

Benefiting Brain Chemistry with L-Tryptophan

The promise of benefiting brain and behavior with dietary alterations has intrigued clinicians and researchers for decades. In particular, evidence supporting the effectiveness of amino acid supplementation with L-tryptophan (TRP) for behavioral conditions like aggression and obsessive-compulsive disorder is mounting.

TRP is an essential amino acid and the precursor to the neurotransmitter serotonin. Although the liver metabolizes over ninety percent of plasma TRP, a certain amount leaves the liver and enters the brain. There, tryptophan hydroxylase converts TRP to 5-hydroxytryptophan (5-HTP), which 5-hydroxytryptophan decarboxylase turns to 5-hydroxytryptamine (5-HT), or serotonin.

Researchers began intensively focusing on the effects of TRP supplementation in the 1970's. Drs. Richard and Judith Wurtman at the Massachusetts Institute of Technology noted that reductions in brain serotonin played a pivotal role in the development of mood and behavioral disorders. Serotonin affects several central nervous system functions, including sleep, mood, aggression, pain, anxiety, memory, eating behavior, temperature regulation, hormonal regulation, and motor behavior. The Wurtmans and others postulated and proved that dietary supplementation of serotonin precursors such as tryptophan could improve mood and behavior significantly. More recently, studies on orally administered 5-HTP show that this serotonin precursor also benefits the psyche.

TRP occurs in low concentration (<1%) in most protein sources. In order to gain access to the brain, it must compete with other large neutral amino acids (LNAA) via a common transport mechanism. Low-protein diets sway the ratio of TRP to LNAA in favor of TRP, so that more TRP is transported into the brain. Dietary supplementation of TRP can likewise increase the ratio of TRP to other LNAA's, and afford TRP an advantage when vying for entry into the brain. Tryptophan hydroxylase, the rate-limiting enzyme that converts TRP to serotonin, is normally only half-saturated with TRP, so that increased intake of TRP modifies the plasma TRP/LNAA ratio, manipulating brain levels of TRP and subsequently driving serotonin synthesis and metabolism.

Over the past few decades, research has shown that TRP may be helpful for both humans and animals with depression, aggression, and obsessive compulsive disorders. In one study, Rhesus monkeys demonstrating compulsive self-injurious behaviors improved significantly after receiving three weeks of dietary TRP supplementation; cerebrospinal fluid from these individuals revealed significant increased in 5-hydroxyindoleacetic acid (5-HIAA), a serotonin metabolite.

Serotonin precursors may aid in treating obesity via appetite suppression, since brain serotonin affects satiety and macronutrient (protein vs. carbohydrate) selection. Administration of 5-HTP causes transient increases in plasma serotonin concentration; large doses of 5-HTP cause short-term decreases in food intake, particularly of carbohydrate-rich food.

The serotonergic system plays a significant role in obsessive-compulsive behaviors. For example, feather picking behavior is linked to low 5HT neurotransmission in the forebrain. Avian studies have demonstrated that chronic increases of TRP in the diet significantly decrease feather picking behavior. A 2004 study in *Applied Animal Behaviour Science* noted that TRP administration significantly increased the ratio of TRP to LNAA in the plasma of the birds. TRP supplementation significantly escalated the turnover of serotonin in the hippocampus and archistriatum in the brain, as well as elsewhere in the forebrain.

A 2000 study published in the *Journal of the American Veterinary Medical Association (JAVMA)* evaluated the effect of high- and low-protein diets, both with and without TRP supplementation, on canine behavior. The authors looked specifically at the effects of dietary protein on dogs with canine aggression, territorial aggression, and hyperactivity. Because of serotonin's effects on mood, they hypothesized that low-protein diets and diets supplemented with TRP would reduce not only aggression, but also excitability and reactivity. Although the diets did not influence fearfulness, hyperactivity, or excitability, dogs fed low protein diets plus TRP were less territorially aggressive, and dogs on either high-protein diets supplemented with TRP or low protein diets with or without TRP supplementation displayed less dominance aggression. Similar reductions in aggression have been noted in other studies on chickens and primates.

Amino acid supplements comprise just one type of a general class of compounds known as "nutraceuticals", which are substances, orally administered, that promote good health. Nutraceuticals are neither foods nor drugs. Although the Food and Drug Administration Center for Veterinary Medicine (FDA-CVM) is responsible for enforcing all aspects of the Food, Drug and Cosmetic Act that apply to foods and drugs for animal use, the agency has assigned most nutraceuticals to a status of low regulatory importance. Thus, nutraceuticals marketed for animal use continue to be widely available despite concerns regarding the safety and efficacy of these products. In a 2001 *JAVMA* article on the "Evaluation of nutraceuticals, dietary supplements, and functional food ingredients for companion animals", John E. Bauer recommends that veterinarians consider four important characteristics of nutraceuticals when discussing the use of these products with their clients: Product quality, Efficacy, Tolerance, and Safety (PETS). For product quality, Bauer states that veterinarians should obtain information on the quality, purity, and ingredients as well as quality-control procedures in place during processing. They should also ask the manufacturer to supply any supportive documentation of product efficacy.

Will the animal be able to tolerate the product, or will the supplement cause bad odor, nausea, anorexia, or interactions with drugs. Finally, is the product safe, especially when given over long period of time?

Notwithstanding the widespread popularity among humans in favor of TRP and 5-HTP for mood disorders and weight control, some veterinary practitioners remain concerned about potential toxicity of TRP, 5-HTP, their possible contaminants, and even amino acid supplementation in general. Production of synthetic TRP as a serotonergic agent halted abruptly in 1989 after an outbreak of eosinophilia-myalgia syndrome in humans was linked with TRP intake. The toxic products eventually linked to one Japanese manufacturer, but the exact cause and contaminants responsible for the outbreak still remain unclear. As with all supplement recommendations made for animal patients, veterinarians recommending TRP or 5-HTP should proceed cautiously, monitor their patients closely, and report adverse outcomes.

