Nucleus accumbens

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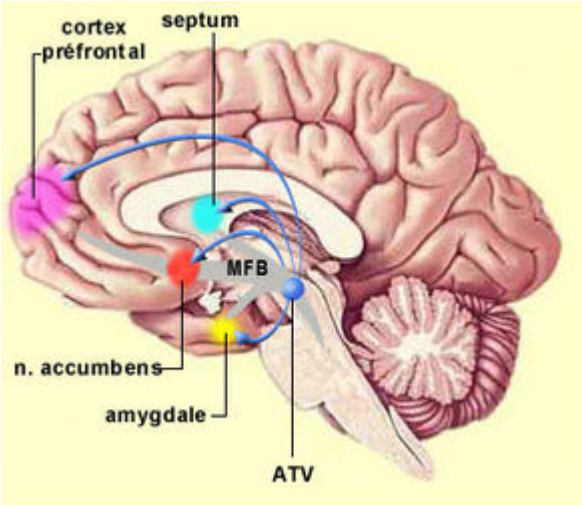
Brain: Nucleus accumbens



Nucleus accumbens visible in red.

Latin	*nucleus accumbens septi*
NeuroNames	*hier-259*
MeSH	*Nucleus+Accumbens*
NeuroLex ID	*birnlex_727*

The **nucleus accumbens** (NAcc), also known as the **accumbens nucleus** or as the **nucleus accumbens septi** (Latin for *nucleus adjacent to the septum*) is a region of the human brain in the basal forebrain rostral to the preoptic area.[1] The nucleus accumbens and the olfactory tubercle collectively form the ventral striatum, which is part of the basal nuclei.[2]

Each brain hemisphere has its own nucleus accumbens. It is located where the head of the caudate and the anterior portion of the putamen meet just lateral to the septum pellucidum. The nucleus accumbens can be divided into two structures—the nucleus accumbens core and the nucleus accumbens shell. These structures have different morphology and function.

Research has indicated the nucleus accumbens has an important role in pleasure including laughter, reward, and reinforcement learning, as well as fear, aggression, impulsivity, addiction, and the placebo effect.[3][4][5][6]

Cell types

The principal neuronal cell type found in the nucleus accumbens is the medium spiny neuron. The neurotransmitter produced by these neurons is gamma-aminobutyric acid (GABA), one of the main inhibitory neurotransmitters of the central nervous system. These neurons are also the main projection or output neurons of the nucleus accumbens.

While 95% of the neurons in the nucleus accumbens are medium spiny GABA-ergic projection neurons, other neuronal types are also found such as large aspiny cholinergic interneurons.

Output and input

Output

The output neurons of the nucleus accumbens send axon projections to the basal ganglia and the ventral analog of the globus pallidus, known as the ventral pallidum (VP). The VP, in turn, projects to the medial dorsal nucleus of the dorsal thalamus, which projects to the prefrontal cortex as well as the striatum. Other efferents from the nucleus accumbens include connections with the substantia nigra, and the pontine reticular formation.[1]

Input

Major inputs to the nucleus accumbens include prefrontal association cortices, basolateral amygdala, and dopaminergic neurons located in the ventral tegmental area (VTA), which connect via the mesolimbic pathway. Thus the nucleus accumbens is often described as one part of a cortico-striato-thalamo-cortical loop.

Dopaminergic input from the VTA is thought to modulate the activity of neurons within the nucleus accumbens. These terminals are also the site of action of highly-addictive drugs such as cocaine and amphetamine, which cause a manifold **increase in dopamine levels in the nucleus accumbens.**

Another major source of input comes from the CA1 and ventral subiculum of the hippocampus to the dorsomedial area of the Nucleus accumbens. The neurons of the hippocampus have a noteworthy correlation to slight depolarizations of cells in the nucleus accumbens, which makes them more positive and therefore more excitable. The correlated cells of these excited states of the medium spiny neurons in the Nucleus accumbens are shared equally between the subiculum and CA1. The subiculum neurons are found to hyperpolarize (increase negativity) while the CA1 neurons "ripple" (fire > 50 Hz) in order to accomplish this priming.[7]

Research

Addiction and drug use

Research using microdialysis has shown that the levels of dopamine in the extracellular fluid of the nucleus accumbens increase when rats are injected with addictive drugs such as cocaine, heroin, nicotine, or alcohol.[8] This increase in dopamine is believed to be responsible for the reinforcing effects that later stimulate drug-taking behavior. Functional-imaging studies in humans have shown that environmental cues associated with addictive drugs releases dopamine in the nucleus accumbens. However, when administered methylphenidate, drug addicted subjects had a much smaller release of dopamine in this area than non-addicted subjects. These **findings suggest** the notion that the nucleus accumbens is associated with the beginnings of drug addiction and the dorsal striatum is responsible for the augmentation of the drug habit.[8]

The nucleus accumbens has been targeted by stereotactic surgery for ablation as a treatment in China for alcoholism.[9]

Pleasure and reinforcement

Although the nucleus accumbens has traditionally been studied for its role in addiction, it plays an equal role in processing many rewards such as food and sex. The nucleus accumbens is selectively activated during the perception of pleasant, emotionally arousing pictures and during mental imagery of pleasant, emotional scenes.[10][11] A 2005 study found that it is involved in the regulation of emotions induced by music,[12] perhaps consequent to its role in mediating dopamine release. The nucleus accumbens plays a role in rhythmic timing and is considered to be of central importance to the limbic-motor interface (Mogensen).

In the 1950s, James Olds and Peter Milner implanted electrodes into the septal area of the rat and found that the rat chose to press a lever which stimulated it. It continued to prefer this even over stopping to eat or drink. This suggests that the area is the "pleasure center" of the brain and is involved in reinforcement learning.[13] In rats, *stimulation of the ventral tegmental area causes the release of dopamine in the nucleus accumbens* much in the same way as addictive drugs and natural reinforcers, such as water or food, initiate the release of dopamine in the nucleus accumbens.[14] The same results have been seen in human subjects in functional imaging studies. For example, increased dopamine concentration is seen in the extracellular fluid of the nucleus accumbens when subjects believed they were being given money, and when heterosexual males were presented pictures of attractive women.[15]

Wanting

The activation of dopamine in the nucleus accumbens is central to "wanting". Dopamine release in the accumbens occurs in anticipation of reward, and facilitates many kinds of approach and goal-oriented behaviors like exploration, affiliation, aggression, sexual

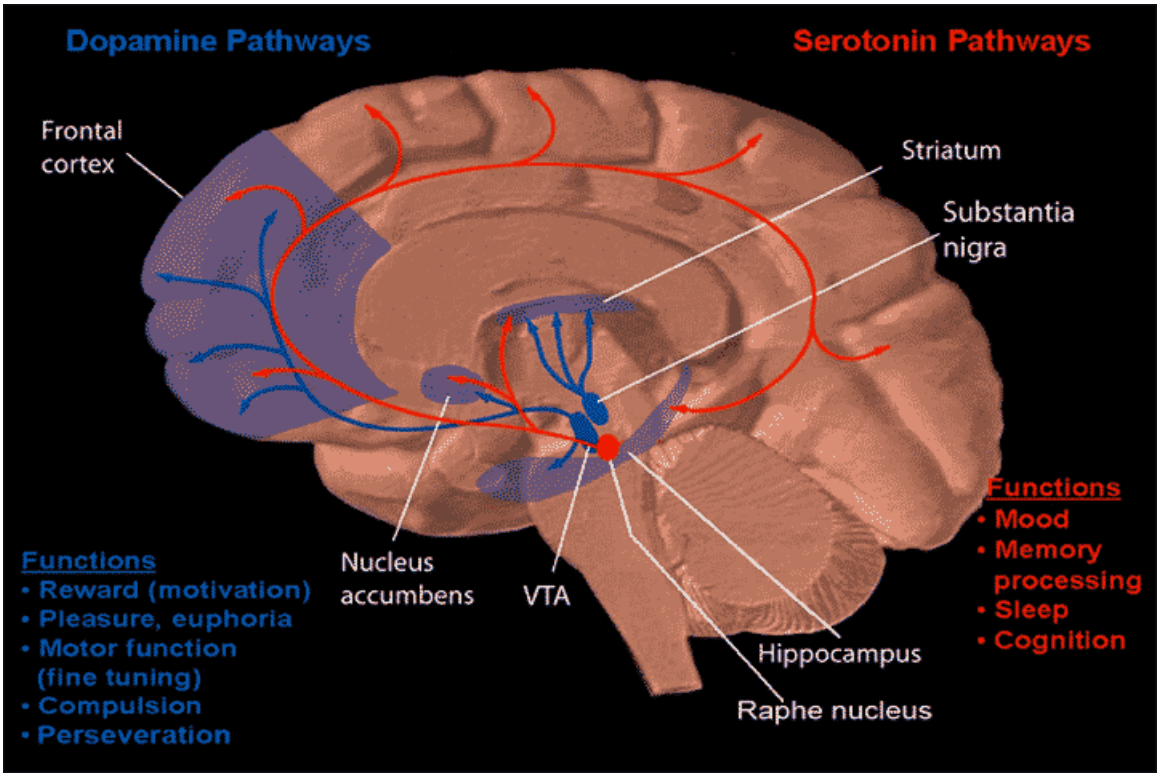
behavior, and food hoarding. Lesions to the nucleus accumbens reduce the motivation to work for reward.[16]

Maternal behavior

An fMRI study conducted in 2005 found that when mother rats were in the presence of their pups the regions of the brain involved in reinforcement, including the nucleus accumbens, were highly active.[17] Levels of dopamine increase in the nucleus accumbens during maternal behavior, while lesions in this area upset maternal behavior.[18] When human mothers are presented pictures of their children, fMRIs show an increased brain activity in the nucleus accumbens and other reinforcing brain regions and a decrease in activity in areas of the brain involved with negative emotions.[*citation needed*]

Deep brain stimulation

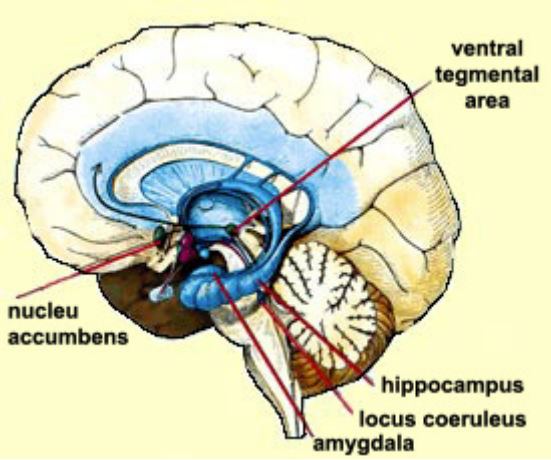
In April 2007, two research teams reported on having inserted electrodes into the nucleus accumbens in order to use deep brain stimulation to treat severe depression.[19] In 2010 experiments reported that deep brain stimulation of the nucleus accumbens was successful in decreasing depression symptoms in 50% of patients who did not respond to other treatments such as electroconvulsive therapy.[20]



THE PLEASURE CENTRES AFFECTED BY DRUGS

The nucleus accumbens definitely plays a central role in the reward circuit. Its operation is based chiefly on two essential neurotransmitters: dopamine, which promotes desire, and serotonin, whose effects include satiety and inhibition. Many animal studies have shown that all drugs increase the production of dopamine in the nucleus accumbens, while reducing that of serotonin.

But the nucleus accumbens does not work in isolation. It maintains close relations with other centres involved in the mechanisms of pleasure, and in particular, with the **ventral tegmental area (VTA)**.



Located in the midbrain, at the top of the brainstem, the VTA is one of the most primitive parts of the brain. It is the neurons of the VTA that synthesize dopamine, which their axons then send to the nucleus accumbens. The VTA is also influenced by endorphins whose receptors are targeted by opiate drugs such as heroin and morphine.

Another structure involved in pleasure mechanisms is the **prefrontal cortex**, whose role in planning and motivating action is well established. The prefrontal cortex is a significant relay in the reward circuit and also is modulated by dopamine.

The locus coeruleus, an alarm centre of the brain and packed with norepinephrine, is another brain structure that plays an important role in drug addiction. When stimulated by a lack of the drug in question, the locus coeruleus drives the addict to do anything necessary to obtain a fix.

Three structures in the limbic system also play an active part in the pleasure circuit and, consequently, in drug dependency. The first is the **amygdala**, which imparts agreeable or disagreeable affective colorations to perceptions.

The second is the **hippocampus**, the foundation of memory, which preserves the agreeable memories associated with taking the drug and, by association, all of the details of the environment in which it is taken. Sometime in the future, these details may reawaken the desire to take the drug and perhaps contribute to recidivism in the patient.

The third structure, the most anterior portion of the **insular cortex**, or insula, is regarded as part of the limbic system and is thought to possibly play a role in the active pleasure-seeking associated both with food and with psychoactive substances. **Damasio** proposed that this part of the cortex tells us about the bodily states associated with our emotional experiences. In this way, the insula might also contribute to the conscious aspect of our needs and desires.