An Overview of Dopamine

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The Stories Behind Parkinson's Disease and Dopamine

In 1817, James Parkinson published "*An Essay On The Shaking Palsy*," which was the first medical document to describe Parkinson's. Parkinson named this disorder shaking palsy (paralysis agitans). However, Dr. Jean-Martin Charcot understood its importance of this report and disease after reading the essay, which he referred to as "*la maladie de Parkinson*," and the name was established.

In 1957, Dr. Arvid Carlsson demonstrated that dopamine was a brain neurotransmitter. He then found that depletion of dopamine promoted a loss of movement control. Furthermore, he reported that the precursor to dopamine, L-DOPA (or Levodopa), alleviated some of the symptoms of Parkinson's. For these achievements, the Nobel Prize in Physiology or Medicine was given to Dr. Carlsson in 2000.

Dopamine and Brain Chemistry 101

Dopamine is classified as a neurotransmitter, and it is found mostly in the central nervous system. The amino acid tyrosine, usually derived from dietary proteins, enters the brain in the circulating blood. Tyrosine is taken up into catecholamine neurons by amino acid transporters in the brain. The conversion of tyrosine to dihydroxyphenylalanine (L-DOPA) is catalyzed by the enzyme tyrosine hydroxylase. L-DOPA is converted to dopamine by the enzyme DOPA decarboxylase. This enzyme quickly changes L-DOPA to dopamine, that supplying the enzyme (DOPA decarboxylase) with additional substrate (L-DOPA) leads to increased product formation (dopamine), which is the basis of L-DOPA (or Levodopa) treatment for Parkinson's.

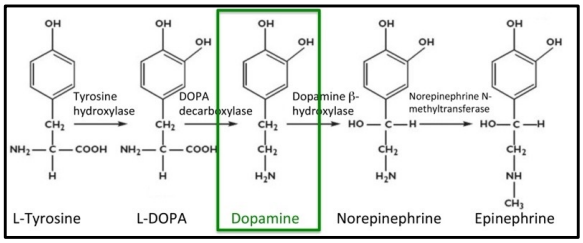
Neural Synapse and Dopamine Receptors

If you are reading this over morning coffee or tea, and as you pick up the cup, you need dopamine to activate neurons to allow your fingers to grip, move, and aim the cup to your mouth. How the brain and body function so effortlessly to accomplish our body movements is almost magical.

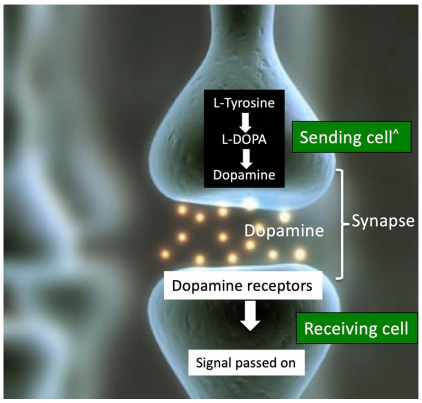
Dopamine is a chemical messenger, or neuro-transmitter. Neurotransmitters are endogenous sub-stances that transmit signals across a synapse from one neuron to another "target" neuron or to another nerve fiber, a muscle fiber, or some other structure.

There are 5 different dopamine receptors (D1, D2, D3, D4, and D5) that provide for all of the physiological functions of dopamine. Simply think of dopamine as a key that can unlock 5 similar but different locks (see Figure). The key (dopamine)-lock (dopamine receptors) interaction initiates a series of signals to the target neuron. It is important to note that dopamine receptors are G protein-coupled receptors (GPCR's), which means that when dopamine binds to the receptor signals are initiated by the receptor and the cell.

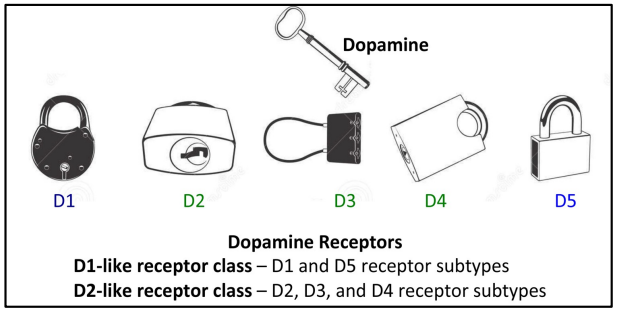
Synthesis of Dopamine



Dopamine Signaling and Synapse



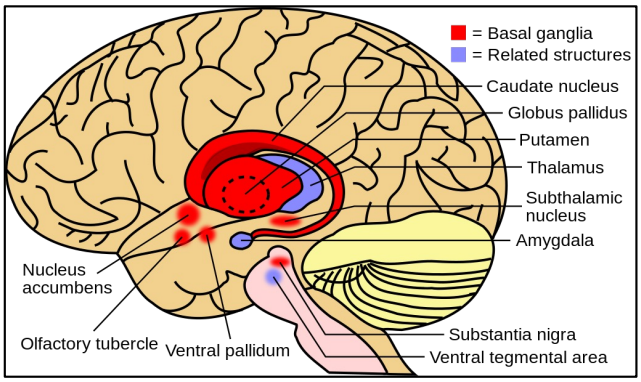
Dopamine Receptors



Basal Ganglia

Basal ganglia circuits affect movements of the contralateral body. Contralateral is occurring on or in conjunction with the opposite side of the body. As shown in the drawing on the rught, the basal ganglia is situated at the base of the forebrain brain and consists of four subcortical nuclei: striatum (caudate nucleus, putamen, and nucleus accumbens); globus pallidus (internal and external segments); subthalamic nucleus; and substantia nigra (pars compacta and pars reticulata; they are considered components of the midbrain). The basal ganglia nuclei help regulate movement, which increases and decreases motor activity, respectively.

Basal Ganglia*



*Drawing from Wikipedia

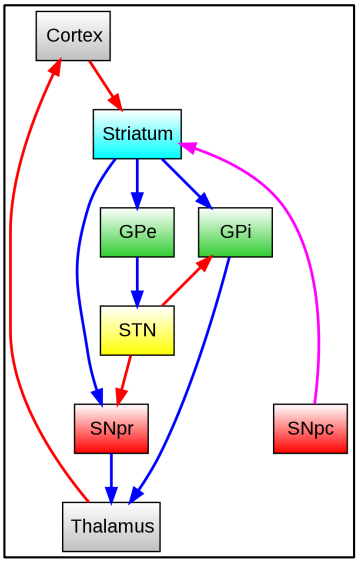
The Nigrostriatal Pathway

The frontal lobes send an excitatory signal through glutamate to the striatum. The striatum then sends additional inhibitory signals to the globus pallidus internus and the pars reticulata of the substantia nigra neurons. As a result, the globus pallidus internus and substantia nigra pars reticulata have lost their ability to inhibit the thalamus. The thalamus is now 'uncoupled' and is able to contact the cerebral cortex and says, let's move; and this signals the motor neurons down the spinal cord resulting in the desired movement.

The nigrostriatal pathway describes the link provided by dopamine between the corpus striatum and the substantia nigra. Dopamine comes from the pars compacta region of the substantia nigra. Dopamine binds to dopamine-type-1 receptors on the neurons of the striatum, which stimulates these cells. Thus, dopamine causes an increase in movement because it activates the striatum, and this is called the Direct Pathway. The Direct Pathway inhibits the internal segment of the globus pallidus.

By contrast, the striatal neurons that support the Indirect Pathway project to the external segment of the globus pallidus. From there, they contact the subthalamic nucleus, which then project to the internal segment of the globus pallidus. In the nigrostriatal pathway, the striatum with D2-type-dopamine receptors receives inhibitory dopaminergic innervation from the pars compacta of the substantia nigra. Ultimately, the Indirect Pathway turns down the thalamus motor, and then follows the motor cortex; thus, motor activity is diminished.

Direct and Indirect Nigrostriatal Pathways*

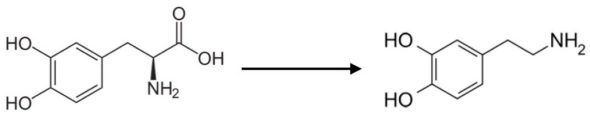


*Drawing from Wikipedia

Dopamine Physiology

Role	Physiological Action/Activity
Movement	Dopamine has a key function in controlling our movements; dopamine is part of the basal ganglia motor loop in the brain.
Reward, pleasure, and motivation	Dopamine is part of the brain's reward/pleasure system; providing feelings of pleasure and helps to motivate us doing these activities.
Cognition	Dopamine helps control the information flow of memory, attention and problem solving In the frontal lobes of the brain.
Attention	Dopamine helps in focus and attention. Vision augments the dopamine response in the brain, which then helps us focus
Sleep regulation	Dopamine helps regulate the "circadian rhythm" in the pineal gland, which is the brain process to adapt to the time of the day (light and dark cycles).
Psychosis and addiction	Dysfunction of the dopamine system is also associated with psychosis and schizophrenia. Cocaine and amphetamines have been found to inhibit the re-uptake of dopamine. Thus, amphetamines and cocaine greatly increase dopamine levels; their use can cause psychosis.

Dopamine: A Symbol of Hope



L-Dopa (Levodopa) is converted enzymatically in the brain to Dopamine.

"Levodopa/Carbidopa provides the spark to positively fire the motor neurons for better movement, posture, balance, and coordination in Parkinson's."
Frank C. Church