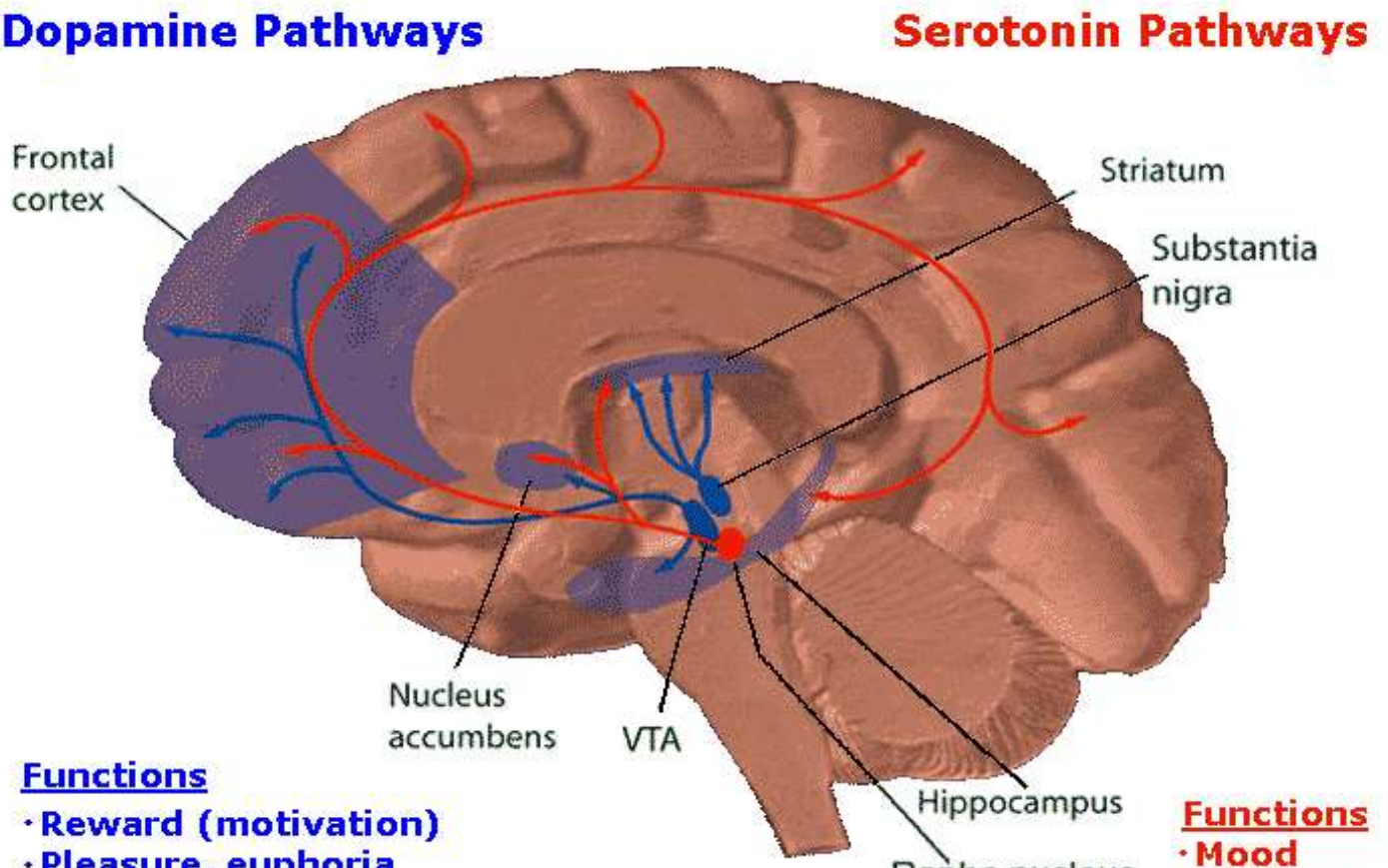
The Functions of Serotonin & Dopamine in the Brain!



Functions

- **Reward (motivation)**
- **Pleasure, euphoria**
- **Motor function (fine tuning)**
- **Compulsion**
- **Perseveration**

Functions

- **Mood**
- **Memory processing**
- **Sleep**
- **Cognition**

Serotonin

From Wikipedia, the free encyclopedia

Serotonin (pronounced /ˌsɛrəˈtoʊnən/) is a monoamine neurotransmitter. It is found extensively in the gastrointestinal tract of animals, and about 80 to 90 percent of the human body's total serotonin is located in the enterochromaffin cells in the gut, where it is used to regulate intestinal movements.[1][2] The remainder is synthesized in serotonergic neurons in the central nervous system (CNS) where it has various functions, including control of appetite, mood and anger.

Function

Serotonin functions as a neurotransmitter in nerve systems of simple as well as complex animals. In the roundworm *Caenorhabditis elegans* serotonin activates the muscles used for feeding, while octopamine suppresses them.[4] Serotonin diffuses to serotonin-sensitive neurons, which control the animal's perception of nutrient availability. Artificial depletion of serotonin or increase of octopamine cues behavior that is typical of a low-food environment: *C. elegans* becomes more active, and mating and egg-laying is suppressed, while the opposite occurs if serotonin is increased or octopamine is decreased in this animal.[5]

The role of serotonin in animals with a more complex nerve system is in perceptions of more complex life situations such as, for example, social rank. If a lobster is injected with serotonin, it behaves like a dominant animal, while octopamine causes subordinate behavior.[6]

Frightened crayfish flips its tail to flee, and the effect of serotonin on this behavior depends on the animal's social status. Serotonin inhibits the fleeing reaction in subordinates, but enhances it in socially dominant or isolated individuals. Social experience alters the proportion between different serotonin receptors which have opposing effects on the fight-or-flight response. [7]

Serotonergic signaling plays an important role in the modulation of human mood, anger and aggression. Individuals of *C.elegans* facing stress (eg. a low-food environment) resume normal behaviour if given serotonin-increasing drugs. The same drugs have similar effects in humans; the action of serotonin on the worms' mating and egg-laying resembles its effects on human sexuality.[*citation needed*]

Serotonin has broad activities in the brain, and genetic variation in serotonin receptors and the serotonin transporter, which facilitates re-uptake of serotonin into presynapses, have been implicated in neurological diseases. Drugs targeting serotonin-induced pathways are being used in the treatment of many psychiatric disorders. One focus of clinical research is the influence of genetics on serotonin action and metabolism in psychiatric settings. Such studies have revealed that the variation in the promoter region of the serotonin transporter protein accounts for nearly 10% of total variance in anxiety-related personality,[8] and the effect of this gene on depression was found to interact with the environment.[9]

Levels of serotonin in the brain show association with aggression,[10] and a mutation in the gene which codes for the 5-HT_{2A} receptor may double the risk of suicide for those with that genotype.[11]

In the ultimatum game, participants whose serotonin levels have been artificially lowered will reject unfair offers more often than players with normal serotonin levels.[12]

Serotonin also has effects on appetite, sleep and general metabolism. In the blood, the major storage site is platelets, which collect serotonin from plasma. Bleeding causes serotonin release which constricts blood vessels.[13] Irritants present in food trigger the enterochromaffin cells to release serotonin to increase peristaltic movements for emptying of the gut. Leakage of intestinal serotonin into the bloodstream at a rate faster than the platelets can absorb it increases free serotonin in the blood, which activates 5HT3 receptors in the chemoreceptor trigger zone that stimulate vomiting. [14]

Serotonin also acts as a growth factor. Liver damage increases cellular expression of 5-HT2A and 5-HT2B receptors.[15] Serotonin present in the blood then stimulates cellular growth to repair liver damage.[16] 5HT2B receptors also activate osteoblasts, which build up bone.[17] However, serotonin also activates osteoclasts, which degrade bone.[18][19]

Serotonin in the central nervous system is not essential to viability in some mammals, as shown for mice that are genetically altered so that they are unable to produce serotonin in the brain stem. These mice can live into adulthood and even give birth to live pups.[20] Although brain serotonin is not essential for viability, its ablation causes impairment such as growth retardation, 50% mortality in the first four weeks of postnatal life, and effects on various physiological and behavioral pathways that originate from the autonomic nervous system. Specifically, mice dams that lack serotonin in the brain are less able to rear pups and show more aggression towards other mice.[20]

[edit] Pathology

Defective signalling of serotonin in the brain may be the root cause of sudden infant death syndrome (SIDS). Scientists from the European Molecular Biology Laboratory in Monterotondo, Italy,[30] 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 that low levels of serotonin in the animals' brainstems, which control heartbeat and breathing, may have caused sudden death, researchers said in the July 4, 2008 issue of Science.[31]

If neurons that make serotonin — serotonergic neurons — are abnormal in infants, there is a risk of sudden infant death syndrome (SIDS).[32][33] Low levels of serotonin may also be associated with intense spiritual experiences.[34]

Recent research conducted at Rockefeller University shows that both in patients who suffer from depression and in mice that model the disorder, levels of the p11 protein are decreased. This protein is related to serotonin transmission within the brain.[35]

Obsessive-compulsive disorder (OCD) can be a debilitating disorder with the following two anxiety-related essential features: obsessions (undesirable, recurrent, disturbing thoughts) and compulsions (repetitive or ritualized behaviors). SSRIs, and other medicines which alter serotonin levels, have been approved to be used to treat symptoms of OCD.

Dopamine

From Wikipedia, the free encyclopedia

Dopamine is a neurotransmitter occurring in a wide variety of animals, including both vertebrates and invertebrates. In the brain, this phenethylamine functions as a neurotransmitter, activating the five types of dopamine receptors — D_1, D_2, D_3, D_4, and D_5, and their variants. Dopamine is produced in several areas of the brain, including the substantia nigra and the ventral tegmental area.[1] Dopamine is also a neurohormone released by the hypothalamus. Its main function as a hormone is to inhibit the release of prolactin from the anterior lobe of the pituitary.

Dopamine can be supplied as a medication that acts on the sympathetic nervous system, producing effects such as increased heart rate and blood pressure. However, because dopamine cannot cross the blood-brain barrier, dopamine given as a drug does not directly affect the central nervous system. To increase the amount of dopamine in the brains of patients with diseases such as Parkinson's disease and dopa-responsive dystonia, L-DOPA (levodopa), which is the precursor of dopamine, can be given because it can cross the blood-brain barrier.

[edit] Functions in the brain

Dopamine has many functions in the brain, including important roles in behavior and cognition, voluntary movement, motivation and reward, inhibition of prolactin production (involved in lactation), sleep, mood, attention, and learning. Dopaminergic neurons (i.e., neurons whose primary neurotransmitter is dopamine) are present chiefly in the ventral tegmental area (VTA) of the midbrain, the substantia nigra pars compacta, and the arcuate nucleus of the hypothalamus.

A common hypothesis, though not uncontroversial[4], is that dopamine has a function of transmitting reward prediction error. According to this hypothesis, the phasic responses of dopamine neurons are observed when an unexpected reward is presented. These responses transfer to the onset of a conditioned stimulus after repeated pairings with the reward. Further, dopamine neurons are depressed when the expected reward is omitted. Thus, dopamine neurons seem to encode the prediction error of rewarding outcomes. In nature, we learn to repeat behaviors that lead to maximize rewards. Dopamine is therefore believed to provide a teaching signal to parts of the brain responsible for acquiring new behavior. Temporal difference learning provides a computational model describing how the prediction error of dopamine neurons is used as a teaching signal.

In insects, a similar reward system exists, using octopamine, a chemical relative of dopamine.

Movement

Via the dopamine receptors, D_{1-5}, dopamine reduces the influence of the indirect pathway, and increases the actions of the direct pathway within the basal ganglia. Insufficient dopamine biosynthesis in the dopaminergic neurons can cause Parkinson's disease, in which a person loses the ability to execute smooth, controlled movements.

[edit] Cognition and frontal cortex

In the frontal lobes, dopamine controls the flow of information from other areas of the brain. Dopamine disorders in this region of the brain can cause a decline in neurocognitive functions, especially memory, attention, and problem-solving. Reduced dopamine concentrations in the prefrontal cortex are thought to contribute to attention deficit disorder. It has been found that D1 receptors[7] as well as D4 receptors[8] are responsible for the cognitive-enhancing effects of dopamine. On the converse, however, anti-psychotic medications act as dopamine antagonists and are used in the treatment of positive symptoms in schizophrenia, although the older, so-called "typical" antipsychotics most commonly act on D2 receptors[9], while the atypical drugs also act on D1, D3 and D4 receptors[10][11].

[edit] Regulating prolactin secretion

Dopamine is the primary neuroendocrine inhibitor of the secretion of prolactin from the anterior pituitary gland.[12] Dopamine produced by neurons in the arcuate nucleus of the hypothalamus is secreted into the hypothalamo-hypophysial blood vessels of the median eminence, which supply the pituitary gland. The lactotrope cells that produce prolactin, in the absence of dopamine, secrete prolactin continuously; dopamine inhibits this secretion. Thus, in the context of regulating prolactin secretion, dopamine is occasionally called **prolactin-inhibiting factor** (**PIF**), **prolactin-inhibiting hormone** (**PIH**), or **prolactostatin**. Prolactin also seems to inhibit dopamine release, such as after orgasm, and is chiefly responsible for the refractory period.

[edit] Motivation and pleasure

Main article: motivation

[edit] Reinforcement

Dopamine is commonly associated with the **pleasure system** of the brain, providing feelings of enjoyment and reinforcement to motivate a person proactively to perform certain activities. Dopamine is released (particularly in areas such as the nucleus accumbens and prefrontal cortex) by naturally rewarding experiences such as food, sex, drugs, and neutral stimuli that become associated with them. Recent studies indicate that aggression may also stimulate the release of dopamine in this way. This theory is often discussed in terms of drugs such as cocaine, nicotine, and amphetamines, which directly or indirectly lead to an increase of dopamine in the mesolimbic reward pathway of the brain, and in relation to neurobiological theories of chemical addiction, arguing that this dopamine pathway is pathologically altered in addicted persons.[13][14][15]

Dopamine, learning, and reward-seeking behavior

Dopaminergic neurons of the midbrain are the main source of dopamine in the brain.[16] Dopamine has been shown to be involved in the control of movements, the signaling of error in prediction of reward, motivation, and cognition. Cerebral dopamine depletion is the hallmark of Parkinson's disease.[16] Other pathological states have also been associated with dopamine dysfunction, such as schizophrenia, autism, and attention deficit hyperactivity disorder in children, as well as drug abuse.

Dopamine is closely associated with reward-seeking behaviors, such as approach, consumption, and addiction.[16] Recent researches suggest that the firing of dopaminergic neurons is a motivational substance as a consequence of reward-anticipation. This hypothesis is based on the evidence that, when a reward is greater than expected, the firing of certain dopaminergic neurons increases, which consequently increases desire or motivation towards the reward.[16] However, recent research finds that while some dopaminergic neurons react in the way expected of reward neurons, others do not and seem to respond in regard to unpredictability.[17] This research finds the reward neurons predominate in the ventromedial region in the substantia nigra pars compacta as well as the ventral tegmental area. Neurons in these areas project mainly to the ventral striatum and thus might transmit value-related information in regard reward values.[17] The nonreward neurons are predominate in the dorsolateral area of the substantia nigra pars compacta which projects to the dorsal striatum and may relate orienting behaviour.[17] It has been suggested that the difference between these two types of dopaminergic neurons arises from their input: reward linked ones have input from the basal forebrain while the nonreward related ones from the lateral habenula.[17]

[edit] Sociability

Sociability is also closely tied to dopamine neurotransmission. Low D2 receptor-binding is found in people with social anxiety. Traits common to negative schizophrenia (social withdrawal, apathy, anhedonia) are thought to be related to a hypodopaminergic state in certain areas of the brain. In instances of bipolar disorder, manic subjects can become hypersocial, as well as hypersexual. This is credited to an increase in dopamine, because mania can be reduced by dopamine-blocking anti-psychotics.[23]

[edit] Processing of pain

Dopamine has been demonstrated to play a role in pain processing in multiple levels of the central nervous system including the spinal cord [24], periaqueductal gray (PAG)[25], thalamus [26], basal ganglia[27][28] insular cortex [29][30] and cingulate cortex.[31] Accordingly, decreased levels of dopamine have been associated with painful symptoms that frequently occur in Parkinson's disease.[32] Abnormalities in dopaminergic neurotransmission have also been demonstrated in painful clinical conditions, including burning mouth syndrome,[33] fibromyalgia [34][35] and restless legs syndrome.[36] In general, the analgesic capacity of dopamine occurs as a result of dopamine D2 receptor activation; however, exceptions to this exist in the PAG, in which dopamine D1 receptor activation attenuates pain presumably *via* activation of neurons involved in descending inhibition.[37] In addition, D1 receptor activation in the insular cortex appears to attenuate subsequent pain-related behavior.

[edit] Salience

Dopamine may also have a role in the salience of potentially important stimuli, such as sources of reward or of danger.[38] This hypothesis argues that dopamine assists decision-making by influencing the priority, or level of desire, of such stimuli to the person concerned.

[edit] Behavior disorders

Deficient dopamine neurotransmission is implicated in attention-deficit hyperactivity disorder, and stimulant medications used to successfully treat the disorder increase dopamine neurotransmission, leading to decreased symptoms.[39]

The long term use of levodopa in Parkinson's disease has been linked to the so-called dopamine dysregulation syndrome.[40]

[edit] Latent inhibition and creative drive

Dopamine in the mesolimbic pathway increases general arousal and goal directed behaviors and decreases latent inhibition; all three effects increase the creative drive of idea generation. This has led to a three-factor model of creativity involving the frontal lobes, the temporal lobes, and mesolimbic dopamine.[41]

[edit] Chemoreceptor trigger zone

Dopamine is one of the neurotransmitters implicated in the control of nausea and vomiting via interactions in the chemoreceptor trigger zone. Metoclopramide is a D2-receptor antagonist that functions as a prokinetic/antiemetic.

[edit] Links to psychosis

Main article: Dopamine hypothesis of schizophrenia

Abnormally high dopamine action has also been strongly linked to psychosis and schizophrenia,[42] Dopamine neurons in the mesolimbic pathway are particularly associated with these conditions. Evidence comes partly from the discovery of a class of drugs called the phenothiazines (which block D_2 dopamine receptors) that can reduce psychotic symptoms, and partly from the finding that drugs such as amphetamine and cocaine (which are known to greatly increase dopamine levels) can cause psychosis.[43] Because of this, most modern antipsychotic medications, for example, risperidone, are designed to block dopamine function to varying degrees.