

# Anxiety, Stress, and Depression- a Supplement Approach

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Anxiety and depression may arise from imbalances in neurotransmitters, such as serotonin, norepinephrine, dopamine, GABA, and glutamate. Just as many prescription drugs are hypothesized to treat anxiety or depression by restoring balance at a neurotransmitter level, certain supplements may do the same. The amino acids tryptophan and 5-HTP are precursors to serotonin, which in turn is a precursor to melatonin; the amino acids phenylalanine and tyrosine are precursors to dopamine, which in turn is a precursor to norepinephrine. Thus, "targeted amino acid therapy" with one or more of the above supplements may alleviate the symptoms of depression and/or anxiety in some individuals. The amino acid taurine is a precursor to GABA, an inhibitory neurotransmitter. The amino acid theanine is an antagonist to glutamate, an excitatory neurotransmitter. One or both of these supplements may be beneficial in the treatment of anxiety and/or depression. Norm Shealy, MD, PhD, a pioneer in holistic medicine, founder of the American Holistic Medical Association in 1978, and author of many books, including *Ninety Days to Stress Free Living*, reports that he has identified taurine deficiency in 88% of his patients with depression.

There is no certain way of determining in advance whether a given individual might benefit from 5-HTP, tyrosine, taurine, theanine, or a combination of these supplements. Questionnaires such as included in the bestseller, *The UltraMind Solution* by Mark Hyman, MD (2008) may help to guide treatment. Some practitioners find measurement of urine neurotransmitter levels helpful as a guide to prescribing treatment – this test is readily available, but the several hundred dollar cost may not be covered by health insurance. I personally am skeptical of the value of this diagnostic test. An alternative dietary supplement approach to targeted amino acid therapy is to take a supplement which contains multiple amino acids in one supplement – these broad spectrum amino acid supplements are referred to as 'free form amino acids,' and anecdotally, some individuals with anxiety and/or depression experience symptom relief when they take such a supplement. Several companies market free form amino acid supplements.

The biochemical pathway by which 5-HTP is converted to serotonin and by which tyrosine is converted to dopamine require vitamins and minerals (scientifically referred to as coenzymes) to facilitate the enzymatic reactions – vitamins B6, B12, and folate as well as the minerals magnesium and zinc are cofactors in these biochemical pathways. Thus, supplementation with these vitamins and minerals may be beneficial in some individuals with anxiety or depression. In a given individual, a genetic variation labeled a genetic polymorphism might interfere with conversion of vitamin B6, B12, or folate into the active form that is used in the body. Genetic testing for these polymorphisms (other than for folate) is not yet widely available, is not covered by insurance, and is expensive. An empiric approach to treatment may involve the administration of activated forms of these vitamins as a supplement. Methylfolate or 5-methyltetrahydrofolate, methylcobalamin, and pyridoxal 5'-phosphate are the activated forms of folate, vitamin B12, and vitamin B6 respectively. There are several supplements on the market which contain the activated forms of vitamin B6, vitamin B12, and folate in a single pill.

Stress may arise primarily from an underlying imbalance in neurotransmitters, or it may arise from environmental factors (a stressful home life, financial difficulties, loss of a job, inadequate sleep). The

effects of stress on the body are mediated by the hypothalamus in the brain; stress is often correlated with an imbalance in functioning of the adrenal gland. In many individuals the condition labeled in holistic medicine as 'adrenal fatigue' is a consequence of stress rather than a cause; it nonetheless may require treatment. Adaptogens by definition are herbs which balance adrenal function. *Rhodiola rosea* is one of the best studied herbs for anxiety and depression. Additional adaptogens include *Cordyceps*, *Panax ginseng*, *Eleutherococcus*, and licorice, as well as a variety of other Ayurvedic herbs and Traditional Chinese Medicine herbs. Many supplements contain a combination of adaptogens. When stress arises from environmental factors, a variety of mind-body approaches that are outside of the scope of this narrative may also be beneficial.

Anxiety, stress, and depression are often associated with inflammation and immune system imbalance. Researchers are uncertain whether the inflammation and immune system dysfunction are precursors to these conditions or a consequence. Either way, some individuals with anxiety, stress, and depression feel better when taking supplemental fish oil. Fish oil contains EPA and DHA (omega 3 fatty acids). EPA is an immediate biochemical precursor to anti-inflammatory substances in the body named prostaglandins and leukotrienes. Flax contains ALA, an omega 3 fatty acid which is a biochemical precursor to EPA and DHA. Thus flax is also anti-inflammatory. However, the efficiency of the biochemical conversion of ALA to EPA and then to DHA is poor – published reports indicate that on average, less than 20% of ALA is converted to EPA, and as little as 5% of ALA is converted to DHA. Fish oil and flax (oil and meal) readily oxidize (turn rancid) – it is advisable to prepare flax meal daily by grinding flax seed, rather than purchasing flax meal, and to store open fish oil containers in the refrigerator. Some experts recommend against the use of flax oil based on a concern that even if packaged in a dark bottle and refrigerated upon opening, the oil may turn rancid very quickly.

Vitamin D has anti-inflammatory and immune balancing actions in the body. Vitamin D is not truly a vitamin; humans synthesize vitamin D in the skin from cholesterol when exposed to ultraviolet B sunlight. Note that SPF 15 sunscreen blocks approximately 97% of the conversion of cholesterol to vitamin D, and the rotation of the earth around the sun is such that in the northern half of the United States, no UV-B rays of sunlight penetrate the ozone in the upper atmosphere between mid October and mid April. Vitamin D status can be estimated by a blood test, a 25-hydroxy vitamin D level, which is a standard test in conventional medicine. This approximately \$60 test may or may not be covered by health insurance. A 25 hydroxy vitamin D level above 30 ng/ml (75 nmol/L) is considered a normal level.

However, some individuals with anxiety and depression subjectively report a dramatic improvement in symptoms only when a vitamin D level > 50 ng/ml is achieved. The hypothesis to explain this observation is that these individuals may have a genetic polymorphism of the vitamin D receptor, such that vitamin D does not bind well to the receptor, and that this poor binding is overcome by achieving higher levels of vitamin D. BEWARE that vitamin D is a fat soluble vitamin (as are vitamins A, E, and K), and too much is toxic. As a general rule of thumb, an individual will not experience toxicity unless the 25 hydroxy vitamin D level is > 100 ng/ml.