5-HTP (5-Hydroxytryptophan) vs. Prozac (SSRIs)
by Ward Dean, MD, James South, MA, and Jim English

Neurotransmitters are specialized biochemicals that nerve cells use to talk to each other. Serotonin is one of some ten major brain neurotransmitters. Deficiencies of serotonin in the brain have been linked to a number of disparate conditions, including: depression (especially the agitated, anxious, irritable type), (1-6) anxiety, (7) suicide, (8) alcoholism, (9) violent behavior, (8) PMS, (10) obesity, (10,11) compulsive gambling, (12) insomnia, (13) carbohydrate craving, (10) SAD (seasonal affective disorder), (10) and migraine headaches. (14)

Serotonin nerve circuits promote feelings of well-being, calmness, personal security, relaxation, confidence and concentration. (15) Serotonin circuits also help counterbalance the tendency of two other major neurotransmitters in the brain -- dopamine and noradrenaline -- to encourage overarousal, fear, anger, tension, aggression, violence, obsessive-compulsive actions, overeating, anxiety and sleep disturbances. (15) Many people suffer from various degrees of brain serotonin deficiency, leading to a host of mental, emotional and behavioral problems. To understand why brain serotonin deficiency is becoming more common in modern society, it is necessary to look at how the brain makes serotonin.

Serotonin Function
Serotonin (5HT), dopamine, and noradrenaline are the three main monoamine neurotransmitters -- mono because each one is made from a single, specific amino acid. Serotonin is made from tryptophan, while dopamine and noradrenaline are made from tyrosine and phenylalanine. Since the blood-brain barrier prevents serotonin from being imported from outside the brain, all serotonin used by our brain cells must be made within the neurons. Normally the blood-brain barrier serves as a protective device to prevent toxins from entering the brain. But this protection comes at a price -- even friendly molecules, such as amino acids needed by the brain, are limited by this barrier.

When nutrients are allowed to cross the blood-brain barrier they must be ferried by specialized transport molecules, much as passengers being transported on a bus. This process creates a special bottleneck for serotonin. Serotonin itself cannot pass through the blood-brain barrier, while its precursor, tryptophan, must share its transport bus with five other amino acids -- leucine, isoleucine, valine, tyrosine and phenylalanine.

In any normal diet, animal protein-based or vegetarian, tryptophan is the least plentiful of all 20 food amino acids. Thus, tryptophan is typically outnumbered as much as 9:1 in its competition to secure its transport through the blood-brain barrier into the brain. Eating a high-protein diet in an attempt to increase dietary tryptophan (a typical diet provides only 1-1.5 grams/day) only increases its competition even more. Ironically, the only dietary strategy that increases brain tryptophan supply is a high-carbohydrate, low-protein diet. When large amounts of carbohydrates are eaten, the body secretes large amounts of the hormone insulin to lower the resulting high blood sugar. In addition to lowering blood sugar levels, insulin also clears most of the five amino acids that compete with tryptophan for a ride to the brain. The result is that tryptophan has the bus to itself, allowing plenty of tryptophan to reach the brain. (10)

Carbohydrates for Stress

This dietary strategy is instinctively known and practiced by many Americans who eat large amounts of carbohydrates, including candy, cake, pie, bread, chips, ice cream, etc., when they are feeling stressed, depressed or anxious. The resulting increase in brain serotonin levels suppresses arousal and anxiety, and promotes a (temporary) sense of well-being and security. Unfortunately, this strategy comes at a high price. The same insulin which enhances brain serotonin levels also increases the conversion of the fats, carbohydrates and amino acids cleared from the blood into stored body fat! Hence the carbohydrate addiction/ obesity/serotonin connection. (10)

Tryptophan vs. 5-HTP

In the 1970s, the American health food industry began to provide an alternative method of getting more tryptophan to the brain -- tryptophan supplements. Many people found that 500 to 3,000 mg of supplementary tryptophan daily provided practical relief from depression, PMS, insomnia and obsessive-compulsive disorders. In 1989, the FDA removed tryptophan from the American health food market due to a mysterious outbreak of a rare but serious ailment -- eosinophilia myalgia (EMS). This EMS epidemic was later traced to a single batch of contaminated tryptophan from a Japanese producer. Thirteen years later, although tryptophan has been proven to be safe (and is currently available in baby food formulas, intravenous feeding solutions, and veterinary products) the FDA still shows no signs of allowing tryptophan back onto the market as a dietary supplement.

Fortunately, a safe, natural and effective alternative to tryptophan has been researched for over 30 years. This substance is L-5-Hydroxytryptophan (5-HTP). 5-HTP is not produced by bacterial fermentation (as was the tainted tryptophan) nor chemical synthesis, but is extracted from the seeds of the Griffonia plant.

Tryptophan to Serotonin Conversion

When neurons convert tryptophan into serotonin, they must first use a vitamin B3-dependent enzyme to convert tryptophan into 5-HTP. A vitamin B6-dependent enzyme is then used to convert 5-HTP into serotonin. One researcher noted, There are several advantages of considering L-5-HTP, as opposed to L-tryptophan, as being the major determinant in elevating brain serotonin levels: L-5-HTP is not degraded by tryptophan pyrrolase to kynurenine, the major pathway for peripheral degradation of L-tryptophan (about 98 percent). Furthermore, L-5-HTP easily crosses the blood-brain barrier ... (1) Additionally, it should be noted that 5-HTP is not incorporated into proteins, as is tryptophan; nor is 5-HTP used to make vitamin B3, as is tryptophan. Thus, in comparison to tryptophan, 5-HTP is virtually a guided missile that is directly targeted to increasing brain serotonin levels. Strikingly, some studies have shown better results using 200 to 300 mg of 5-HTP per day as an antidepressant than other studies using 2000 to 3,000 mg or more of tryptophan per day.
(17)

A placebo-controlled, double-blind study reported in 1992 found excellent results treating obesity using doses of 5-HTP as high as 900 mg daily, with minimal side effects (the greatest side effect being diarrhea or upset stomach)! (11) In one study, the antidepressant effects of 5-HTP was compared with fluvoxamine, a prescription Prozac-like drug used in Europe (Fig. 1).

The 5-HTP patients showed slightly better treatment response than the fluvoxamine group, yet had significantly fewer and less severe side effects. The researchers note: Regarding tolerance and safety, however, oxitriptan [5-HTP] proved superior to fluvoxamine as was apparent from a marked difference in severity of untoward side effects between the two compounds. The study presented here ...strongly confirm[s] the efficacy of 5-HTP as an antidepressant. (4)

Prozac

In a society that has made the book Listening to Prozac a mega-bestseller, some may still consider serotonin-selective re-uptake inhibitor (SSRI) drugs such as Prozac the gold standard of managing the serotonin-deficiency syndrome, even though the Poeldinger study showed 5-HTP to be superior to a major SSRI, fluvoxamine. A study reported by Risch and Nemeroff demonstrates, however, that even those successfully treated with SSRIs (ignoring their frequent and sometimes serious side effects) are dependent upon their brains' producing adequate serotonin from either tryptophan or 5-HTP. SSRIs work by conserving existing brain serotonin supplies by keeping more serotonin in the synaptic gap between neurons. They achieve this through preventing enzymatic degradation of synaptic serotonin (Fig. 2). SSRIs do not enhance serotonin production. Risch and Nemeroff state: ...depressed patients were treated with low-tryptophan diets that were supplemented with high doses of neutral amino acids [which compete with tryptophan for transport through the blood-brain barrier]... Remitted depressed subjects receiving serotonergic antidepressants (e.g. fluoxetine [Prozac], fluvoxamine) who were challenged with low-tryptophan diet supplemented with neutral amino acids promptly relapsed into severe clinical depression. When the tryptophan supplementation was provided, the patients promptly recovered... (3)

The many successful published studies using 5-HTP show that 5-HTP, by naturally elevating brain serotonin, can alleviate the serotonin-deficiency syndrome without any help from SSRI drugs. Yet the study related by Risch and Nemeroff eloquently shows that the success of SSRI drugs is crucially dependent upon the brain producing adequate serotonin (from either tryptophan or 5-HTP), and that brain serotonin production is the controlling or rate-limiting variable underlying the apparent success of SSRIs. It appears that the more logical and economically sound choice to alleviate conditions that result from the serotonin deficiency syndrome is 5-HTP, the serotonin precursor of the deficient substance.