Treatment of Nutritional and Metabolic Disorders in Psychiatry: Integrative or Integrated?

This article highlights evidence-based treatment with herbs and nutrients with good tolerability and potential benefit when integrated into psychiatric practices.

After decades of mind/brain-focused subspecialization, psychiatry is now reconsidering the whole person. “Integrative medicine” is being used to denote the strategic combining of standard treatments (eg, medication, psychotherapies) with evidence-based complementary and alternative approaches (eg, herbs, nutrients, acupuncture, neuro-therapy). “Integrated medicine” refers to the practice of using a multidisciplinary treatment team (physicians, psychologists, social workers, and occupational and physical therapists). The goals of both integrative and integrated care are to address the biological, psychological, and social needs of the patient.

This article highlights evidence-based treatment with herbs and nutrients with good tolerability and potential benefit when integrated into psychiatric practices. The other two articles in this Special Report are intended to refresh and update your knowledge of nutritional and metabolic disorders commonly encountered in psychiatric patients. Psychiatrists can diagnose conditions such as vitamin deficiencies, nutrient deficiencies, hypothyroidism, and obesity, and they can treat or refer patients with these ailments. Sarris and colleagues have proposed that integrative mental health (a subdivision of integrative medicine) encompass mainstream mental health treatments, evidence-based complementary and alternative approaches, healthy lifestyle changes, and socio-cultural issues. The evolving concept of integrative mental health appears to encompass the goals and practices of integrated medicine. Modern medicine is probing the biological bases of nutritional supplements and herbs to understand their therapeutic actions. Identifying active constituents and improving extraction processes will allow further development of natural combinations and synthetic analogues and consequently will expand treatment options.

**Nutrients**

*B vitamins, folate, S-adenosylmethionine.* Depression and nonresponse to antidepressant medication have been associated with B vitamin and folate deficiencies. Patients with a history of substance abuse, poor diet, chronic illness, and age-related decline are at greater risk for vitamin B and folate deficiencies. Methylation, the transfer of methyl groups, is essential for production of key cellular components such as proteins, phospholipids, and neurotransmitters. S-adenosylmethionine (SAMe) is the body’s most active methyl donor: folate and vitamin B12 are essential cofactors in the
methylation cycle. Antidepressant augmentation with folic acid or folinic acid was shown to significantly improve scores on the Hamilton Depression Rating Scale.2

SAMe has been found to be more effective than placebo and as effective as standard antidepressants for treating depression. Compared with prescription antidepressants, SAMe has fewer adverse effects (e.g., no weight gain or sexual dysfunction) and a faster onset of action, and as an adjunct, SAMe increases response to antidepressants.

SAMe deficiency occurs often in patients with Parkinson disease, particularly in those treated with L-dopa, which depletes SAMe and leads to treatment-resistant depression. In such cases, high doses of SAME effectively alleviate depression and, in many cases, improve parkinsonian symptoms. **Omega-3 fatty acids.** In addition to maintaining neuronal cell membrane fluidity, omega-3 fatty acids modulate neurotransmitter signaling, calcium ion influx, and secretion of cytokines. Modern dietary habits may be the cause of omega-3 fatty acid insufficiency. Some findings suggest that omega-3 fatty acids (eicosapentaenoic acid and docosahexaenoic acid) may be beneficial in unipolar and bipolar depression.3

The evidence is different for MDD. Significant methodological problems and publication bias were found in 13 randomized controlled trials reviewed in a meta-analysis.4 Although the proportions of omega-6 fatty acids and omega-3 fatty acids in cell membranes may contribute to the development of depression, the evidence that omega-3 fatty acids contribute significantly to the treatment of MDD is weak.

In perinatal depression, omega-3 fatty acid supplementation is especially effective in improving mood, replenishing depleted fatty acid stores, and supporting neonatal and postnatal brain development. An initial randomized controlled study of children aged 6 to 12 years with ADHD found that omega-3 fatty acids were safe and effective.5

N-acetylcysteine, inositol, minerals. N-acetylcysteine, a precursor to the major antioxidant glutathione, was found to augment mood stabilizers in patients with bipolar disorder.6 In a double-blind, randomized, placebo-controlled study of 140 patients with chronic schizophrenia, N-acetylcysteine reduced akathisia and negative symptoms on the Positive and Negative Syndrome Scale.7 Modulation of glutamate may contribute to the demonstrated benefits of N-acetylcysteine in depression, panic disorder, obsessive-compulsive disorder (OCD), bipolar depression, and trichotillomania.

Preliminary randomized clinical trials suggest that inositol, a phospholipid precursor, may be a useful adjunctive treatment for bipolar disorder and panic disorder, as well as for depression, OCD, bulimia nervosa, and binge eating disorder, although the evidence for the last 4 is limited.8-11 In persons with zinc, iron, or copper insufficiency, supplementation may be helpful in treating depression as well as hyperactivity and impulsiveness in ADHD.

**Phytomedicinal herbs**

Concerns about potential herb-drug interactions prevent many physicians from integrating plant extracts into psychiatric practice. However, most of the herbs that are useful in psychiatric patients have very few, if any, significant adverse effects.

Adaptogens are herbs whose roots, leaves, petals, stamen, and/or berries contain biologically active constituents that when extracted enhance the ability of organisms to resist numerous kinds of stressors—including physical activity, psychological stress, toxic exposures, excess heat or cold, infections, inflammation, hormonal changes, and malignancies. To qualify as an adaptogen, the extracts must be low in adverse effects and well tolerated by most people. More recently, these plant extracts are being redefined as metabolic regulators.

Arctic root, rose root, golden root (Rhodiola rosea). This ancient medicinal herb produces over a hundred bioactive compounds in its roots that act as antioxidants, antimicrobials, mitochondrial energy enhancers, antidepressants, selective estrogen receptor modulators, and more. Extensive research has shown that high-grade extracts can improve cellular repair and physical and intellectual performance, particularly under stress. Evidence supports the role of adaptogens in neuroendocrine regulation of the hypothalamic-pituitary-adrenal axis and in gene expression of key mediators of stress-induced signal transduction pathways, such as neuropeptide Y, nitric oxide, membrane-bound G protein signaling pathways, stress-activated protein kinase, and molecular chaperones such as heat shock protein.70 In addition, R. rosea reduced extrapyramidal adverse effects of neuroleptics. Siberian ginseng (Eleutherococcus senticosus or Acanthopanax senticosus). E. senticosus, which grows in northern China and Siberia, improves fatigue, sleep, stamina, mood, and cognitive function with very few adverse effects. One study showed it augmented lithium, reduced conversion to mania, and increased remission rates after 6 weeks.13 Schisandra chinensis. Extracts from Schisandra roots and seeds are used to reduce stress, fatigue,
bipolar depression, tension, anxiety, and weakness. *Schisandra* is also useful in reducing the adverse effects of other medications, such as antidepressants and antipsychotics. Adaptogen combinations such as ADAPT, with *R. rosea*, *E. senticosus*, and *S. chinensis*, exert synergistic therapeutic effects. *Korean ginseng* or *Asian ginseng* (*Panax ginseng*). *P. ginseng* extracts increase blood flow, abstract thinking, reaction time, accuracy, and working memory at daily doses of 300 to 800 mg. However, methodological limitations have been found in studies of ginseng. Moreover, anxiety, insomnia, tachycardia, GI symptoms, headache, and reduced platelet aggregation have been reported with the use of ginseng.

*St John’s wort*. High-quality St John’s wort extracts have been demonstrated to be effective in the treatment of mild to moderate depression and somatoform disorder, with possible benefits in seasonal affective disorder. However, St John’s wort has also been shown to induce cytochrome P-450 3A4, 2C9, and 1A2 isozymes and P-glycoproteins in humans. It can affect serum levels of many medications, including immune suppressants used to prevent organ rejection in transplant patients, digoxin, warfarin, oral contraceptives, theophylline, and protease inhibitors. In addition, St John’s wort can cause phototoxicity, mania in bipolar patients, and serotonin syndrome, particularly in combination with prescription antidepressants. Therefore, it is incumbent on the physician to be knowledgeable about brand quality, inquire about the use of St John’s wort, check for potential herb-drug interactions, and inform the patient of potential risks.

**Conclusion**

Nutritional supplements, particularly the use of daily vitamins has become routine practice. Complementary and alternative medicine approaches, such as hypnosis and acupuncture have gradually gained acceptance in mainstream medical practice. Thousands of articles are published each year on complementary, alternative, and integrative treatments. Rather than being left behind, physicians can safely integrate these valuable treatments into their clinical work by identifying the most effective and best-documented treatments and by learning how to minimize the risks of adverse reactions.

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**References:**


