[Template:Other uses](/wiki/Template:Other_uses" \o "Template:Other uses) [Template:Use dmy dates](/wiki/Template:Use_dmy_dates) [Template:Infobox neurotransmitter](/wiki/Template:Infobox_neurotransmitter) [Template:Chembox](/wiki/Template:Chembox) **Serotonin** ([Template:IPAc-en](/wiki/Template:IPAc-en)[Template:RefnTemplate:RefnTemplate:Refn](/wiki/Template:Refn)) or **5-hydroxytryptamine** (**5-HT**) is a [monoamine neurotransmitter](/wiki/Monoamine_neurotransmitter). Biochemically derived from [tryptophan](/wiki/Tryptophan),[[1]](#cite_note-1) serotonin is primarily found in the [gastrointestinal tract](/wiki/Human_gastrointestinal_tract) (GI tract), blood [platelets](/wiki/Platelet), and the [central nervous system](/wiki/Central_nervous_system) (CNS) of animals, including humans. It is popularly thought to be a contributor to feelings of well-being and [happiness](/wiki/Happiness).[[2]](#cite_note-2) Approximately 90% of the [human body's](/wiki/Human_body) total serotonin is located in the [enterochromaffin cells](/wiki/Enterochromaffin_cells) in the GI tract, where it is used to regulate intestinal movements.[[3]](#cite_note-3)[[4]](#cite_note-4) The serotonin is secreted [luminally](/wiki/Lumen_(anatomy)) and [basolaterally](/wiki/Cell_membrane#Membrane_polarity) which leads to increased serotonin uptake by circulating platelets and activation after stimulation, which gives increased stimulation of myenteric neurons and [gastrointestinal motility](/wiki/Gastrointestinal_physiology#Motility).[[5]](#cite_note-5) |- | colspan ="3" align="center" | **5-HT1 receptor family** signals via [Gi/o](/wiki/Gi_alpha_subunit) inhibition of [adenylyl cyclase](/wiki/Adenylyl_cyclase).

|- | [5-HT1A](/wiki/5-HT1A_receptor) || 3.17 || Memory[Template:Vague](/wiki/Template:Vague) (agonists ↓); learning[Template:Vague](/wiki/Template:Vague) (agonists ↓); anxiety (agonists ↓); depression (agonists ↓); positive, negative, and cognitive symptoms of schizophrenia (partial agonists ↓); analgesia (agonists ↑); [aggression](/wiki/Aggression) (agonists ↓); dopamine release in the prefrontal cortex (agonists ↑); serotonin release and synthesis (agonists ↓)

|- | [5-HT1B](/wiki/5-HT1B_receptor) || 4.32 || Vasoconstriction (agonists ↑); aggression (agonists ↓); bone mass (↓). Serotonin autoreceptor.

|- | [5-HT1D](/wiki/5-HT1D_receptor) || 5.03 || Vasoconstriction (agonists ↑) |- | [5-HT1E](/wiki/5-HT1E_receptor) || 7.53 || |- | [5-HT1F](/wiki/5-HT1F_receptor) || 10 || |- | colspan ="3" align="center" | **5-HT2 receptor family** signals via [Gq](/wiki/Gq_alpha_subunit) activation of [phospholipase C](/wiki/Phospholipase_C).

|- | [5-HT2A](/wiki/5-HT2A_receptor) || 11.55 || Psychedelia (agonists ↑; antagonists ↑); depression (agonists & antagonists ↓); anxiety (antagonists ↓); positive and negative symptoms of schizophrenia (antagonists ↓); norepinephrine release from the [locus coeruleus](/wiki/Locus_coeruleus) (antagonists ↑); glutamate release in the [prefrontal cortex](/wiki/Prefrontal_cortex)

|- | [5-HT2B](/wiki/5-HT2B_receptor) || 8.71 || Cardiovascular functioning (agonists increase risk of pulmonary hypertension), empathy (via the spindle neurons or Von Economo neurons[[15]](#cite_note-15) Rodent experiment shows that neonatal exposure to SSRI's makes persistent changes in the serotonergic transmission of the brain resulting in behavioral changes,[[38]](#cite_note-38)[[39]](#cite_note-39) which are reversed by treatment with antidepressants.[[40]](#cite_note-40) By treating normal and [knockout mice](/wiki/Knockout_mouse) lacking the serotonin transporter with fluoxetine scientists showed that normal emotional reactions in adulthood, like a short latency to escape foot shocks and inclination to explore new environments were dependent on active serotonin transporters during the neonatal period.[[41]](#cite_note-41)[[42]](#cite_note-42) Human serotonin can also act as a [growth factor](/wiki/Growth_factor) directly. Liver damage increases cellular expression of [5-HT2A](/wiki/5-HT2A_receptor) and [5-HT2B receptors](/wiki/5-HT2B_receptor), mediating liver compensatory regrowth (see [Template:Section link](/wiki/Template:Section_link))[[43]](#cite_note-43) Serotonin present in the blood then stimulates cellular growth to repair liver damage.[[44]](#cite_note-44)5HT2B receptors also activate [osteocytes](/wiki/Osteocyte), which build up bone[[45]](#cite_note-45) However, serotonin also inhibits [osteoblasts](/wiki/Osteoblast), through 5-HT1B receptors.[[46]](#cite_note-46)

## Contents

* 1 Cardiovascular growth factor[[edit](/index.php?title=(none)&action=edit&section=12)]
* 2 Pharmacology[[edit](/index.php?title=(none)&action=edit&section=13)]
  + 2.1 Psychedelic drugs[[edit](/index.php?title=(none)&action=edit&section=14)]
  + 2.2 Antidepressants[[edit](/index.php?title=(none)&action=edit&section=15)]
    - 2.2.1 Serotonin syndrome[[edit](/index.php?title=(none)&action=edit&section=16)]
  + 2.3 Antiemetics[[edit](/index.php?title=(none)&action=edit&section=17)]
  + 2.4 Other[[edit](/index.php?title=(none)&action=edit&section=18)]
  + 2.5 Methyl-tryptamines and hallucinogens[[edit](/index.php?title=(none)&action=edit&section=19)]
* 3 Diseases and disorders[[edit](/index.php?title=(none)&action=edit&section=20)]
* 4 Comparative biology and evolution[[edit](/index.php?title=(none)&action=edit&section=21)]
  + 4.1 Unicellular organisms[[edit](/index.php?title=(none)&action=edit&section=22)]
  + 4.2 Plants[[edit](/index.php?title=(none)&action=edit&section=23)]
  + 4.3 Invertebrates[[edit](/index.php?title=(none)&action=edit&section=24)]
  + 4.4 Insects[[edit](/index.php?title=(none)&action=edit&section=25)]
  + 4.5 Growth and reproduction[[edit](/index.php?title=(none)&action=edit&section=26)]
  + 4.6 Aging and age-related phenotypes[[edit](/index.php?title=(none)&action=edit&section=27)]
  + 4.7 Deficiency[[edit](/index.php?title=(none)&action=edit&section=28)]
* 5 Biochemical mechanisms[[edit](/index.php?title=(none)&action=edit&section=29)]
  + 5.1 Biosynthesis[[edit](/index.php?title=(none)&action=edit&section=30)]
  + 5.2 Effects of food content[[edit](/index.php?title=(none)&action=edit&section=31)]
* 6 History[[edit](/index.php?title=(none)&action=edit&section=32)]
* 7 See also[[edit](/index.php?title=(none)&action=edit&section=33)]
* 8 Notes[[edit](/index.php?title=(none)&action=edit&section=34)]
* 9 References[[edit](/index.php?title=(none)&action=edit&section=35)]
* 10 External links[[edit](/index.php?title=(none)&action=edit&section=36)]

#### Cardiovascular growth factor[[edit](/index.php?title=(none)&action=edit&section=12)]

[Template:Main](/wiki/Template:Main) Serotonin, in addition, evokes [endothelial](/wiki/Endothelium) [nitric oxide synthase](/wiki/Nitric_oxide_synthase) activation and stimulates, through a [5-HT1B receptor](/wiki/5-HT1B_receptor)-mediated mechanism, the phosphorylation of p44/p42 mitogen-activated protein kinase activation in bovine aortic endothelial cell cultures.[[47]](#cite_note-47) In blood, serotonin is collected from plasma by platelets, which store it. It is thus active wherever platelets bind in damaged tissue, as a vasoconstrictor to stop bleeding, and also as a fibrocyte mitotic (growth factor), to aid healing.[[48]](#cite_note-48)

## Pharmacology[[edit](/index.php?title=(none)&action=edit&section=13)]

Several classes of [drugs](/wiki/Drugs) target the 5-HT system, including some [antidepressants](/wiki/Antidepressant), [antipsychotics](/wiki/Antipsychotic), [anxiolytics](/wiki/Anxiolytic), [antiemetics](/wiki/Antiemetic), and [antimigraine drugs](/wiki/Migraine), as well as the [psychedelic drugs](/wiki/Psychedelic_drug) and [empathogens](/wiki/Empathogen).

### Psychedelic drugs[[edit](/index.php?title=(none)&action=edit&section=14)]

The psychedelic drugs [psilocin](/wiki/Psilocin)/[psilocybin](/wiki/Psilocybin), [DMT](/wiki/Dimethyltryptamine), [mescaline](/wiki/Mescaline), and [LSD](/wiki/LSD) are [agonists](/wiki/Agonist), primarily at [5HT2A](/wiki/5-HT2A_receptor)/[2C](/wiki/5HT2C_receptor) receptors.[[49]](#cite_note-49)[[50]](#cite_note-50)[[51]](#cite_note-51) The [empathogen-entactogen](/wiki/Empathogen-entactogen) [MDMA](/wiki/MDMA) releases serotonin from synaptic vesicles of neurons.[[52]](#cite_note-52)

### Antidepressants[[edit](/index.php?title=(none)&action=edit&section=15)]

[Template:Main](/wiki/Template:Main) Drugs that alter serotonin levels are used in treating [depression](/wiki/Major_depressive_disorder), [generalized anxiety disorder](/wiki/Generalized_anxiety_disorder) and [social phobia](/wiki/Social_anxiety_disorder). [Monoamine oxidase inhibitors](/wiki/Monoamine_oxidase_inhibitor) (MAOIs) prevent the breakdown of [monoamine neurotransmitters](/wiki/Monoamine_neurotransmitter) (including serotonin), and therefore increase concentrations of the neurotransmitter in the brain. MAOI therapy is associated with many adverse drug reactions, and patients are at risk of [hypertensive emergency](/wiki/Hypertensive_emergency) triggered by foods with high [tyramine](/wiki/Tyramine) content, and certain drugs. Some drugs inhibit the re-uptake of serotonin, making it stay in the synaptic cleft longer. The [tricyclic antidepressants](/wiki/Tricyclic_antidepressants) (TCAs) inhibit the reuptake of both serotonin and [norepinephrine](/wiki/Norepinephrine). The newer [selective](/wiki/Selective_and_non-selective) serotonin reuptake inhibitors ([SSRIs](/wiki/SSRI)) have fewer side-effects and fewer interactions with other drugs.[[53]](#cite_note-53) Certain SSRI medications have been shown to lower serotonin levels below the baseline after chronic use, despite initial increases.[[54]](#cite_note-54) The [*5-HTTLPR*](/wiki/5-HTTLPR) gene codes for the number of serotonin transporters in the brain, with more serotonin transporters causing decreased duration and magnitude of serotonergic signaling.[[55]](#cite_note-55) The [5-HTTLPR polymorphism (l/l)](/wiki/5-HTTLPR_polymorphism_(l/l)) causing more serotonin transporters to be formed is also found to be more resilient against depression and anxiety.[[56]](#cite_note-56)[[57]](#cite_note-57)

#### Serotonin syndrome[[edit](/index.php?title=(none)&action=edit&section=16)]

[Template:Main](/wiki/Template:Main) Extremely high levels of serotonin can cause a condition known as [serotonin syndrome](/wiki/Serotonin_syndrome), with toxic and potentially fatal effects. In practice, such toxic levels are essentially impossible to reach through an [overdose](/wiki/Overdose) of a single antidepressant drug, but require a combination of serotonergic agents, such as an [SSRI](/wiki/SSRI) with an [MAOI](/wiki/MAOI).[[58]](#cite_note-58) The intensity of the symptoms of serotonin syndrome vary over a wide spectrum, and the milder forms are seen even at nontoxic levels.[[59]](#cite_note-59)

### Antiemetics[[edit](/index.php?title=(none)&action=edit&section=17)]

Some [5-HT3 antagonists](/wiki/5-HT3_antagonist), such as [ondansetron](/wiki/Ondansetron), [granisetron](/wiki/Granisetron), and [tropisetron](/wiki/Tropisetron), are important [antiemetic](/wiki/Antiemetic) agents. They are particularly important in treating the [nausea](/wiki/Nausea) and [vomiting](/wiki/Vomiting) that occur during anticancer [chemotherapy](/wiki/Chemotherapy) using cytotoxic drugs. Another application is in the treatment of postoperative nausea and vomiting.

### Other[[edit](/index.php?title=(none)&action=edit&section=18)]

Some serotonergic agonist drugs cause fibrosis anywhere in the body, particularly the syndrome of [retroperitoneal fibrosis](/wiki/Retroperitoneal_fibrosis), as well as [cardiac valve fibrosis](/wiki/Cardiac_fibrosis).[[60]](#cite_note-60)In the past, three groups of serotonergic drugs have been epidemiologically linked with these syndromes. These are the serotonergic vasoconstrictive antimigraine drugs ([ergotamine](/wiki/Ergotamine) and [methysergide](/wiki/Methysergide)),<ref name=Baskin/> the serotonergic appetite suppressant drugs ([fenfluramine](/wiki/Fenfluramine), [chlorphentermine](/wiki/Chlorphentermine), and [aminorex](/wiki/Aminorex)), and certain anti-Parkinsonian dopaminergic agonists, which also stimulate serotonergic 5-HT2B receptors. These include [pergolide](/wiki/Pergolide) and [cabergoline](/wiki/Cabergoline), but not the more dopamine-specific [lisuride](/wiki/Lisuride).[[61]](#cite_note-61) As with fenfluramine, some of these drugs have been withdrawn from the market after groups taking them showed a statistical increase of one or more of the side effects described. An example is [pergolide](/wiki/Pergolide). The drug was declining in use since it was reported in 2003 to be associated with cardiac fibrosis.[[62]](#cite_note-62) Two independent studies published in the [New England Journal of Medicine](/wiki/New_England_Journal_of_Medicine) in January 2007, implicated pergolide, along with [cabergoline](/wiki/Cabergoline), in causing [valvular heart disease](/wiki/Valvular_heart_disease).[[63]](#cite_note-63)[[64]](#cite_note-64) As a result of this, the [FDA](/wiki/Food_and_Drug_Administration) removed pergolide from the U.S. market in March 2007.[[65]](#cite_note-65) (Since cabergoline is not approved in the U.S. for Parkinson's Disease, but for hyperprolactinemia, the drug remains on the market. Treatment for hyperprolactinemia requires lower doses than that for Parkinson's Disease, diminishing the risk of valvular heart disease).[[66]](#cite_note-66)

### Methyl-tryptamines and hallucinogens[[edit](/index.php?title=(none)&action=edit&section=19)]

[Template:For](/wiki/Template:For) Several plants contain serotonin together with a family of related [tryptamines](/wiki/Tryptamine) that are [methylated](/wiki/Methylation) at the [amino](/wiki/Amine) (NH2) and [(OH) groups](/wiki/Hydroxyl), are [*N*-oxides](/wiki/Amine_oxide), or miss the OH group. These compounds do reach the brain, although some portion of them are metabolized by [monoamine oxidase](/wiki/Monoamine_oxidase) enzymes (mainly [MAO-A](/wiki/MAO-A)) in the liver. Examples are plants from the [*Anadenanthera*](/wiki/Anadenanthera) genus that are used in the [hallucinogenic](/wiki/Hallucinogen) [yopo](/wiki/Yopo) snuff. These compounds are widely present in the leaves of many plants, and may serve as deterrents for animal ingestion. Serotonin occurs in several mushrooms of the genus [*Panaeolus*](/wiki/Panaeolus).[[67]](#cite_note-67)

## Diseases and disorders[[edit](/index.php?title=(none)&action=edit&section=20)]

Serotonin in mammals is made by two different [tryptophan hydroxylases](/wiki/Tryptophan_hydroxylase): [TPH1](/wiki/TPH1) produces serotonin in the [pineal gland](/wiki/Pineal_gland)[Template:Citation needed](/wiki/Template:Citation_needed) and the enterochromaffin cells, while [TPH2](/wiki/TPH2) produces it in the [Raphe nuclei](/wiki/Raphe_nuclei) and in the [myenteric plexus](/wiki/Myenteric_plexus). Genetically altered mice lacking TPH1 develop progressive loss of heart strength early on. They have pale skin and breathing difficulties, are easily tired, and eventually die of [heart failure](/wiki/Heart_failure).[[68]](#cite_note-68) Genetically altered mice that lack TPH2 are normal when they are born. However, after three days, they appear to be smaller and weaker, and have softer skin than their siblings. In a [purebred](/wiki/Purebred) strain, 50% of the mutants died during the first four weeks, but in a mixed strain, 90% survived. Normally, the mother [weans](/wiki/Weaning) the litter after three weeks, but the mutant animals needed five weeks. After that, they caught up in growth and had normal mortality rates. Subtle changes in the [autonomic nervous system](/wiki/Autonomic_nervous_system) are present, but the most obvious difference from normal mice is the increased aggressiveness and impairment in maternal care of young.[[69]](#cite_note-69)Despite the blood-brain barrier, the loss of serotonin production in the brain is partially compensated by intestinal serotonin. The behavioural changes become greatly enhanced if one crosses TPH1- with TPH2-lacking mice and gets animals that lack TPH entirely.[[70]](#cite_note-70) In humans, defective signaling of serotonin in the brain may be the root cause of [sudden infant death syndrome](/wiki/Sudden_infant_death_syndrome) (SIDS). Scientists from the European Molecular Biology Laboratory in Monterotondo, Italy[[71]](#cite_note-71) genetically modified lab mice to produce low levels of the neurotransmitter serotonin. The results showed the mice suffered drops in heart rate and other symptoms of SIDS, and many of the animals died at an early age. Researchers now believe low levels of serotonin in the animals' brainstems, which controls heartbeat and breathing, may have caused sudden death.[[43]](#cite_note-43)If neurons that make serotonin — serotonergic neurons — are abnormal in human infants, there is a risk of [sudden infant death syndrome](/wiki/Sudden_infant_death_syndrome) (SIDS).[[72]](#cite_note-72) Recent research conducted at [Rockefeller University](/wiki/Rockefeller_University) shows, in both patients who suffer from depression as well as mice that model the disorder, levels of the [p11 protein](/wiki/P11_protein) are decreased. This protein is related to serotonin transmission within the brain.[[73]](#cite_note-73) Depletion of serotonin is common between disorders such as obsessive-compulsive disorder, depression, and anxiety. However, Dr. Marazziti and his researchers at the University of Pisa in Italy found that depletion of serotonin also occurs in people who have recently fallen in love. This leads to the obsessive component associated with early stages of love.[[74]](#cite_note-74) Consumption of an average amount of alcohol (0.8g/kg of body weight) has been shown to decrease tryptophan by about 25%, leading to a similar decrease in serotonin. The sexual and impulsive behavior resulting from an intoxicated state is at least partially an effect of the decrease in serotonin because serotonin regulates these behaviors.[[74]](#cite_note-74)

## Comparative biology and evolution[[edit](/index.php?title=(none)&action=edit&section=21)]

### Unicellular organisms[[edit](/index.php?title=(none)&action=edit&section=22)]

Serotonin is used by a variety of single-cell organisms for various purposes. [SSRIs](/wiki/SSRIs) have been found to be toxic to algae.[[75]](#cite_note-75) The gastrointestinal parasite [*Entamoeba histolytica*](/wiki/Entamoeba_histolytica) secretes serotonin, causing a sustained secretory diarrhea in some patients.[[76]](#cite_note-76)[[77]](#cite_note-77) Patients infected with *E. histolytica* have been found to have highly elevated serum serotonin levels, which returned to normal following resolution of the infection.[[78]](#cite_note-78) *E. histolytica* also responds to the presence of serotonin by becoming more virulent.[[79]](#cite_note-79) This means serotonin secretion not only serves to increase the spread of enteamoebas by giving the host diarrhea but also serves to coordinate their behaviour according to their population density, a phenomenon known as [quorum sensing](/wiki/Quorum_sensing). Outside the gut of a host, there is nothing that the entoamoebas provoke to release serotonin, hence the serotonin concentration is very low. Low serotonin signals to the entoamoebas they are outside a host and they become less virulent to conserve energy. When they enter a new host, they multiply in the gut, and become more virulent as the enterochromaffine cells get provoked by them and the serotonin concentration increases.

### Plants[[edit](/index.php?title=(none)&action=edit&section=23)]

In drying [seeds](/wiki/Seeds), serotonin production is a way to get rid of the buildup of poisonous [ammonia](/wiki/Ammonia). The ammonia is collected and placed in the [indole](/wiki/Indole) part of L-[tryptophan](/wiki/Tryptophan), which is then [decarboxylated](/wiki/Decarboxylation) by [tryptophan decarboxylase](/wiki/Aromatic_L-amino_acid_decarboxylase) to give tryptamine, which is then [hydroxylated](/wiki/Hydroxylation) by a [cytochrome P450 monooxygenase](/wiki/Cytochrome_P450_monooxygenase), yielding serotonin.[[80]](#cite_note-80) However, since serotonin is a major gastrointestinal tract modulator, it may be produced by plants in fruits as a way of speeding the passage of seeds through the digestive tract, in the same way as many well-known seed and fruit associated laxatives. Serotonin is found in [mushrooms](/wiki/Mushroom), [fruits](/wiki/Fruits) and [vegetables](/wiki/Vegetable). The highest values of 25–400 mg/kg have been found in nuts of the [walnut](/wiki/Walnut) (*Juglans*) and [hickory](/wiki/Hickory) (*Carya*) genera. Serotonin concentrations of 3–30 mg/kg have been found in [plantains](/wiki/Plantain_(cooking)), [pineapples](/wiki/Pineapple), [banana](/wiki/Banana), [kiwifruit](/wiki/Kiwifruit), [plums](/wiki/Plum), and [tomatoes](/wiki/Tomato). Moderate levels from 0.1–3 mg/kg have been found in a wide range of tested vegetables.[[81]](#cite_note-81) Serotonin is one compound of the poison contained in [stinging nettles](/wiki/Stinging_nettle) (*Urtica dioica*), where it causes pain on injection in the same manner as its presence in insect venoms (see below). It is also naturally found in *Paramuricea clavata*, or the Red Sea Fan.[[82]](#cite_note-82) Serotonin and tryptophan have been found in chocolate with varying cocoa contents. The highest serotonin content (2.93 µg/g) was found in chocolate with 85% cocoa, and the highest tryptophan content (13.27–13.34 µg/g) was found in 70–85% cocoa. The intermediate in the synthesis from tryptophan to serotonin, 5-hydroxytryptophan, was not found.[[83]](#cite_note-83)

### Invertebrates[[edit](/index.php?title=(none)&action=edit&section=24)]

Serotonin functions as a neurotransmitter in the nervous systems of simple, as well as complex, animals. For example, in the roundworm [*Caenorhabditis elegans*](/wiki/Caenorhabditis_elegans), which feeds on bacteria, serotonin is released as a signal in response to positive events, e.g., finding a new source of food or in male animals finding a female with which to mate.[[84]](#cite_note-84) When a well-fed worm feels bacteria on its [cuticle](/wiki/Cuticle), [dopamine](/wiki/Dopamine) is released, which slows it down; if it is starved, serotonin also is released, which slows the animal down further. This mechanism increases the amount of time animals spend in the presence of food.[[85]](#cite_note-85) The released serotonin activates the muscles used for feeding, while [octopamine](/wiki/Octopamine_(neurotransmitter)) suppresses them.[[86]](#cite_note-86) Serotonin diffuses to serotonin-sensitive neurons, which control the animal's perception of nutrient availability.

If [lobsters](/wiki/Lobster) are injected with serotonin, they behave like dominant individuals whereas octopamine causes [subordinate behavior](/wiki/Dominance_hierarchy).[[87]](#cite_note-87) A [crayfish](/wiki/Crayfish) that is frightened may [flip its tail](/wiki/Caridoid_escape_reaction) to flee, and the effect of serotonin on this behavior depends largely on the animal's social status. Serotonin inhibits the fleeing reaction in subordinates, but enhances it in socially dominant or isolated individuals. The reason for this is social experience alters the proportion between [serotonin receptors](/wiki/Serotonin_receptor) (5-HT receptors) that have opposing effects on the [fight-or-flight response](/wiki/Fight-or-flight_response).[Template:Clarify](/wiki/Template:Clarify) The effect of [5-HT1 receptors](/wiki/5-HT1_receptor) predominates in subordinate animals, while [5-HT2 receptors](/wiki/5-HT2_receptor) predominates in dominants.[[88]](#cite_note-88)

### Insects[[edit](/index.php?title=(none)&action=edit&section=25)]

Serotonin is evolutionary conserved and appears across the animal kingdom. It is seen in insect processes in roles similar to in the human central nervous system, such as memory, appetite, sleep, and behavior.[[89]](#cite_note-89) Locust swarming is mediated by serotonin, by transforming social preference from aversion to a gregarious state that enables coherent groups.[[90]](#cite_note-90) Learning in flies and honeybees is affected by the presence of serotonin.[[91]](#cite_note-91)[[92]](#cite_note-92) Insect 5-HT receptors have similar sequences to the vertebrate versions, but pharmacological differences have been seen. Invertebrate drug response has been far less characterized than mammalian pharmacology and the potential for species selective insecticides has been discussed.[[93]](#cite_note-93) [Wasps](/wiki/Wasp) and [hornets](/wiki/Hornets) have serotonin in their venom,[[94]](#cite_note-94) as do [scorpions](/wiki/Scorpion).[[95]](#cite_note-95) If flies are fed serotonin, they are more aggressive; flies depleted of serotonin still exhibit aggression, but they do so much less frequently.[[96]](#cite_note-96)

### Growth and reproduction[[edit](/index.php?title=(none)&action=edit&section=26)]

In the nematode [*C. elegans*](/wiki/Caenorhabditis_elegans), artificial depletion of serotonin or the increase of octopamine cues behavior typical of a low-food environment: *C. elegans* becomes more active, and mating and egg-laying are suppressed, while the opposite occurs if serotonin is increased or octopamine is decreased in this animal.[[97]](#cite_note-97) Serotonin is necessary for normal nematode male mating behavior,[[98]](#cite_note-98) and the inclination to leave food to search for a mate.[[99]](#cite_note-99) The serotonergic signaling used to adapt the worm's behaviour to fast changes in the environment affects [insulin](/wiki/Insulin)-like signaling and the [TGF beta signaling pathway](/wiki/TGF_beta_signaling_pathway),[[100]](#cite_note-100) which control long-term adaption.

In the [fruit fly](/wiki/Drosophila_melanogaster) insulin both regulates [blood sugar](/wiki/Blood_sugar) as well as acting as a [growth factor](/wiki/Growth_factor). Thus, in the fruit fly, serotonergic neurons regulate the adult body size by affecting insulin secretion.[[101]](#cite_note-101)[[102]](#cite_note-102) Serotonin has also been identified as the trigger for [swarm behavior](/wiki/Swarm_behavior) in locusts.[[103]](#cite_note-103) In humans, though insulin regulates blood sugar and [IGF](/wiki/Insulin-like_growth_factor) regulates growth, serotonin controls the release of both hormones, modulating insulin release from the [beta cells](/wiki/Beta_cell) in the [pancreas](/wiki/Pancreas) through serotonylation of GTPase signaling proteins.[[11]](#cite_note-11) Exposure to [SSRIs](/wiki/SSRI) during [Pregnancy](/wiki/Gestation) reduces fetal growth.[[104]](#cite_note-104)

### Aging and age-related phenotypes[[edit](/index.php?title=(none)&action=edit&section=27)]

Serotonin is known to regulate aging, learning and memory. The first evidence comes from the study of longevity in [*C. elegans*](/wiki/Caenorhabditis_elegans).[[105]](#cite_note-105) During early phase of aging, the level of serotonin increases, which alters locomotory behaviors and associative memory.[[106]](#cite_note-106) The effect is restored by mutations and drugs (including [mianserin](/wiki/Mianserin) and [methiothepin](/wiki/Methiothepin)) that inhibit [serotonin receptors](/wiki/Serotonin_receptors). The observation does not contradict with the notion that the serotonin level goes down in mammals and humans, which is typically seen in late but not early phase of aging.

### Deficiency[[edit](/index.php?title=(none)&action=edit&section=28)]

Genetically altered *C. elegans* worms that lack serotonin have an increased reproductive lifespan, may become obese, and sometimes present with arrested development at a [dormant larval state](/wiki/Dauer_larva).[[107]](#cite_note-107)[[108]](#cite_note-108)

## Biochemical mechanisms[[edit](/index.php?title=(none)&action=edit&section=29)]

### Biosynthesis[[edit](/index.php?title=(none)&action=edit&section=30)]

[thumb|right|340px|alt= On top an L-tryptophan molecule with an arrow down to a 5-HTP molecule.](/wiki/File:Serotonin_biosynthesis.svg) [Tryptophan hydroxylase](/wiki/Tryptophan_hydroxylase) catalyses this reaction with help of O2 and [tetrahydrobiopterin](/wiki/Tetrahydrobiopterin), which becomes water and [dihydrobiopterin](/wiki/Dihydrobiopterin). From the 5-HTP molecule goes an arrow down to a serotonin molecule. Aromatic L-amino acid decarboxylase or 5-Hydroxytryptophan decarboxylase catalyses this reaction with help of [pyridoxal phosphate](/wiki/Pyridoxal_phosphate). From the serotonin molecule goes an arrow to a 5-HIAA molecule at the bottom ot the image. Monoamine oxidase catalyses this reaction, in the process O2 and water is consumed, and ammonia and hydrogen peroxide is produced.|The pathway for the synthesis of serotonin from tryptophan. In animals including humans, serotonin is [synthesized](/wiki/Biosynthesis) from the [amino acid](/wiki/Amino_acid) L-[tryptophan](/wiki/Tryptophan) by a short [metabolic pathway](/wiki/Metabolic_pathway) consisting of two [enzymes](/wiki/Enzyme): [tryptophan hydroxylase](/wiki/Tryptophan_hydroxylase) (TPH) and [aromatic amino acid decarboxylase](/wiki/Aromatic_L-amino_acid_decarboxylase) (DDC). The TPH-mediated reaction is the rate-limiting step in the pathway. TPH has been shown to exist in two forms: [TPH1](/wiki/TPH1), found in several [tissues](/wiki/Biological_tissue), and [TPH2](/wiki/TPH2), which is a neuron-specific [isoform](/wiki/Protein_isoform).[[68]](#cite_note-68) Serotonin can be synthesized from tryptophan in the lab using *Aspergillus niger* and *Psilocybe coprophila* as catalysts. The first phase to 5-hydroxytryptophan would require letting tryptophan sit in ethanol and water for 7 days, then mixing in enough HCl (or other acid) to bring the pH to 3, and then adding NaOH to make a pH of 13 for 1 hour. *Asperigillus niger* would be the catalyst for this first phase. The second phase to synthesizing tryptophan itself from the 5-hydroxytryptophan intermediate would require adding ethanol and water, and letting sit for 30 days this time. The next two steps would be the same as the first phase: adding HCl to make the pH = 3, and then adding NaOH to make the pH very basic at 13 for 1 hour. This phase uses the *Psilocybe coprophila* as the catalyst for the reaction.[[109]](#cite_note-109) Serotonin taken orally does not pass into the serotonergic pathways of the central nervous system, because it does not cross the [blood–brain barrier](/wiki/Blood–brain_barrier).[[110]](#cite_note-110) However, [tryptophan](/wiki/Tryptophan) and its [metabolite](/wiki/Metabolite) [5-hydroxytryptophan](/wiki/5-hydroxytryptophan) (5-HTP), from which serotonin is synthesized, does cross the blood–brain barrier. These agents are available as [dietary supplements](/wiki/Dietary_supplement), and may be effective serotonergic agents. One product of serotonin breakdown is [5-hydroxyindoleacetic acid](/wiki/5-hydroxyindoleacetic_acid) (5-HIAA), which is excreted in the [urine](/wiki/Urine). Serotonin and 5-HIAA are sometimes produced in excess amounts by certain [tumors](/wiki/Tumor) or [cancers](/wiki/Cancer), and levels of these substances may be measured in the urine to test for these tumors.

### Effects of food content[[edit](/index.php?title=(none)&action=edit&section=31)]

[Template:See also](/wiki/Template:See_also) Consuming purified tryptophan increases brain serotonin whereas eating foods containing tryptophan does not.[[111]](#cite_note-111) This is because the transport system which brings tryptophan across the [blood-brain barrier](/wiki/Blood-brain_barrier) is also selective for the other amino acids contained in protein sources.[[110]](#cite_note-110) High plasma levels of other large neutral amino acids compete for transport and prevent the elevated plasma tryptophan from increasing serotonin synthesis.

## History[[edit](/index.php?title=(none)&action=edit&section=32)]

[Template:Expand section](/wiki/Template:Expand_section) In 1935, Italian [Vittorio Erspamer](/wiki/Vittorio_Erspamer) showed an extract from [enterochromaffin cells](/wiki/Enterochromaffin_cell) made intestines contract. Some believed it contained [adrenaline](/wiki/Adrenaline), but two years later, Erspamer was able to show it was a previously unknown [amine](/wiki/Amine), which he named "enteramine".[[112]](#cite_note-112) In 1948, [Maurice M. Rapport](/wiki/Maurice_M._Rapport), Arda Green, and [Irvine Page](/wiki/Irvine_Page) of the [Cleveland Clinic](/wiki/Cleveland_Clinic) discovered a vasoconstrictor substance in [blood serum](/wiki/Blood_plasma), and since it was a serum agent affecting vascular tone, they named it serotonin.[[113]](#cite_note-113) In 1952, enteramine was shown to be the same substance as serotonin, and as the broad range of physiological roles was elucidated, the abbreviation 5-HT of the proper chemical name 5-hydroxytryptamine became the preferred name in the pharmacological field.[[114]](#cite_note-114) Synonyms of serotonin include: 5-hydroxytriptamine, thrombotin, enteramin, substance DS, and 3-(β-Aminoethyl)-5-hydroxyindole.[[115]](#cite_note-115) In 1953, [Betty Twarog](/wiki/Betty_Twarog) and Page discovered serotonin in the central nervous system.[[116]](#cite_note-116)

## See also[[edit](/index.php?title=(none)&action=edit&section=33)]

* [5-HT2c receptor agonist](/wiki/5-HT2c_receptor_agonist)

## Notes[[edit](/index.php?title=(none)&action=edit&section=34)]

[Template:Reflist](/wiki/Template:Reflist)

## References[[edit](/index.php?title=(none)&action=edit&section=35)]

[Template:Reflist](/wiki/Template:Reflist)

## External links[[edit](/index.php?title=(none)&action=edit&section=36)]

[Template:Commons category](/wiki/Template:Commons_category)

* [5-Hydroxytryptamine MS Spectrum](http://gmd.mpimp-golm.mpg.de/Spectrums/a1a3167e-cbab-45fd-adb6-9addc14e0ec2.aspx)
* [Serotonin bound to proteins](http://www.ebi.ac.uk/pdbe-srv/PDBeXplore/ligand/?ligand=SRO) in the [PDB](/wiki/Protein_Data_Bank)
* [PsychoTropicalResearch](http://www.psychotropical.com/) Extensive reviews on serotonergic drugs and Serotonin Syndrome.
* [Molecule of the Month: Serotonin](http://www.chm.bris.ac.uk/motm/serotonin/home1.htm) at [University of Bristol](/wiki/University_of_Bristol)
* 60-Second Psych: [No Fair! My Serotonin Level Is Low](http://www.sciam.com/podcast/episode.cfm?id=68FC98F1-E48A-251D-8F65277181DB9A4E), [Scientific American](/wiki/Scientific_American)
* [Serotonin Test Interpretation on ClinLab Navigator](http://www.clinlabnavigator.com/Tests/Serotonin.html).
* [Template:Cite journal](/wiki/Template:Cite_journal)
* [The Psychobiology of Serotonin Deficiency Syndrome](http://store.lidtke.com/pages/townsend-letter-tryptophan)

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[Category:Serotonin](/wiki/Category:Serotonin) [Category:Tryptamine alkaloids](/wiki/Category:Tryptamine_alkaloids) [Category:Biogenic amines](/wiki/Category:Biogenic_amines) [Category:Neurotransmitters](/wiki/Category:Neurotransmitters) [Category:TAAR1 agonists](/wiki/Category:TAAR1_agonists) [Category:Serotonin receptor agonists](/wiki/Category:Serotonin_receptor_agonists) [Category:Serotonin releasing agents](/wiki/Category:Serotonin_releasing_agents) [Category:Hydroxyarenes](/wiki/Category:Hydroxyarenes) [Category:Peripherally selective drugs](/wiki/Category:Peripherally_selective_drugs)