Nutritional Influences on Illness
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Aggressive Behavior and L-Tryptophan

Serotonin, a major neurotransmitter, has been found to play an important role in modulating aggressive behavior. Impulsive, violent, and suicidal behaviors have repeatedly been shown to be associated with a reduction in serotonergic activity in the central nervous system.\(^1\)

Alcohol ingestion, which is well known to magnify the potential for aggression,\(^2\) appears to transiently increase brain serotonin turnover.\(^3\) While initially this effect would improve mood, it results in further serotonin depletion, thereby promoting aggressive behavior.

Tryptophan is the dietary precursor of serotonin, and the combination of excessive alcohol intake and a low-tryptophan diet has been found to be associated with both decreased brain serotonin and increased aggression.\(^4\) In a study of alcoholic impulsive offenders with antisocial personality disorder, aggressive behavior was found to be related to depressed cerebrospinal fluid (CSF) serotonin levels. Moreover, depressed CSF levels of a serotonin metabolite (5-HIAA) were associated with elevated CSF testosterone levels. While the 5-HIAA levels were related to impulsivity, the CSF testosterone levels were related to aggressiveness and interpersonal violence.\(^5\)

In addition to alcoholics, depressed CSF 5-HIAA levels have also been found in suicidal/aggressive patients and violent offenders who were not alcoholic.\(^6,7\)

Several lines of evidence suggest that the amount of tryptophan in the diet relates closely to aggressive behavior. For example, rats given a diet almost lacking in tryptophan develop aggressive behavior towards mice.\(^8\) In humans, tryptophan intake is inversely correlated with aggressive traits.\(^9,10\) Moreover, bimodal seasonal emotional patterns are related to plasma L-tryptophan availability, and this data matches known seasonal patterns for the prevalence of violent suicide and depression.\(^11\)

Tryptophan must compete with other large neutral amino acids to cross the blood-brain barrier; therefore, the ratio of the amount of tryptophan to the amount of competing amino acids (tryptophan ratio) may provide a rough indication of the availability of tryptophan in the brain for conversion into serotonin. Kitahara has calculated the dietary tryptophan ratio for 18 European countries to attempt to relate it to homicide rates. While initially no correlation was found between tryptophan ratios and homicide, once social and cultural differences were controlled for, low tryptophan ratios were indeed found to be associated with high homicide rates.\(^12\)

A more direct method of examining the relationship between the tryptophan ratio and aggression is by measuring the actual ratio in the blood plasma. When a group of depressed alcoholics was evaluated in this manner, those with a history of aggression – including suicide attempts – also had the lowest tryptophan ratios.\(^13\)

L-Tryptophan Supplementation

If a low tryptophan ratio is associated with aggressive behavior, will tryptophan supplementation reduce that behavior? Dietary tryptophan was manipulated in social groups of vervet monkeys by providing them with amino
acid mixtures that were tryptophan-free, nutritionally balanced, or excessively high in tryptophan. These mixtures were shown to have a marked effect on plasma tryptophan levels.

During spontaneous activity, the only effect of the different mixtures was increased aggression in the males on the tryptophan-free mixture. During competition for food, however, while the tryptophan-free mixture continued to increase male aggression, the high-tryptophan mixture reduced aggression in both males and females. These data suggest that tryptophan supplementation may be most effective in reducing aggression during times of stress.

When hospitalized male schizophrenics were given L-tryptophan, only those patients with high levels of hostility and a high lifetime frequency of aggressive incidents benefited; these patients showed a lessening of hostility and depression, a reduction in ward incidents, and improvement on a standardized psychiatric rating scale. In another study of 20 aggressive patients, while 6 grams of tryptophan daily for one month failed to reduce the number of violent incidents, it significantly reduced the need for potent medications to control violent or agitated behavior.

The rate of firing of serotonergic neurons in the brain increases as the level of behavioral arousal increases; thus increased serotonin levels would be more likely to influence brain function at higher levels of arousal. Indeed, this fact probably explains why the vervet monkeys only responded to tryptophan supplementation when they were put under competitive stress. It also may explain why altered tryptophan levels failed to affect aggression in a study of normal human males, while overaroused, hostile, and aggressive psychiatric patients responded well.

Both clinical and anecdotal evidence suggest that 500 to 1,500 mg of supplementary tryptophan, taken at bedtime on a regular basis, is frequently sufficient to relieve symptoms due to serotonin-deficiency. Surprisingly, higher dosages may not be as effective, due to activation of tryptophan pyrrolase, a key enzyme in the metabolism of tryptophan in the liver.

Since niacinamide, a form of vitamin B3, inhibits liver tryptophan pyrrolase, the addition of at least 100 mg of the vitamin with each meal should increase tryptophan’s efficacy. Similarly, since vitamin B6 activates the enzyme that converts tryptophan to serotonin, 25 to 50 mg of this

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vitamin once or twice daily with meals may also increase its efficacy.17

In the conversion of tryptophan to serotonin, the intermediate step is its conversion to 5-hydroxytryptophan (5-HTP). Surprisingly, supplementation with 5-HTP may increase aggressive behavior, apparently because, while tryptophan appears to exclusively enhance the serotonergic system, 5-HTP also appears to enhance the catecholaminergic system.18

Dr. Werbach cautions that the nutritional treatment of illness should be supervised by physicians or other practitioners whose training prepares them to recognize serious illness and to integrate nutritional interventions safely into the treatment plan.

Notes


7. Van Praag HM. Affective disorders and aggression disorders: evidence for a common biological mechanism. Suicide Life Threat Behav. 1986;16(2):103-132.


If you treat patients with psychological symptoms, you will want a copy of Dr. Werbach’s thoroughly revised and expanded second edition of Nutritional Influences on Mental Illness. For more information on his books, see the Third Line Press web page (www.third-line.com) or contact Third Line Press directly (4751 Viviana Drive, Tarzana, California 91356, USA; 818-996-0076; fax: 818-774-1575; tlp@third-line.com).