

# Mental Health

## *Not All in the Mind—Really a Matter of Cellular Biochemistry*

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**T**he adage of “the mind is a terrible thing to waste” is especially true when it comes to nutrition and its effects on mental disease. The literature has numerous studies that indicate multiple nutritional deficiencies as contributors to mental illnesses and their symptoms. From this research, we can extrapolate that fueling an individual, based on his or her biochemical needs, heightens neurologic performance.

This is an approach that differs from standard pharmaceutical prescribing, which, in most cases, downplays symptoms rather than focusing on their actual causes. Symptoms and efficient neurologic functioning are the body’s and brain’s responses to either health or illness.

Today, we know the power of thoughts. . .not just as creative, thinking beings but the power that positive thoughts have on human lives. Taking this further, a brain that may require more of a certain nutrient, or has a deficiency of several nutrients, cannot be expected to perform properly and, thus, will experience mental symptoms. What follows are a select group of “mental health” conditions that reflect just as much a state of body as they do a state of mind. The artificial division of mind from body is much the same as division of one’s nose from one’s face, or the proverbial trees from the forest.

### **Anxiety**

Anxiety is more prevalent today. A permanent fixture in many people’s lives, anxiety affects not only the mind, but also the body and day-to-day living as well. Anxiety can be defined in two different ways, the first as an apprehensive, uneasy state of mind, typically the result of anticipated events (i.e., life stressors), and the second, more clinical, terminology characterizes anxiety as an abnormal, overwhelming feeling of apprehension or fear that is punctuated by physiologic reactions such as tension, sweating, and a rapid pulse. Regardless of the definition, anxiety affects both the mind and the body to varying degrees and more people experience these feelings in their lives today.

The current prevalence of anxiety in the population (particularly Americans) is undoubtedly caused by people working longer hours while attempting to balance their relationships with family and home responsibilities. It is no wonder that more people experience stress and anxiety today than ever before. Thus, many more people are seeking treatment to relieve their suffering.

It is estimated that 19 million adults in the United States suffer from anxiety disorders, with a cost estimated to be nearly \$42 billion dollars per year. Nearly \$23 billion have been spent for repeated medical visits by patients seeking relief from symptoms caused by anxiety that appear to be physical illnesses. People with anxiety are 3–5 times more likely to see a doctor and are 6 times more likely to be hospitalized for these disorders than those without such problems.<sup>1</sup>

The economic and individual burdens of anxiety disorders are high because these conditions can be chronic and quite disabling. People with anxiety disorders utilize primary health care providers more than they use psychiatric medical personnel, exerting a large cost on the health care system itself.

These patients seek medical care more often, in part, because of increased concerns about their health and the manifestations of racing heart, insomnia, shortness of breath, and other physical presentations. Only 30 percent of individuals afflicted with anxiety disorders seek treatment for their conditions and 30 million people will experience some type of anxiety disorder at some point in their lives.<sup>2</sup>

Two B vitamins and magnesium may be helpful for addressing anxiety-related disorders.

#### *Niacin*

Nicotinamide, a form of the B vitamin niacin (vitamin B<sub>3</sub>), is known to have similar effects to benzodiazepenes on the brain.<sup>3</sup> Nicotinamide acts to stimulate the gamma-aminobutyric acid (GABA)–benzodiazepine receptor complex, an inhibitory neuron grouping, thereby exerting a calming effect by modulating these specific neurons.<sup>4</sup> Experiments designed to test the efficacy of nicotinamide and brain function revealed that GABA nerve receptors were less stimulated when nicotinamide was lacking in the test subjects and that reintroduction of nicotinamide led to a calming effect on the GABA receptors.<sup>5</sup> Supplementation with adequate amounts of nicotinamide may possibly contribute to fewer anxiety symptoms.

#### *Pyridoxine*

Pyridoxine (vitamin B<sub>6</sub>) is an important coenzyme in the biosynthesis of the neurotransmitters GABA, dopamine, and serotonin, all of which are affected in anxiety. Deficiency of pyridoxine causes an increased sympathetic discharge and hypertension in animals that has been hypothesized to reflect a decrease in production of the previously mentioned neurotransmitters. In addition, adding pyridoxine to the diets of these animals lowered

their blood pressure.<sup>6</sup> In a separate study that investigated the use of magnesium and pyridoxine on anxiety-related premenstrual syndrome (PMS) symptoms, investigators found that women who were given 200 mg of magnesium with 50 mg of pyridoxine per day experienced significant reductions in anxiety-related PMS symptoms, such as nervous tension, irritability, and generalized anxiety.<sup>7</sup>

### Magnesium

Magnesium supplementation has a broad reputation for producing a calmative effect on patients with anxiety symptoms and/or high stress levels. Decreased levels of nervousness and decreased insomnia were noted in patients who were given 200 mg of magnesium combined with 400 mg of calcium,<sup>8</sup> while another researcher noted an association between magnesium deficiency and anxiety symptoms.<sup>9</sup>

In a study investigating the use of magnesium in postsurgical patients to alleviate pain, patients were infused with magnesium both during and following surgery and were evaluated for anxiety levels. Patients who received the magnesium infusion required significantly less pain medication (morphine and fentanyl) compared to subjects in a control group who received no magnesium. The magnesium-treated group reported less anxiety as well.<sup>10</sup>

Magnesium deficiency is common in the typical American diet. One large survey determined that adequate magnesium was lacking in nearly 72 percent of diets, that 50 percent of people consume less than 75 percent of the recommended daily allowance (RDA) of magnesium, and that 30 percent of these people ate less than 50 percent of the RDA for magnesium.<sup>11</sup> People who take oral contraceptives or diuretics and who overuse laxatives may be at risk of magnesium deficiency as well.

## Bipolar Disorder

Bipolar disorder, also known as manic depression, is a condition that is punctuated by wide changes in mood, thought, energy levels, and behavior. Depression and mania can occur cyclically or episodically, and episodes of mixed mania and depression can appear as well, becoming increasingly frequent leading to disruptions in all aspects of a person's life. Affecting approximately 2.3 million adults in the United States,\* or nearly 1.2 percent of the population, ages 18 years and older in any given year,<sup>12</sup> bipolar disorder typically begins in late adolescence. The average age at onset of the first episode of mania is in the early 20s.<sup>13</sup>

Bipolar disorder is a familial disorder. Two thirds of people with bipolar disorder have one close relative with bipolar disorder or depression, proving that bipolar disorder has a genetic component.<sup>14</sup> Studies of twins have indicated that if one twin has the mood disorder, the chances of an identical twin having it are three times higher than that of a fraternal twin, and the concor-

dance rate among identical twins is 80 percent whereas it is only 16 percent for fraternal twins.<sup>15</sup> The cause of bipolar disorder is not only genetically linked however. The approach to this and other psychopathologic diseases is that multiple biologic and psychologic factors interact to create the condition.

Two B vitamins and some botanicals can be used to help mitigate symptoms of this disorder.

### Folic Acid

Folic acid (vitamin B<sub>9</sub>) is closely linked to proper brain functioning, especially regarding mania and depression. The roles of folic acid in psychiatric conditions have been relatively well-researched and many interesting conclusions can be drawn between this essential nutrient and bipolar disorder. In addition, folate levels are closely related to the pharmaceutical treatments for mania and depression, with folate levels being negatively affected.

A survey of 45 patients diagnosed with mania showed that these patients had red-blood-cell folate levels that were slightly less than 20 percent of subjects in a healthy control group.<sup>16</sup> A review of folic acid and its role in neurobiology by Young and Ghadirian revealed the following information:<sup>17</sup>

- Folic-acid deficiency is quite common among people with various psychiatric disorders.
- Absorption of folate is inhibited by anticonvulsant medications (which are used in the standard treatment of bipolar disorder).
- Patients' psychiatric symptoms are associated with folate deficiency.
- Several studies have demonstrated that folate is effective for treating psychiatric symptoms in folate-deficient patients.
- Folic-acid deficiency will lower brain levels of two chemicals (S-adenosylmethionine (SAME) and 5-hydroxytryptamine (5-HT)), which are closely involved in proper brain function. SAME is known to have antidepressant properties and will elevate levels of 5-HT in the brain, leading researchers to conclude that deficiency of folate is related to decreased levels of brain 5-HT.

### Cobalamin

Cobalamin (vitamin B<sub>12</sub>) is another well-known nutrient for which a deficiency can lead to psychiatric symptoms; this has been reported in the medical literature for several decades.<sup>18</sup> A case report and study by Evans, et al. describes the occurrence of manic psychosis that occurred in patients. Although there were no apparent hematologic manifestations of vitamin B<sub>12</sub> deficiency, there were changes in the patients' electroencephalograms along with other organic mental changes.<sup>19</sup> The authors of this study performed a review of the literature, citing the causal link between vitamin B<sub>12</sub> deficiency and brain dysfunction, leading the scientists to suggest that the manifestation of psychiatric symptoms may occur prior to other standard manifestations (macrocytic anemia and spinal-cord disease) and that all patients with neuropsychiatric diseases should be screened for vitamin B<sub>12</sub> deficiency.

### Botanical Medicines

Lavender (*Lavendula officinalis*) has mild relaxant effects and is used traditionally for addressing restlessness, insomnia, depres-

\*Narrow WE. One-year prevalence of depressive disorders among adults 18 and over in the U.S.: NIMH ECA prospective data. Population estimates based on U.S. Census estimated residential population age 18 and over on July 1, 1998. Unpublished table.

sion, and nervousness. Lavender preparations are commonly derived from the plant oil; internal ingestion is contraindicated. When inhaled, the constituents of lavender oil lead to relaxation and decreased alertness.<sup>20</sup> Inhalation of lavender-oil scents may modulate feelings of anxiety in patients with mania.

Lemon balm (*Melissa officinalis*) is another botanical medicine with mild calming effects and the ability to reduce alertness,<sup>21</sup> which is useful for treating nervous anxiety as well as other nonrelated medical problems. Brain function is directly affected (terpenes are thought to act on some of the inhibitory neurons [GABA] in the brain, thereby eliciting their calmative effects).<sup>22</sup> A study utilizing both valerian (*Valeriana officinalis*) and lemon balm produced improvements in the amounts and quality of sleep in subjects who took this herbal combination.<sup>23</sup>

## Depression

Approximately 19 million American adults suffer from clinical depression; this number is equivalent to nearly 9.5 percent of the adult population with depression in a given year.<sup>24</sup> Almost twice as many women (12 percent) as men (6.6 percent) are affected by depressive disorders each year. These numbers are equivalent to 12.4 million women and 6.4 million men in the United States.\* Depressive disorder (which includes major depressive disorder, dysthymic disorder, and bipolar disorder) accounts for three of the leading causes of disability in the United States and other developed nations (major depressive disorder ranks as number 1). Many people who suffer from depressive disorders suffer from other disorders as well,<sup>25</sup> including anxiety.

Major depressive disorder can develop at almost any age. However, it occurs most commonly in a person's mid-20s while dysthymic disorder often begins in childhood, adolescence, or early adulthood.<sup>13</sup> Depressive disorder is a mental illness that involves the mind as well as the body. The disorder disrupts the way patients sleep and eat and how they perceive the world and themselves.

## 5-HTP

5-Hydroxytryptophan (5-HTP) is a precursor substance to the neurotransmitter serotonin. 5-HTP is related to the amino acid L-tryptophan, which is converted in the body into 5-HTP. 5-HTP is able to cross into the brain and augment supplies of serotonin and, because of this, acts as an effective treatment for depression. Insufficient activity of serotonin (including other neurotransmitters) is a key element in the currently accepted view of neurobiologists regarding the pathogenesis of depression.

One review article of the various precursor treatments for depression noted that such therapies hold a therapeutic value in treating depression and that more research is needed to confirm additional efficacy.<sup>26</sup>

Another review article noted that the efficacy of 5-HTP was "high" for treating disorders such as depression, binge eating, and insomnia.<sup>27</sup> Used as a nutritional food supplement, 5-HTP is a beneficial adjunctive treatment for patients with depression.

Although the greatest task in medicine is identifying and removing the cause of disease, (which, in most cases of depression is inadequate activity/supply of serotonin), this nutrient can act as a bridge to bolster a patient's neurochemistry while other nutritional treatments can be used that may, in principle, restore brain neurotransmitter functioning. As a patient's symptoms decrease, tapering supplemental 5-HTP down will allow the patient to continue functioning normally.

## Vitamin C

Vitamin C, or ascorbic acid, is a nutrient that seems to always capture attention no matter what investigational study it undergoes. In a review of the clinical effects of ascorbic-acid deficiency in people, Hodges et al. noted that depression is one of the first symptoms of scurvy in humans who were experimentally subjected to deficient vitamin C diets.<sup>28</sup>

Indeed, scurvy is relatively rare in modern life. However, diets containing low amounts of vitamin C are not, especially with increasing processed-food diets on the rise.

### Condition–Nutrient Cross-Reference Chart

	Anxiety	Bipolar	Depression	ADD/ADHD	Schizophrenia
Ascorbate (vitamin C)			1000–2000 mg		
Pyridoxine (vitamin B <sub>6</sub> )	200 mg				
Cobalamin (vitamin B <sub>12</sub> )		1000 mg			
Magnesium	400 mg				
Niacin (vitamin B <sub>3</sub> )	300 mg				
Folate (vitamin B <sub>9</sub> )		1000 mg			
5-Hydroxytryptophan			150–300 mg		
Hypericum (from St. John's wort; <i>Hypericum perforatum</i> )			300 mg		
Lavender ( <i>Lavendula officinalis</i> )		Inhale essential oil			
Lemon balm ( <i>Melissa officinalis</i> )		80–100 mg			
Zinc				5 mg	
Phosphatidyl serine				300 mg	
Essential fatty acids				2000 mg	2000–3000 mg

## Dosing Recommendations

Nutrient	Dosing
Pyridoxine (vitamin B <sub>6</sub> )	50–100 mg per day, in divided doses
Cobalamin (vitamin B <sub>12</sub> )	1000 mg per day, in divided doses
Magnesium	400 mg per day, in divided doses
Folate (vitamin B <sub>9</sub> )	1000 mg per day
Ascorbate (vitamin C)	1000–2000 mg per day, in divided doses
Nicotinamide (vitamin B <sub>3</sub> )	1000 mg per day, 2 times per day
5-Hydroxytryptophan	150–300 mg per day
Phosphatidyl serine	300 mg per day
Zinc	5 mg per day
Fatty acids	3–4 g per day (eicosapentaenoic acid/dehydroepiandrosterone in ratio of 180:120 mg, respectively)
Lavender ( <i>Lavendula officinalis</i> )	Essential oil, inhaled scent 3 times per day
Lemon balm ( <i>Melissa officinalis</i> )	80–100 mg, 3 times per day
Hypericum	300 mg, 3 times per day (standardized to 0.3% hypericin or 5% hyperforin content)

Additional studies on vitamin C and scurvy revealed an interesting link between psychiatric patients and vitamin C levels. A study on psychiatric patients (some of whom had bipolar depression) revealed that many of these individuals were in a state of low vitamin C saturation, or “subacute” scurvy.<sup>29</sup> This and another study involving a similar population of psychiatric patients also demonstrated decreased vitamin C loads, or borderline scurvy, without the patients actually manifesting the symptoms of this disease.<sup>30</sup>

### *St. John's Wort*

One of the most investigated botanical medicines from a phytochemical aspect, St. John's wort (*Hypericum perforatum*) is a viable alternative to standard pharmacotherapy for depression. A literature review of the effects of St. John's wort reveals the efficacy of this herbal medicine in affecting several biochemical pathways that play a central role in depression and its pathogenesis, including the monoamine oxidase, serotonin, GABA, and dopamine neurotransmitter systems.<sup>31</sup>

The extracts of this plant have been intensely studied for the last decade and are now considered viable medicine for depression. A review of the mechanisms of action(s) of *Hypericum's* constituents include the ability to bind to GABA receptors, downregulate beta-adrenergic receptors, and upregulate serotonin 5-HT(2) receptors. These effects lead to positive changes in neurotransmitter concentrations in areas of the brain that are implicated in depression.<sup>32</sup>

## Attention Deficit Disorder/Attention Deficit Hyperactivity Disorder

Attention deficit disorder/attention deficit hyperactivity disorder (ADD/ADHD) is one of the most common mental disorders among children today. Three (3)–5 percent of all children (2–3 times as many boys are affected than girls) or nearly 2 million American children have ADD/ADHD according to the National Institute of Mental Health.<sup>33</sup> This statistic correlates to one child in each classroom in the United States having the disorder.

No solitary causative factor has been identified as responsible for the different behavior patterns observed in ADD/ADHD. The disorder is only diagnosed by observing certain characteristic behavior patterns over time; no other clear physical signs can be seen.

A recent report issued by the Centers for Disease Control and Prevention noted that nearly 1.6 million elementary school-age children have a diagnosis of ADD/ADHD and a national survey revealed that the parents of 7 percent of children ages 6–11 years old were told by health care professionals that their children had ADD/ADHD.<sup>34</sup> The report also included the following demographic information:

- Boys are nearly three times as likely to have ADD/ADHD than girls.
- White children were twice as likely than Hispanic and Black children to have a diagnosis of ADHD
- While children with health insurance were diagnosed with ADD/ADHD more often than children without health insurance, and children with ADD/ADHD use more health care services including mental health services than those without ADD/ADHD.

Two key nutrients can be used to address ADD/ADHD.

### *Phosphatidylserine*

Phosphatidylserine is a biologic phospholipid molecule. Phospholipids are one of the main components of cellular membranes in the human body that stabilize the other constituents of which cellular membranes are comprised. Phosphatidylserine is the main phospholipid of human brain cells and regulates cellular functions, such as controlling the internal environment of the cell, communication between cells, signal transduction, release of secretory vesicles, and regulation of cell growth and division.<sup>35</sup>

Phosphatidylserine is beneficial for several different brain functions, not including its contribution to nerve-cell synaptic membranes, a key anatomic aspect of nerve-signal production and transmission. As a supplement, this nutrient's benefits

include increased neurologic energy via facilitated synaptic communication and increased production, release, and effectiveness of the neurotransmitter dopamine.<sup>36</sup>

One study that investigated using phosphatidylserine supplementation to treat patients with ADD/ADHD resulted in a slightly greater than 90-percent improvement in these cases, with doses of 200–300 mg per day, for up to 4 months, providing the greatest resolution of symptoms.<sup>37</sup> Supplemental administration of phosphatidylserine is thought to normalize brain-lipid content, thereby assisting the return of normalized function of neuronal cells.<sup>38</sup>

### Zinc

A collection of studies has revealed that this mineral is low in people with ADD/ADHD<sup>39</sup> and that lower serum zinc levels were found in children with ADD/ADHD compared to children without the disorder.<sup>40</sup> A relationship exists between levels of free fatty acids in the blood and zinc in children with ADD/ADHD. These children, compared to controls without ADD/ADHD, were found to have low blood levels of zinc and free fatty acids.<sup>41</sup>

These results indicate that a deficiency of zinc may contribute to the development of ADD/ADHD; one study hypothesized that the low levels of free fatty acids may be a result of the decreased zinc levels.

Another interesting study revealed a relationship between the responsiveness to standard stimulant pharmacotherapy and zinc levels in the body: Low zinc levels equated to poor responses to the medication.<sup>42</sup> Zinc is a cofactor in neurotransmitter synthesis and affects dopamine metabolism indirectly. Dopamine is a neurotransmitter that is believed to be involved in ADD/ADHD (low levels of dopamine are associated with ADD/ADHD and dopamine supplementation has alleviated some ADD/ADHD symptoms.)<sup>43</sup>

## Schizophrenia

A chronic, severe, and disabling condition of the brain, schizophrenia is marked by symptoms, such as hearing internal voices and believing that other people may be reading one's mind, controlling one's thoughts, or plotting against one. This is terrifying to the person experiencing the disease. People with schizophrenia are fearful and withdrawn and their speech and behavior often appear to be disorganized and incomprehensible. Often, the first signs of schizophrenia emerge as troubling changes in behavior.

This disorder is one of the most common mental illnesses. One estimate is that 1 of every 100 people is affected by schizophrenia, a statistic that equates to 1 percent of the population.<sup>44</sup> It is estimated that more than 2 million Americans suffer from this illness in a given year. Found throughout the world, schizophrenia affects men and women equally. Schizophrenia seems to appear earlier in men than women (men usually develop signs in their early 20s whereas women develop signs in their late 20s to early 30s). It has been estimated that the cost of schizophrenia to society approached \$32.5 billion dollars per year in the United States alone in a given year.<sup>44</sup>

Fatty acids may be helpful for mitigating the effects of this devastating illness.

### Fatty Acids

Much evidence is indicative of the role of disordered membrane phospholipid metabolism in schizophrenia. A relatively new theory of schizophrenia describes a disorder of membrane phospholipid metabolism that is associated with an increased loss of polyunsaturated fatty acids (PUFAs) from the cellular membrane via enhanced activity of phospholipase A2.<sup>45</sup> Membrane changes that occur from this process may have adverse effects on the brain, where sequential coordination of millions of neurons are dependent on cohesive functioning on the cellular membrane.

Additional evidence of the fatty-acid link to schizophrenia includes the theory of abnormal brain turnover of phospholipids, detected by magnetic resonance imaging, and reduced cellular membrane levels of omega 3- and omega-6 polyunsaturated fatty acids. In addition, four of five trials using eicosapentaenoic acid (EPA) to treat schizophrenia yielded positive results.<sup>46</sup>

Increased phospholipid breakdown and decreased levels of PUFAs, especially arachidonic acid (AA) have been demonstrated throughout the literature.<sup>47</sup> Researchers are currently delving into the various physiologic functions of membrane phospholipids and PUFAs and their roles in schizophrenia. Most of this research hints at altered cellular signaling and how it relates to neurobiologic manifestations of schizophrenia and therapeutics.

Giving patients who have schizophrenia a mixture of PUFAs (a ratio of 180:120 mg of EPA/dehydroepiandrosterone respectively) and antioxidant vitamins (a ration of 400 IU:500 mg of vitamins E and C, respectively) two times per day for 4 months, produced significant reductions in psychopathology based on the outcome scores of several psychiatric rating scales.<sup>48</sup> In a comprehensive review of the scientific databases containing descriptions of clinical trials utilizing PUFAs to treat schizophrenia symptoms, it was determined that using PUFAs to treat the disorder produced favorable results in these patients, with few side-effects, if any.<sup>49</sup>

## Conclusions

Nutritional deficiencies can play roles in mental illness and addressing such disorders or their symptoms can be helpful for patients who seek relief. More research will reveal more about the mind-body link in these disorders. □

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