufficiency**

Conditions that increase the risk of nutrient insufficiency include older age, diabetes, alcohol abuse, eating disorders, pregnancy, parenteral nutrition, and lower economic status. In addition, any medical condition that affects the gastrointestinal tract can impair absorption of essential vitamins. Neurological complications in association with bariatric surgery have been garnering attention in recent years. These neurological complications may involve the entire nervous systems, ranging from diffuse encephalopathy to peripheral neuropathy to myopathy. Up to 16 percent of patients who undergo bariatric surgery may experience peripheral neuropathy. This may be due, in part, to the prevalence of malnutrition among morbidly obese patients prior to their bariatric surgery.

Among healthy elderly people who are free of major chronic illnesses, age-related decline in neurological function of the peripheral nervous system has been attributed to metabolic factors, such as plasma glucose levels, even if these factors are within the normal range. Studies have also shown that these age-related declines in peripheral nerve function are more common in men than women.

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Neuropathies arising from suboptimal nutritional status may manifest either acutely, subacutely or chronically and may be either demyelinating or axonal. Peripheral neuropathy with coexistent myelopathy—also known as myeloneuropathy—has also been observed with nutritional deficiencies of vitamin B12 and copper.3

**Keys Nutrients for Normal Nerve Function**

The link between nutrition and nerve function is not surprising, as the nervous system relies on nearly all of the essential nutrients for effective functioning.6 A proper diet in the form of adequate protein, minerals and vitamins is also required for full motor function. While overt, clinical vitamin deficiencies are uncommon—even among the elderly—biochemical or subclinical vitamin deficiencies may arise due to age-related changes in gastrointestinal absorption and/or vitamin metabolism.7

**B Complex Vitamins**

The B vitamins are significant for healthy nerve function because subclinical deficiencies in these vitamins are relatively common in the general population and specifically among older adults, who may have a reduced ability to absorb both folate and protein-bound vitamin B12. Perhaps the most common neuropathy associated with vitamin B deficiency is beriberi, which occurs in response to vitamin B1 (thiamine) deficiency. Thiamine diphosphate, the active metabolite of thiamine, is an essential co-factor in cellular respiration, ATP production, neurotransmitter synthesis and myelin sheath maintenance. As only about 20 days’ worth of thiamine are stored in the body, thiamine deficiency can begin to manifest in as little as three weeks. The recommended daily allowance for thiamine ranges from 1.0 milligrams per day for young healthy adults to 1.5 milligrams per day for breastfeeding women. In the U.S., thiamine deficiency is rare except in certain conditions such as chronic alcohol abuse, eating disorders and weight reduction surgery.3

Folate and vitamin B12 (cobalamin) play fundamental roles in central nervous system (CNS) function at all ages, including nucleotide and DNA synthesis and tissue growth, differentiation, and repair. Vitamin B12 is also integral for the conversion of L-methylmalonyl coenzyme A into succinal coenzyme A, which is essential for formation of the myelin sheath.3 Deficiencies in these B vitamins may lead to neurological and neuropsychiatric disorders. In addition to folate and vitamin B12, vitamin B6 (pyridoxine) is also important for normal nerve function. Vitamin B6 is a co-factor in the irreversible synthesis of several essential neurotransmitters, including epinephrine, norepinephrine, serotonin, and -aminobutyrate.7 Vitamin B6 is unique in that either deficiency or excess can cause neuropathy. Deficiency in this vitamin is reported to produce peripheral neuropathy and convulsions.8 The recommended daily allowance of vitamin B6 is 1.3 milligrams per day, with an upper intake limit of 100 milligrams per day.9

The primary pathological effect of vitamin B12 deficiency on the nervous system in demyelination, or subacute combined system degeneration, which affects both the central and peripheral nervous systems.10 Other symptoms that may be associated with biochemical

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10– Green R. Evidence for the role of vitamin B-12 in normal brain function. In: Green R, chairman. The role of folate and vitamin B-12 in...
or clinical vitamin B₁₂ deficiency include peripheral neuropathy, impaired memory, dementia, delirium, megaloblastic anemia, and pancytopenia.¹¹

Although clinical vitamin B₁₂ deficiency is relatively rare, mild, subclinical deficiency is present in an estimated 3.2 percent of adults aged 51 and older.¹² According to the Institute of Medicine, 75–90 percent of people with a clinically relevant vitamin B₁₂ deficiency have neurological disorders, and in about 25 percent of cases these are the only clinical manifestations of the deficiency.¹³ Patients with type 2 diabetes represent an at-risk population for vitamin B₁₂ deficiency with an estimated prevalence of 22 percent.¹⁴ Among patients with type 2 diabetes who have severe neuropathy, vitamin B₁₂ replacement has been shown to result in significant improvement in pain and paresthesias.¹⁵

**Figure 1. Vitamin Deficiencies and the Nervous System**¹⁶

<table>
<thead>
<tr>
<th>Compound</th>
<th>Deficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin A</td>
<td>Vision problems, such as night blindness</td>
</tr>
<tr>
<td></td>
<td>Decreased sense of taste</td>
</tr>
<tr>
<td>Vitamin B₁ (Thiamine)</td>
<td>BeniBeri, with distal sensory loss, burning pain, paresthesia, muscle weakness, headache In some cases, co-existent Wernicke's encephalopathy</td>
</tr>
<tr>
<td>Vitamin B₂ (Riboflavin)</td>
<td>Peripheral nerve damage Visual problems, including burning and sensitivity to light</td>
</tr>
<tr>
<td>Vitamin B₃ (Pantothenic Acid)</td>
<td>Rarely, fatigue, headaches and burning sensation in the hands and feet</td>
</tr>
<tr>
<td>Vitamin B₆ (Pyridoxine)</td>
<td>General numbness, paresthesias or burning pain in the hands and feet Decreased distal sensation Ataxia and mild distal weakness</td>
</tr>
<tr>
<td>Vitamin B₉ (Folic Acid)</td>
<td>Peripheral neuropathy Memory disorders</td>
</tr>
<tr>
<td>Vitamin B₁₂ (Cobalamin)</td>
<td>Subacute combined degeneration Neuropsychiatric symptoms Peripheral neuropathy Optic neuropathy</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>Linked to Parkinson's disease, Alzheimer’s disease, depression, cognitive decline</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>Ataxia Hyporeflexia Loss of proprioception and vibration Decreased sensation Proximal muscle weakness</td>
</tr>
</tbody>
</table>

Folate supplementation has been reported to be effective in the treatment of polyneuropathies and peripheral neuropathies associated with folate deficiency.¹⁷ High-dose vitamin B treatment (folic acid 0.8 mg, vitamin B₉ 20 mg and vitamin B₁₂ 0.5 mg) has been shown to lower plasma homocysteine levels and slow shrinkage of whole brain volume over two years among patients

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¹³– Allen LH. How common is vitamin B-12 deficiency? Am J Clin Nutr 2009;89:693S-696S.


with baseline elevated plasma homocysteine levels.\textsuperscript{18} It has also been shown to reduce—by as much as seven-fold—cerebral atrophy in the gray matter regions most vulnerable to the Alzheimer’s disease process, including the medial temporal lobe, among elderly people with mild cognitive impairment and high homocysteine levels.\textsuperscript{19}

**Vitamin D**

While the role of vitamin D in calcium metabolism has been studied extensively, our understanding of its role in nervous system development and function is still in its infancy. However, the importance of vitamin D in healthy brain development and function has been gaining support over the past decade.

Multiple lines of evidence suggest that vitamin D is a neuroactive steroid that leads to alterations in brain neurochemistry and adult brain function.\textsuperscript{20,21} Adult deficiencies of vitamin D have been associated with a variety of adverse CNS outcomes, including Parkinson’s disease, Alzheimer’s disease, depression, and cognitive decline. Interestingly, in one case study, correction of vitamin D deficiency in a type 1 diabetic patient with severe neuropathy led to reversal of neuropathic symptoms.\textsuperscript{22}

The ability of vitamin D metabolites to regulate certain neurotrophic factors and influence inflammation has led to the suggestion that calcitriol—also known as 1,25-dihydroxycholecalciferol or 1,25-dihydroxyvitamin D$_3$—is neuroprotective.\textsuperscript{23} The proposed mechanism behind these neuroprotective effects is regulation of proteins that either decrease the levels or inhibit the toxicity of reactive oxygen species.\textsuperscript{24}

**Vitamin E**

The nervous system is highly susceptible to damage associated with oxidative stress caused by free radicals, which increases with aging and leads to nerve damage.\textsuperscript{25} Vitamin E includes a group of eight structurally-related, lipid-soluble, chain-breaking antioxidants—four tocopherols and four tocotrienols—that act as free radical scavengers. Alpha-tocopherol is the most abundant and bioavailable antioxidant form of vitamin E in human tissues, and the recommended daily allowance of alpha-tocopherol is 15 milligrams per day.\textsuperscript{26,27}

The biological relevance and neuroprotective properties of vitamin E may extend beyond its antioxidant activity. More recently, vitamin E has been shown to play critical roles in signaling, membrane fluidity, and gene regulation.\textsuperscript{25} Animal studies have shown that low alpha-tocopherol levels in the brain induce downregulation of genes involved in myelination, neuronal vesicle transport, and glial functions.\textsuperscript{28}

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\textsuperscript{21} Eyles DW, Burne THJ, McGrath JJ. Vitamin D, effects on brain development, adult brain function and the links between low levels of vitamin D and neuropsychiatric disease. Frontiers in Neuroendocrinology 2013;34:47-64.


Other Nutrients

- Vitamin A—An increasing body of evidence demonstrates that retinoid signaling plays an important role in the function of the mature brain. As such, adequate nutritional status of vitamin A—the parent compound of the retinoids—may be important for adult brain function. 29

- Vitamin K —An emerging nutrient in nervous system function, vitamin K participates in the synthesis of sphingolipids, which are present in high concentrations in brain cell membranes. In recent years, studies have linked alterations in sphingolipid metabolism to age-related cognitive decline and neurodegenerative diseases. 30

- Boron—Boron has not yet been recognized as an essential nutrient, but data from animal and human studies suggest that boron may be important for cell membrane function, mineral and hormone metabolism and enzyme reactions. 31 Even relatively short periods of restricted dietary boron intake can have a negative impact on brain function and various cognitive and psychomotor tasks. When compared to older adults with a dietary boron intake of approximately 3.25 mg/day, older adults with low dietary boron intake exhibited increased low-frequency electroencephalogram (EEG) activity, which is linked to reduced mental alertness, impaired memory and poorer performance on vigilance and psychomotor tasks. 32,33 Restrict dietary boron intake was also associated with significantly poorer performance on tasks emphasizing manual dexterity, hand-eye coordination, attention, perception, short-term memory, and long-term memory. 34

The upper intake level set by the Institute of Medicine for adults is 20 mg/day. 35 Average daily intake of boron from food sources ranges between 1.7 and 7 milligrams per day. 36 The recommended dietary allowance has not been established, but no toxicity has been identified and supplementation with up to one to three milligrams of boron per day is considered to be safe.

- Zinc —Zinc acts as a neuromodulator at excitatory synapses and plays a significant role in the stress response, as well as the function of zinc-dependent enzymes that contribute to maintaining brain compensatory capacity. Alterations in zinc homeostasis have been reported in both Parkinson’s and Alzheimer’s disease, as well as in seizures and traumatic brain injury. There is also a growing body of evidence that age-related changes to the brain—frequently associated with a decline in brain function and impaired cognitive performance—could be related to dysfunctions affecting intracellular zinc ion availability.

Zinc supplementation may be useful for preventing age-related neurodegenerative disorders, as well as for preserving overall health in the context of zinc deficiency.

which is common among the elderly. Dietary supplementation with physiological doses of zinc restores deranged immune-endocrine functions in aging and enhances resistance to infections in the elderly, but to date, the full impact of zinc supplementation on brain function is yet to be determined. What is certain is that a narrow range of zinc ions is beneficial for cell functions and high zinc ion concentrations can be toxic. As such, the effect of zinc supplementation is strictly dependent on the dose and length of treatment. Studies have shown a beneficial effect of supplementation with 15 mg/day of zinc over a period of 1–7 months, in association with other micronutrients, on the cognitive functions of elderly individuals.

- Copper—Copper deficiency has long been recognized as a cause of hematologic abnormalities. More recently, copper deficiency has been reported in association with peripheral neuropathy, myelopathy or myeloneuropathy. While copper deficiency is rare among the general population, it may be found in patients with prior gastric surgery and in the setting of excessive intake of zinc supplements.

**Supporting Nerve Health with Multi-Nutrient Supplementation**

The cells of the central and peripheral nervous system require specific nutrients in order to carry out their specialized functions, and a growing body of evidence supports the need for adequate nutritional status to prevent vitamin and mineral deficiencies that adversely affect nerve health.

Formulated by licensed physicians using evidence-based research and strict quality criteria, the Forté Elements Brain & Nerve supplement is specifically designed to support brain and nerve health. Forté Elements is the industry leader in mediceuticals, nutritional support systems that meet stringent, pharmaceutical-grade standards of manufacture and target the unique nutrient needs dictated by a particular health condition or situation.

Unlike other dietary supplements marketed for nerve health, the Forté Elements Brain & Nerve supplement has met the following criteria to be categorized as a mediceutical:

1. Formulated to support a specific health condition or situation
2. Contains only non-synthetic, pharmaceutical-grade ingredients that are Generally Recognized as Safe (GRAS)
3. Contains elements that have been validated by clinical research for the specific health condition or situation, as published in peer-reviewed journals
4. Conforms to pharmaceutical-grade dosage standards for the specific health condition or situation
5. Is produced in FDA-compliant manufacturing facilities using pharmaceutical-grade manufacturing practices
6. Is accompanied by a Certificate of Analysis confirming that product ingredients meet the mediceutical standard and are as listed on the product label

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Forté Elements Nerve Supplement

Data from the National Health and Nutrition Examination Survey show that intakes of vitamins A, C, D, E, K, and folate are low in a significant proportion of the elderly population in the U.S.44 Nutritional deficiencies among older adults may be due to a reduced capacity for self-care and nutrition or decreased nutrient absorption, metabolism, storage, and utilization, which can lead to neuropathies.

Decline in nerve function may contribute to overall morbidity and reduced quality of life. Research has shown that declines in peripheral nerve function in older adults may not solely be the consequence of the aging process, but may instead be a combination of the consequences of aging, gender, and potentially modifiable metabolic factors.5

Physical exercise seems to not only slow the loss of nerve cells in areas of the brain involved in memory, but also maintain the function of the remaining nerve cells.45 Appropriate multi-nutrient supplementation with the Forté Elements Brain & Nerve Supplement may also play a role in health nerve function and may help to preserve the compensatory capacity of the brain or prevent the onset of neuropathic or neurodegenerative diseases.

A fusion of science and practical medical experience unlike anything that has come before.