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Research Article

A Review on Neurotransmitters: Dopamine & Serotonin

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Abstract

Dopamine, and serotonin are essential neurotransmitters that contribute to a wide range of physiological and psychological processes, influencing our mood, behaviour, social interactions, and overall well-being. While dopamine is primarily associated with the brain's reward system, motivation, and motor control, serotonin is known for its involvement in mood regulation, emotional well-being, and social behaviour. Both neurotransmitters are involved in complex interactions with other neurotransmitter systems and brain regions, influencing a wide range of physiological and psychological processes. Dysregulation of these neurotransmitter systems can have significant implications for mental health and may contribute to the development of various neurological and psychiatric disorders. Therefore, understanding the pharmacology of these two neurotransmitters is crucial for developing treatments for a wide range of neurological and psychiatric conditions.

Key words: antimicrobial; human microflora; agar disc diffusion assays; minimum inhibitory concentration; synergistic effects; additive effects; phytochemical composition;bioactive compounds

Introduction

Neurotransmitters are chemical messengers that transmit signals across synapses, and from neurons to other cells in the body, like muscle cells or glands. They play an important role in the communication within the nervous system and are essential for regulating various physiological and psychological processes [1]. There are several types of neurotransmitters, each with specific functions such as dopamine, serotonin, norepinephrine, acetylcholine, gamma-aminobutyric acid (GABA), glutamate, and endorphins. Some neurotransmitters like monoamines, norepinephrine, serotonin may be present at different stages of development. Monoamines are detectable before neurons become fully differentiated. Norepinephrine is, elevated in the notochord, even during the early stages of embryo development; excitatory amino acids emerge later in ontogenesis and glutamate during the perinatal period and then it is stabilized [2]. Serotonin plays a role in morphogenesis, contributing to the shaping of bodily structures. However, hypoxia can interfere with the formation of neuronal circuitry, potentially leading to long-term adverse effects on the body [3-4].

Neurotransmitters are synthesized within neurons involving enzymes and precursor molecules. After synthesis they are stored in vesicles at the presynaptic terminal of neurons. When an action potential arrives at the presynaptic terminal, it triggers the release of neurotransmitters into the synaptic cleft where it binds to specific receptor molecules on the postsynaptic membrane of the target cell. This binding triggers a series of biochemical events within the postsynaptic cell, leading to changes in its electrical activity. The effects on target cells can be excitatory (promoting the generation of action potentials) or inhibitory (reducing the generation of action potential), depending on the type of receptor activated. After its effect on the target cell, they are removed from the synaptic cleft through various mechanisms like reuptake by transporters on the presynaptic membrane, enzymatic degradation, or diffusion away from the synapse.

They play diverse roles in the nervous system, including regulating mood, emotion, cognition, motor control, sleep, appetite, and stress response. Imbalances in neurotransmitter levels have been implicated in various neurological and psychiatric disorders, such as depression, anxiety disorders, schizophrenia, Parkinson's disease, and Alzheimer's disease. In this review article we discuss the role of two important neurotransmitters dopamine and serotonin.

1.Dopamine is a neurotransmitter commonly known as pleasure chemical. It works as a neuromodulator controlling motor control and reward motivated behavior [5-6]. It is produced in the dopaminergic neurons in the ventral tegmental area of the mid brain, substantia nigra pars compacta, and arcuate nucleus of hypothalamus. In the field of pharmacology, dopamine confers motivational salience [7-9], meaning it enhances the output of stimuli or events that motivate us to complete tasks, rewarding those that encourage focus while discouraging those that cause distraction [10]. Disruption of the motivational salience system has been associated with a range of psychiatric disorders such as addiction, schizophrenia, and depression. Dopamine is rapidly absorbed from the

small intestine and, it inhibits the secretion of prolactin from anterior pituitary gland.

Synthesis and Degradation: It is synthesized in neurons and medulla of adrenal glands [11-12].

L-Phenylalanine → L-Tyrosine → L-DOPA → Dopamine

L-DOPA can be synthesized from essential amino acid phenylalanine or from non-essential tyrosine [13]. Drugs that influence dopamine synthesis typically act on enzymes involved in these pathways. As L-DOPA is commonly used in the treatment of Parkinson's disease to increase dopamine levels in the brain. The degradation of dopamine occurs by oxidoreductases, although it is also vulnerable to oxidation via direct interaction with oxygen, resulting in the formation of quinones along with various free radicals. Cofactors such as ferric iron /catalysts can accelerate this oxidation process. The production of quinones and free radicals formed by dopamine autoxidation has the potential to harm cells, suggesting that this mechanism may play a role in the cell damage observed in conditions like Parkinson's disease, attention deficit hyperactivity disorder, Tourette syndrome, schizophrenia, bipolar disorder, addiction. and other neuro diseases [14-15].

Receptors and Pharmacodynamics: Several drugs exert its effects by binding to and activating dopamine receptors located on postsynaptic neurons. There are several subtypes of dopamine receptors, classified into D1-like (D1 and D5) and D2-like (D2, D3, and D4) and human trace amine associated receptor1(hTAAR1) receptor families [16-17]. D1 to D5 receptors are metabotropic and G protein coupled receptors exerting their effects via increase/ decrease of cAMP second messengers [18]. D1 receptors can be excitatory via opening of Na channels and inhibitory via opening of K channels whereas D2 like inhibit target neurons. Thus, its impact on a target neuron is contingent upon the types of receptors present on the neuron's membrane and the internal reactions of that neuron to the second messenger cAMP. Among all receptors, D1 receptors are the most abundant in the human nervous system, followed by D2 receptors, D3, D4, and D5 receptors are found in significantly lower quantities. Drugs can bind these receptors, either as agonists (mimicking dopamine's effects) or antagonists (blocking dopamine's effects). Antipsychotic medications, act on dopamine D2 receptor antagonists, reducing dopamine neurotransmission in certain brain regions to alleviate psychotic symptoms in conditions like schizophrenia.

Psychostimulants of dopamine are amphetamine, methylphenidate, nicotine, opioid, cocaine which acts on mesolimbic pathway increasing its release from synaptic vesicles in the synaptic cleft, resulting in increased neurotransmission and ability to do work (task saliency) and arousal (wakefulness) [19-21]. Additionally, substances that directly stimulate dopamine receptors, such as recreational drugs, can have profound effects on mood and behaviour. Drugs like bupropion, are used as antidepressants and smoking cessation aids. They inhibit the reabsorption of dopamine into presynaptic neurons after its release into the synaptic cleft thus prolonging the presence of dopamine in the synaptic space, enhancing neurotransmission. Few D2 receptor binding have been reported in persons suffering from negative schizophrenia.

Dopamine induces positive chronotropic and inotropic effects on myocardial tissue, leading to increased heart rate and cardiac contractility. These effects are achieved directly by stimulating beta-adrenoceptors and indirectly by promoting the release of norepinephrine from storage sites within sympathetic nerves. In the brain, dopamine acts as an agonist to the five dopamine receptor subtypes (D1, D2, D3, D4, D5).

Found in: it is found in pulp and peels of red and yellow banana at levels of 40-50 ppm by weight [22]. Plants, such as potatoes, avocados, broccoli, and Brussels sprouts, may contain dopamine at levels of 1 ppm or higher. Citrus fruits like oranges, tomatoes, spinach, beans, and other plants have dopamine concentrations below 1 ppm. Plants synthesize dopamine from the amino acid tyrosine utilizing biochemical pathways similar to those in animals where it undergoes various metabolic pathways, yielding melanin and a different alkaloid as byproducts. L-DOPAs highest concentration present in leaves and beans pod of *Mucuna puriens* and some in *Vicia faba* [23-24]. It is present in highest concentration 4.4% dry weight in marine green algae Ulvaria obscura thus reducing its consumption by snails and isopods [25].

Other functions: it also acts as a paracrine messenger. It dilates blood vessels, in kidneys it increases sodium and urine excretion, in pancreas it reduces insulin secretion as a result glucose is increased helping in body's fight and flight function and activating epinephrine. In gut it reduces the gastrointestinal motility and protects intestinal mucosa.

We can naturally increase its level by listening to good music, doing works which we enjoy/ visit to memorable places and maintaining a healthy diet.

Symptoms of high dopamine (hyperdopaminergic**):** agitation, hypomania, psychosis, hyperactivity/ hypersexuality, paranoia, sleep disturbances.

Symptoms of low dopamine: aches and pains, tremors, difficulty in swallowing/ moving, muscle spasms, stiffness, insomnia/ excessive sleeping.

1. **Serotonin** is a multifaceted neurotransmitter with widespread effects throughout the body. It is a monoamine (5-hydroxytryptamine), neurotransmitter in the brain and nervous system. In the brain, it is involved in mood regulation and is often referred to as the "feel-good" neurotransmitter because it contributes to feelings of well-being and happiness. Imbalances in its levels have been associated with various psychiatric disorders like depression, anxiety, and obsessive-compulsive disorder (OCD). It plays role in regulating mood, appetite, sleep, memory, and other physiological functions like sleep, thermoregulation, sexual activity, vomiting, vasoconstrictions and biological rhythms [26-27]. It is primarily found in the gastrointestinal tract, blood platelets, and central nervous system.

Synthesis and Degradation: is synthesized from the amino acid tryptophan, stored in vesicles and released upon neuronal stimulation. The conversion of tryptophan to 5-hydroxytryptophan (5-HTP) by the enzyme tryptophan hydroxylase requires oxygen and the cofactor tetrahydrobiopterin [28-30].

In the 2nd step 5-HTP is converted to serotonin by the enzyme L-amino acid decarboxylase (AADC), also known as DOPA decarboxylase which removes carboxyl group from 5-HTP, resulting in the formation of serotonin.

Tryptophan→ 5-hydroxytryptophan → Serotonin

The degradation pathway involves the enzyme monoamine oxidase (MAO) which forms 5-hyroxyindoleacetaldehyde by oxidative deamination of serotonin and aldehyde dehydrogenase (ALDH) which forms 5-hyroxyindoleacetic acid and is excreted in urine.

Serotonin → 5-hydroxyindoleacetaldehyde → 5-hyroxyinoleacetic acid → Urine

Receptors and Pharmacodynamics: its receptors are proteins on the cell surface. They are classified into HT families, from 5-HT1 to 5-HT7, based on their structure and function where "5-HT" stands for 5-hydroxytryptamine. It acts as a hallucinogenic drug. All HT receptors are G protein coupled receptors which activates intracellular second messengers except HT3 which is ion channel [31]. 5-HT1 receptors: are involved in regulating neurotransmitter release, and controls mood, anxiety, and cognition. Drugs for 5-HT1 are used to treat migraine and some psychiatric disorders. 5-HT2 receptors are distributed in the central

nervous system and are involved in functions, including mood regulation, perception, and appetite. Drugs for 5-HT2 receptors are used in the treatment of depression, schizophrenia etc. 5-HT3 receptors are ion channels, allowing the passage of ions across the cell membrane when activated by serotonin. They are primarily found in the central and peripheral nervous systems and regulates nausea, vomiting, and pain perception. 5-HT4 receptors are found in the gastrointestinal tract (GIT), where they regulate gastro intestinal motility, vasoconstriction and secretion. Drugs targeting 5-HT4 receptors are used to treat constipation and irritable bowel syndrome. 5-HT6 and 5-HT7 receptors are located in the brain involved in regulating cognition, memory, and mood.

Drugs like selective serotonin reuptake inhibitors (SSRIs) are prescribed for depression and anxiety as they increase its levels in the brain. They inhibit the reuptake of serotonin, allowing more of it to remain in the synaptic space between neurons, thereby enhancing its effects.

Found in: it is found in all bilateral animals like worms, insects, fungi and plants [32-33]. In animals, it is synthesized in neurons located in the raphe nuclei of the brainstem and released into synapses where it binds to serotonin receptors on target neurons, transmitting signals. In plants it controls growth regulation, flowering, xylem sap exudation, ion permeability and plant morphogenesis [34-39]. In fruits and vegetables, it is found in banana, pine apple, tomato, walnut, basil, green onion, spinach, chicory, lettuce, Chinese cabbage, sedum, Griffonia, scarlet runner bean, raintree [40-45]. In microorganisms it plays roles in microbial physiology, such as cell growth, stress response, and communication within microbial communities. It is synthesized by amoeba in the GIT causing diarrhoea in humans [46].

Other Functions: it plays roles in appetite/ digestion, sleep-wake cycles, sexual function, and cognitive function. Disruptions in serotonin signalling have been implicated in a range of conditions beyond mood disorders, like irritable bowel syndrome, migraines, and cardiovascular disorders

Symptoms of high Serotonin (Serotonin syndrome)**:** restlessness, agitation, confusion, dilated pupils, headache, tremors, sweating, high body temperature (hyperthermia), high heart rate (tachycardia), nausea, vomiting, diarrhoea, seizures, loss of consciousness.

Symptoms of low Serotonin: depression, anxiety, mood swings, irritability, insomnia, fatigue, decreased appetite, impaired cognition, GIT problems.

Table 1: Basic differences and similarity between neurotransmitters

	Dopamine	Serotonin
Differences		
Functions	associated with the brain's reward system, involved in regulating feelings of pleasure, motivation, and reinforcement. movement, cognition, attention, and mood	"happiness" neurotransmitter involved in regulating mood, emotions, and social behaviour, sleep-wake cycles, appetite, digestion, and cognitive functions memory and learning
Brain regions	produced in substantia nigra and ventral tegmental area, has widespread projections throughout the brain, in striatum, prefrontal cortex, and limbic system	produced in the raphe nuclei of the brainstem, with projections extending in cerebral cortex, limbic system, and hypothalamus
Receptors	exerts its effects by binding to dopamine receptors, which are classified into several subtypes (D1 through D5) distributed throughout the brain and have diverse functions	serotonin receptors (H1-H7), are widely distributed in the brain and mediate various physiological and behavioural responses
Disorders	Dysregulation of dopamine is implicated in several neurological and psychiatric disorders, Parkinson's disease schizophrenia, attention deficit hyperactivity disorder (ADHD), and addiction	Imbalances in serotonin are linked to mood disorders such as depression and anxiety, obsessive-compulsive disorder (OCD), eating disorders, and certain types of migraines
Medication	Medications affecting dopamine levels or receptor activity are used to treat Parkinson's disease, schizophrenia, and ADHD	Medications targeting serotonin as selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), and serotonin agonists, are prescribed for depression, anxiety disorders, and other mood-related conditions
Similarity		
Regulation of mood		
Regulation of sleep		
Regulation of movement		
Reward and motivation		
Reward and motivation		

Conclusion:

Dopamine and serotonin are two essential neurotransmitters that play distinct but interconnected roles in regulating various aspects of brain function and behaviour. Imbalances in dopamine and serotonin levels implicated in numerous neurological and psychiatric disorders, including mood disorders, schizophrenia, Parkinson's disease, ADHD, and addiction.

Understanding the differences and similarities between dopamine and serotonin is important for developing targeted therapeutic interventions to treat these disorders. Medications that modulate dopamine or serotonin levels and receptor activity are widely used in clinical practice to manage symptoms associated with these conditions. Further research into the mechanisms underlying dopamine and serotonin function will continue to shed light on their roles in health and disease, potentially leading to the development of more effective treatments and interventions.

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Conflicts of Interest

There is no conflict of interest to be disclosed.

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