Serotonin and tryptophan

Serotonin is a brain hormone that promotes restful sleep, comfort and satiety. When serotonin levels are low, depression, anxiety, insomnia, and the urge to eat occur.

Serotonin is a neurotransmitter produced by the amino acid tryptophan, which induces feelings of security, relaxation and confidence. Serotonin decreases due to enzymatic breakdown (12) which occurs with a lack of L-tryptophan in the diet and with age (1-3). When a serotonin deficiency exists, sleep disturbances (8, 9), anxiety, depression, fibromyalgia, the desire to eat excessively (5-7), cravings and compulsive carbohydrate consumption (18) occur. Eating carbohydrates facilitates the transformation of L-tryptophan into serotonin (4, 18).

The amino acid L-tryptophan is necessary to produce serotonin in the brain. Although many foods contain tryptophan, one’s diet may not provide the L-tryptophan needed to produce sufficient amounts of serotonin. Furthermore, enzymes that occur with inflammation and aging break down L-tryptophan before it becomes serotonin.

Tryptophan is one of the eight essential amino acids present in the human diet, and it is also the least abundant. An adult needs at least 250 mg per day to maintain a good nitrogen balance (10). L-tryptophan is a serotonin precursor, but its entry into the blood-brain barrier is hindered by competition from other amino acids. A typical diet provides 1,000 to 1,500 mg/day of tryptophan, as part of the proteins, along with other competing amino acids (11). Therefore, a high protein diet is not a good solution to increase levels of serotonin in the brain. It is necessary to ingest tryptophan in a quickly bioavailable form, without other competing amino acids, while minimizing the effect of enzymatic degradation.

The metabolism of tryptophan in the body

Tryptophan can be metabolized through three different mechanisms:

1. It can be incorporated into the proteins of the body’s tissues.
2. It can be converted into serotonin and melatonin.
3. It can be transformed into indolamines, carbon dioxide, adenosine triphosphate (ATP) or niacin.

There are two specific enzymes that can transform L-tryptophan: tryptophan 2, 3-dioxygenase (TDO) and indolamine 2, 3-dioxygenase (IDO). TDO increases when the plasma concentrations of L-tryptophan exceed the levels necessary for the production of serotonin. This enzyme oxidizes L-tryptophan, creating carbon dioxide, water and ATP (13, 14). The oral intake of larger amounts of L-tryptophan fails to produce more serotonin because it induces more TDO and depletes the L-tryptophan. On the other hand, IDO can degrade L-tryptophan, even when circulating levels are low (14, 15). This enzyme is found in macrophages and dendritic cells and increases with inflammatory states, HIV infection and aging (16, 17).

When TDO or IDO act on the L-tryptophan, L-tryptophan can no longer be converted into serotonin, melatonin, or be incorporated into proteins.
Aging reduces serotonin levels

With aging, increased levels of inflammatory cytokines induce the enzyme IDO (indolamine 2, 3-dioxygenase) to degrade L-tryptophan. As a result, if you ingest large amounts of L-tryptophan (4,000 mg/day or more), more serotonin is not produced because TDO is induced and greater IDO activity degrades what little L-tryptophan remains in the blood.

Different pathways for the production of serotonin

There are four major factors that facilitate the synthesis of serotonin, which in turn influences the metabolism of tryptophan by facilitating its conversion or decreasing its degradation. These are:

- **The presence of lysine.** This competes with the amino acid tryptophan on the same oxidative degradation pathway. This means that in the presence of lysine, L-tryptophan is less oxidized (29).
- **The presence of niacinamide.** When systemic inflammation is present, the ingestion of niacinamide reduces the degradation of tryptophan (27, 28).
- **The presence of turmeric.** This plant can limit the induction of IDO. As a result, L-tryptophan is proportionally less degraded (30).
- **The presence of cofactors that facilitate the conversion of L-tryptophan into serotonin, such as vitamin B6 (19, 20).**

Dosage and advantages of tryptophan

The amino acid tryptophan is found in many foods as a protein. When taken alone in the form of an amino acid, it has excellent long-term tolerability. The doses used for different symptoms are:

- In general, a dose of 3,000 mg of L-tryptophan is sufficient to maintain the synthesis of serotonin in the human brain for eight to twelve hours (33).
- Although a dose of 250 mg improves sleep quality, the lowest dose of L-tryptophan for the treatment of insomnia can range from a minimum of 1,000 mg to 4,000 mg the first week, and from 500 to 1,000 mg the second. It usually takes repeated doses for any improvement to be observed (31).
- With a daily dosage of 6,000 mg of L-tryptophan, mood swings, tension and irritability can be decreased in women with premenstrual syndrome (26).
- Depression decreases with the intake of L-tryptophan (21), even in alcoholics (22). A recommended standard dosage is 50-300 mg of L-tryptophan or its metabolite 5-hydroxytryptophan three times a day for 2-4 weeks (23-25).
- Dosages of 3,500 mg / day have been used to help patients stop smoking (32).

L-tryptophan does not cause difficulties in waking up in the morning (31).

Vitamins, aminoacids and plant extracts: how do they affect our mood?

**Pyridoxine:** Also known as vitamin B6. It modulates the production of serotonin and GABA. These are both neurotransmitters that help control depression and anxiety (50), including depression associated with PMS (51).

**Theanine:** The amino acid found in tea. Its calming effect (52) is the result of increased production of GABA and dopamine. It also has a neuroprotective effect on the brain (53).

**Taurine:** Taurine is abundant in the heart and other muscles. It calms the brain and protects it from excess glutamate (54). It is also an indirect regulator of oxidative stress (55). Taurine has many functions at the cellular level, including its role as a neurotransmitter, a trophic factor in the development of the central nervous system, the maintenance of the structural integrity of the membrane, and the regulation of calcium transport and homeostasis; it also functions as a neuromodulator and a neuroprotector (56, 58). It has a proven anti-depressive effect in mice and plays a role in the regulation of learning and memory (57), in addition to its neuroprotective action (58). Another of its properties is its beneficial effect on anxiety control (59).

**Ashwagandha:** Reduces anxiety (62, 63) and increases GABA (61), producing a calming effect. This plant also influences the circadian sleep rhythm (60), inhibits lipid peroxidation (80) and has a protective effect on the skin’s collagen (64).

References


10. Altman PL, Dittner DS (Editors), Metabolism Bethesda, Maryland: Federation of American Societies for Experimental Biology, 1968.


