10 Basal Nuclei (Basal Ganglia)

CHAPTER OBJECTIVE

- To describe the basal nuclei and their connections
- To relate basal nuclei functions to diseases commonly affecting this area of the nervous system

A 58-year-old man goes to a neurologist because he has noticed the development of a slight tremor of his left hand. The tremors involve all of the fingers and the thumb and are present at rest but cease during voluntary movement.

On examination, the patient tends to perform all his movements slowly, and his face has very little expression and is almost masklike. On passively moving the patient's arms, the neurologist finds that the muscles show increased tone, with a slight jerky resistance to the movements. When asked to stand up straight, the patient does so but with a stooped posture, and, when he walks, he does so by shuffling across the examining room.

The neurologist makes the diagnosis of Parkinson disease, based on her knowledge of the structure and function of the basal ganglia and their connections to the substantia nigra of the midbrain. She is able to prescribe appropriate drug therapy, which results in a great improvement in the hand tremors.

The basal nuclei play an important role in the control of posture and voluntary movement. Unlike many other parts of the nervous system concerned with motor control, the basal nuclei have no direct input or output connections with the spinal cord.

TERMINOLOGY

The term **basal nuclei** is applied to a collection of masses of gray matter situated within each cerebral hemisphere. They are the corpus striatum, the amygdaloid nucleus, and the claustrum.

Clinicians and neuroscientists use a variety of different terminologies to describe the basal nuclei. A summary of the terminologies commonly used is shown in Table 10-1. The subthalamic nuclei, the substantia nigra, and the red nucleus are functionally closely related to the basal nuclei, but they should not be included with them.

The interconnections of the basal nuclei are complex, but in this account, only the more important pathways are considered. The basal nuclei play an important role in the control of posture and voluntary movement.

CORPUS STRIATUM

The corpus striatum (Fig. 10-1; see also Atlas Plate 5) is situated lateral to the thalamus and is almost completely divided by a band of nerve fibers, the **internal capsule**, into the caudate nucleus and the lentiform nucleus. The term *striatum* is used here because of the striated appearance produced by the strands of gray matter passing through the internal capsule and connecting the caudate nucleus to the putamen of the lentiform nucleus (see below).

Table 10-1 Terminology Commonly Used to Describe the Basal Nuclei

Neurologic Structure	Basal Nucleus (Nuclei)[a]
Caudate nucleus	Caudate nucleus
Lentiform nucleus	Globus pallidus plus putamen
Claustrum	Claustrum
Corpus striatum	Caudate nucleus plus lentiform nucleus
Neostriatum (striatum)	Caudate nucleus plus putamen
Amygdaloid body	Amygdaloid nucleus

[a]The term *basal* has been used in the past to denote the position of the nuclei at the base of the forebrain.

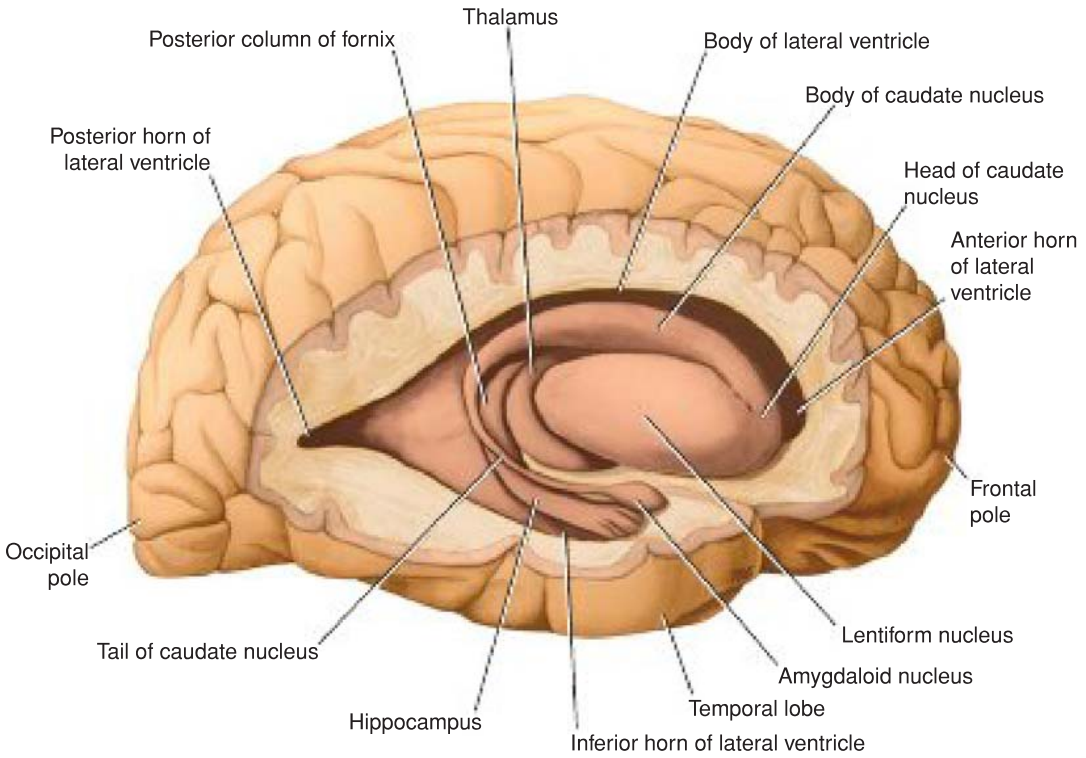


Figure 10-1 Lateral view of the right cerebral hemisphere dissected to show the position of the different basal nuclei.

Caudate Nucleus

The caudate nucleus is a large C-shaped mass of gray matter that is closely related to the lateral ventricle and lies lateral to the thalamus. The lateral surface of the nucleus is related to the internal capsule, which separates it from the lentiform nucleus (Fig. 10-2). For purposes of description, it can be divided into a head, a body, and a tail.

The **head** of the caudate nucleus is large and rounded and forms the lateral wall of the anterior horn of the lateral ventricle (see also Atlas Plate 5). The head is continuous inferiorly with the putamen of the lentiform nucleus (the caudate nucleus and the putamen are sometimes referred to as the **neostriatum** or **striatum**). Just superior to this point of union, strands of gray matter pass through the internal capsule, giving the region a striated appearance, hence the term **corpus striatum**.

The **body** of the caudate nucleus is long and narrow and is continuous with the head in the region of the interventricular foramen. The body of the caudate nucleus forms part of the floor of the body of the lateral ventricle.

The **tail** of the caudate nucleus is long and slender and is continuous with the body in the region of the posterior end of the thalamus. It follows the contour of the lateral ventricle and continues forward in the roof of the inferior horn of the lateral ventricle. It terminates anteriorly in the **amygdaloid nucleus** (see Fig. 10-1).

Lentiform Nucleus

The lentiform nucleus is a wedge-shaped mass of gray matter whose broad convex base is directed laterally and whose blade is directed medially (see Fig. 10-2; see also Atlas Plate 5). It is buried deep in the white matter of the cerebral hemisphere and is related medially to the internal capsule, which separates it from the caudate nucleus and the thalamus. The lentiform nucleus is related laterally to a thin sheet of white matter, the **external capsule**, which separates it from a thin sheet of gray matter, called the **claustrum**. The claustrum, in turn, separates the external capsule from the subcortical white matter of the insula. A vertical plate of white matter divides the nucleus into a larger, darker lateral portion, the **putamen**, and an inner lighter portion, the **globus pallidus**. The paleness of the globus pallidus is due to the presence of a high concentration of myelinated nerve fibers. Inferiorly at its anterior end, the putamen is continuous with the head of the caudate nucleus (see Fig. 10-1).

AMYGDALOID NUCLEUS

The amygdaloid nucleus is situated in the temporal lobe close to the uncus (see Fig. 10-1). The amygdaloid nucleus is considered to be part of the limbic system and is described in Chapter 9. Through its connections, it can influence the body's response to environmental changes. In the sense of fear, for example, it can change

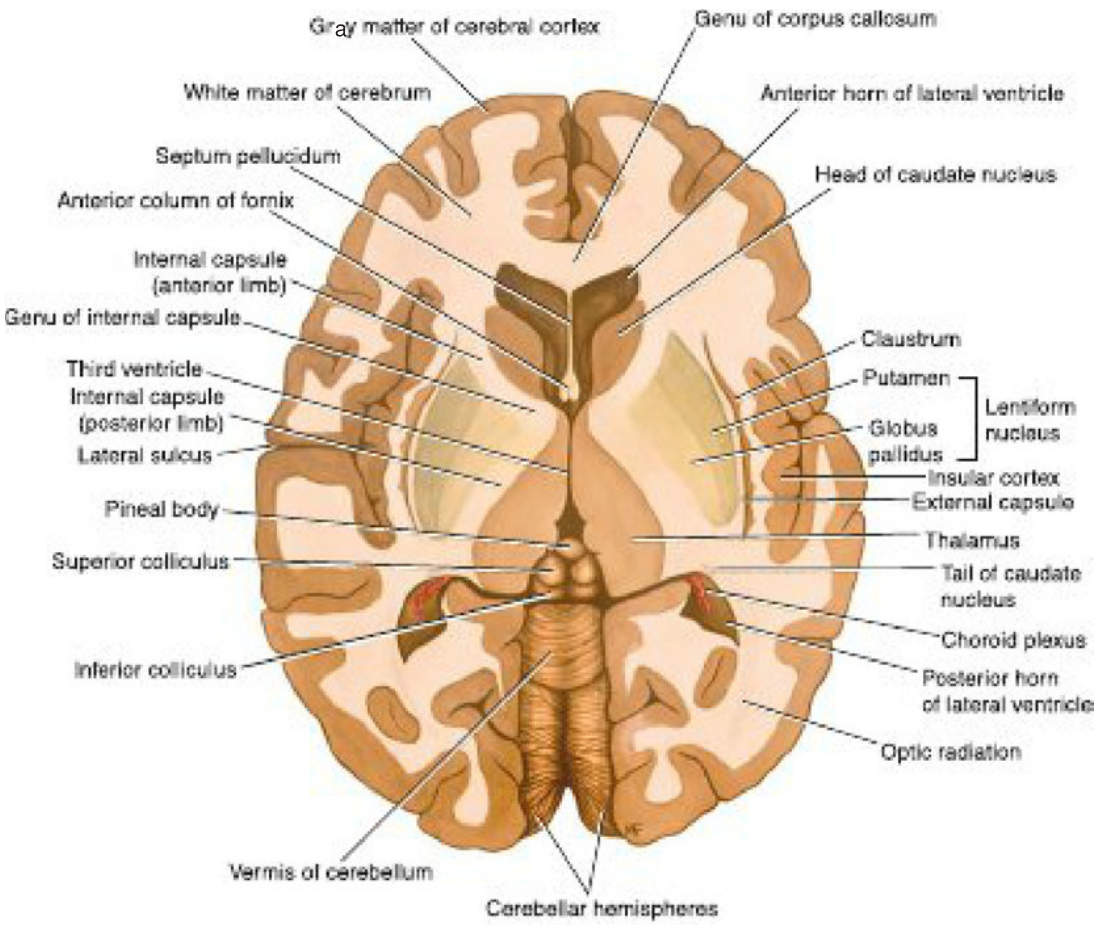


Figure 10-2 Horizontal section of the cerebrum, as seen from above, showing the relationships of the different basal nuclei.

the heart rate, blood pressure, skin color, and rate of respiration.

SUBSTANTIA NIGRA AND SUBTHALAMIC NUCLEI

The substantia nigra of the midbrain and the subthalamic nuclei of the diencephalon are functionally closely related to the activities of the basal nuclei and are described elsewhere (see pp. 211 and 253). The neurons of the substantia nigra are dopaminergic and inhibitory and have many connections to the corpus striatum. The neurons of the subthalamic nuclei are glutaminergic and excitatory and have many connections to the globus pallidus and substantia nigra.

CLAUSTRUM

The claustrum is a thin sheet of gray matter that is separated from the lateral surface of the lentiform nucleus by the external capsule (see Fig. 10-2). Lateral to the claustrum is the subcortical white matter of the insula. The function of the claustrum is unknown.

CONNECTIONS OF THE CORPUS STRIATUM AND GLOBUS PALLIDUS

The caudate nucleus and the putamen form the main sites for receiving input to the basal nuclei. The globus pallidus forms the major site from which the output leaves the basal nuclei.

They receive no direct input from or output to the spinal cord.

Corpus Striatum Afferent Fibers

Projections to the corpus striatum include corticostriate, thalamostriate, nigrostriatal, and brainstem striatal fibers.

Corticostriate Fibers

All parts of the cerebral cortex send axons to the caudate nucleus and the putamen (Fig. 10-3). Each part of the cerebral cortex projects to a specific part of the caudate–putamen complex. Most of the projections are from the cortex of the same side. The largest input is from the sensory motor cortex. Glutamate is the neurotransmitter of the corticostriate fibers (Fig. 10-4).

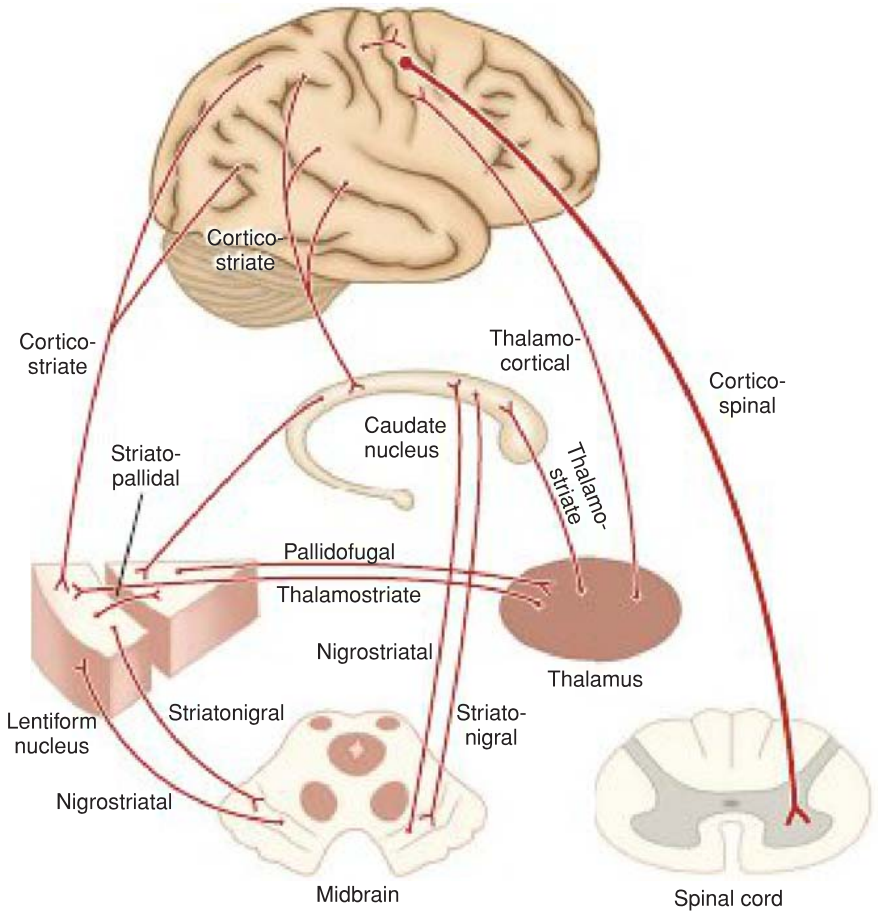


Figure 10-3 Some of the main connections between the cerebral cortex, the basal nuclei, the thalamic nuclei, the brainstem, and the spinal cord.

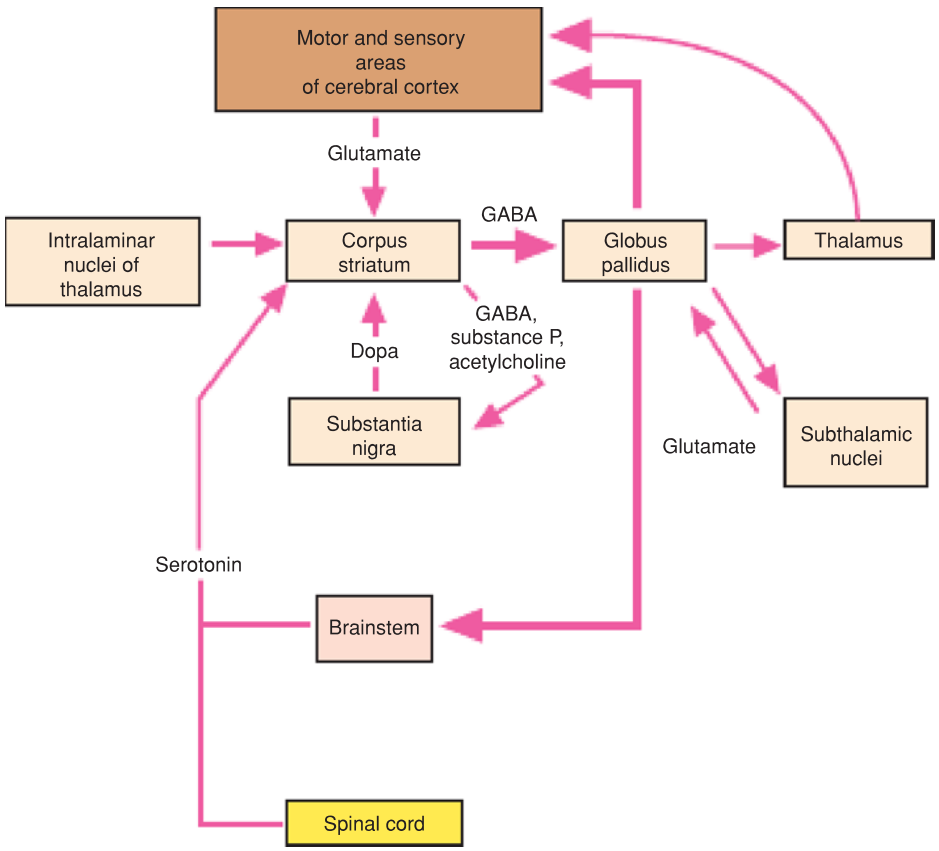


Figure 10-4 Basal nuclei pathways showing the known neurotransmitters.

Thalamostriate Fibers

The intralaminar nuclei of the thalamus send large numbers of axons to the caudate nucleus and the putamen (see Fig. 10-3).

Nigrostriatal Fibers

Neurons in the substantia nigra send axons to the caudate nucleus and the putamen (see Figs. 10-3 and 10-4) and liberate dopamine at their terminals as the neurotransmitter. These fibers are believed to be inhibitory in function.

Brainstem Striatal Fibers

Ascending fibers from the brainstem end in the caudate nucleus and putamen and liberate serotonin at their terminals as the neurotransmitter. These fibers are thought to be inhibitory in function.

Corpus Striatum Efferent Fibers

Projections from the corpus striatum include striatopallidal and striatonigral fibers.

Striatopallidal Fibers

Striatopallidal fibers pass from the caudate nucleus and putamen to the globus pallidus (see Fig. 10-3). They have γ-aminobutyric acid (GABA) as their neurotransmitter (see Fig. 10-4).

Striatonigral Fibers

Striatonigral fibers pass from the caudate nucleus and putamen to the substantia nigra (see Fig. 10-3). Some of the fibers use GABA or acetylcholine as the neurotransmitter, while others use substance P (see Fig. 10-4).

Globus Pallidus Afferent Fibers

Striatopallidal fibers pass from the caudate nucleus and putamen to the globus pallidus. As noted previously, these fibers have GABA as their neurotransmitter (Fig. 10-4).

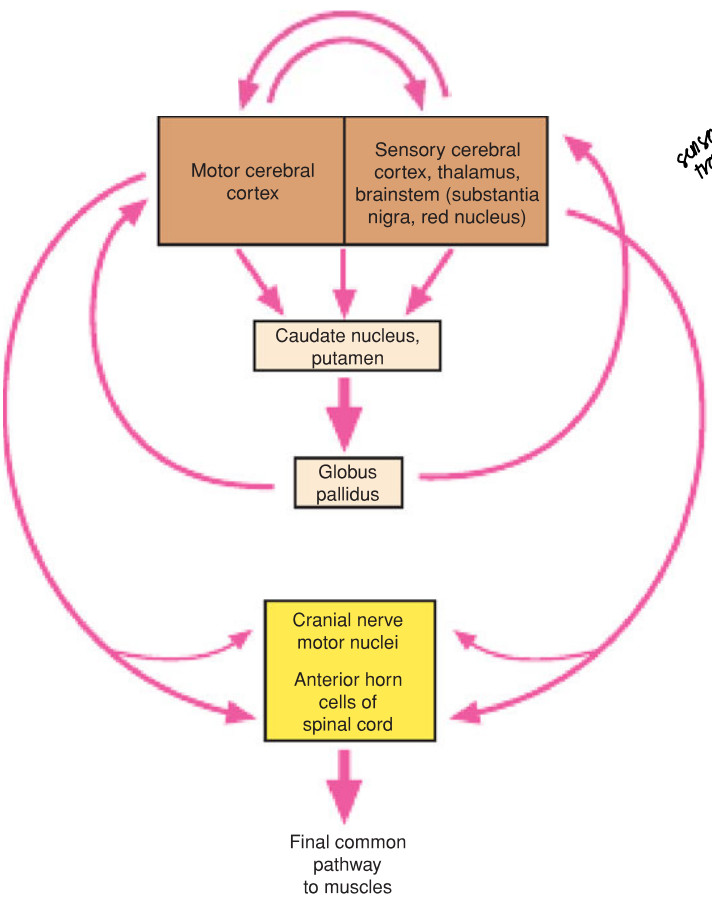
Globus Pallidus Efferent Fibers

Pallidofugal fibers are complicated and can be divided into groups: (1) the **ansa lenticularis**, which pass to the thalamic nuclei; (2) the **fasciculus lenticularis**, which pass to the subthalamus; (3) the **pallidotegmental** fibers, which terminate in the caudal tegmentum of the midbrain; and (4) the **pallidosubthalamic fibers**, which pass to the subthalamic nuclei.

BASAL NUCLEI FUNCTIONS

The basal nuclei (Fig. 10-5) are joined together and connected with many different regions of the nervous system by a very complex number of neurons.

Basically, the corpus striatum receives afferent information from most of the cerebral cortex, the thalamus,



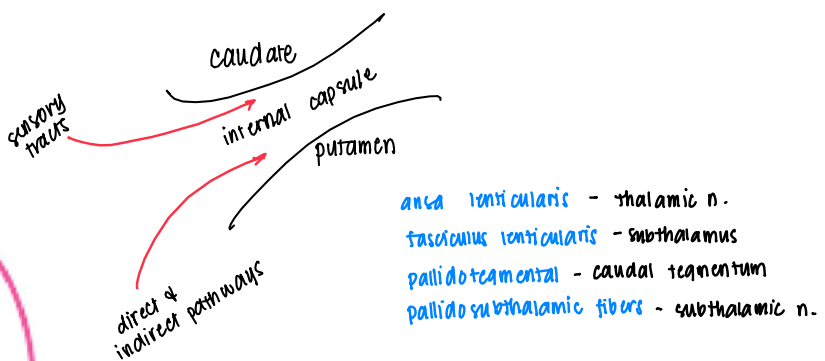


Figure 10-5 Diagram showing the main functional connections of the basal nuclei and how they can influence muscle activity.

the subthalamus, and the brainstem, including the substantia nigra. The information is integrated within the corpus striatum, and the outflow passes back to the areas listed above. This circular pathway is believed to function as follows.

The activity of the basal nuclei is initiated by information received from the premotor and supplemental areas of the motor cortex, the primary sensory cortex, the thalamus, and the brainstem. The outflow from the basal nuclei is channeled through the globus pallidus, which then influences the activities of the motor areas of the cerebral cortex or other motor centers in the brainstem. Thus, the basal nuclei control muscular movements by influencing the cerebral cortex and have no direct control through descending pathways to the brainstem and spinal cord. In this way, the basal nuclei assist in the regulation of voluntary movement and the learning of motor skills.

Writing the letters of the alphabet, drawing a diagram, passing a football, using the vocal cords in talking and singing, and using the eye muscles when looking at an object are a few examples where the basal nuclei influence the skilled cortical motor activities.

Destruction of the primary motor cerebral cortex prevents the individual from performing fine discrete movements of the hands and feet on the opposite side of the body (see p. 290). However, the individual is still capable of performing gross crude movements of the opposite limbs. If destruction of the corpus striatum then takes place, paralysis of the remaining movements of the opposite side of the body occurs.

The basal nuclei not only influence the execution of a particular movement of, say, the limbs but also help prepare for the movements. This may be achieved by controlling the axial and girdle movements of the body and the positioning of the proximal parts of the limbs. The activity in certain neurons of the globus pallidus increases before active movements take place in the distal limb muscles. This important preparatory function enables the trunk and limbs to be placed in appropriate positions before the primary motor part of the cerebral cortex activates discrete movements in the hands and feet.

Clinical Notes

Disorders of the basal nuclei are of two general types. **Hyperkinetic disorders** involve excessive and abnormal movements, such as seen with chorea, athetosis, and ballism. **Hypokinetic disorders** involve a lack or slowness of movement. Parkinson disease includes both types of motor disturbances.

Chorea

In chorea, the patient exhibits involuntary, quick, jerky, irregular movements that are nonrepetitive. Swift grimaces and sudden movements of the head or limbs are good examples.

Huntington Disease

Huntington disease is an autosomal dominant inherited disease, with the onset occurring most often in adult life. Death occurs 15 to 20 years after onset. The disease has been traced to a single gene defect on chromosome 4. This gene encodes a protein, **huntingtin**, the function of which is not known. The codon (CAG) that encodes glutamine is repeated many more times than normal. The disease affects men and women with equal frequency and unfortunately often reveals itself only after they have had children.

Patients have the following characteristic signs and symptoms:

1. **Choreiform movements** first appear as involuntary movements of the extremities and twitching of the face (facial grimacing). Later, more muscle groups are involved, so the patient becomes immobile and unable to speak or swallow.
2. **Progressive dementia** occurs with loss of memory and intellectual capacity.

In this disease, the GABA-secreting, substance P–secreting, and acetylcholine-secreting neurons of the striatonigral-inhibiting pathway degenerate. This results in the dopa-secreting neurons of the substantia nigra becoming overactive; thus, the nigrostriatal pathway inhibits the caudate nucleus and the putamen (Fig. 10-6). This inhibition produces the abnormal movements seen in this disease. Computed tomography scans show enlarged lateral ventricles due to degeneration of the caudate nuclei. Medical treatment of Huntington chorea has been disappointing.

Sydenham Chorea

Sydenham chorea (St. Vitus dance) is a disease of childhood in which rapid, irregular, involuntary movements of the limbs, face, and trunk occur. The condition is associated with rheumatic fever. The antigens of the streptococcal bacteria are similar in structure to the proteins present in the membranes of striatal neurons. The host's antibodies not only combine with the bacterial antigens but also attack the membranes of the neurons of the basal ganglia. This results in the production of choreiform movements, which are fortunately transient, and full recovery is made.

Hemiballismus

Hemiballismus is a form of involuntary movement confined to one side of the body. It usually involves the proximal extremity musculature, and the limb suddenly flies about out of control in all directions. The lesion, which is usually a small stroke, occurs in the opposite subthalamic nucleus or its connections; smooth movements of different parts of the body are integrated in the subthalamic nucleus.

Parkinson Disease

Parkinson disease is a progressive disease of unknown cause that commences between the ages of 45 and 55 years. It is associated with neuronal degeneration in the **substantia nigra** and, to a lesser extent, in the **globus pallidus**, **putamen**, and **caudate nucleus**. The disease affects about 1 million people in the United States.

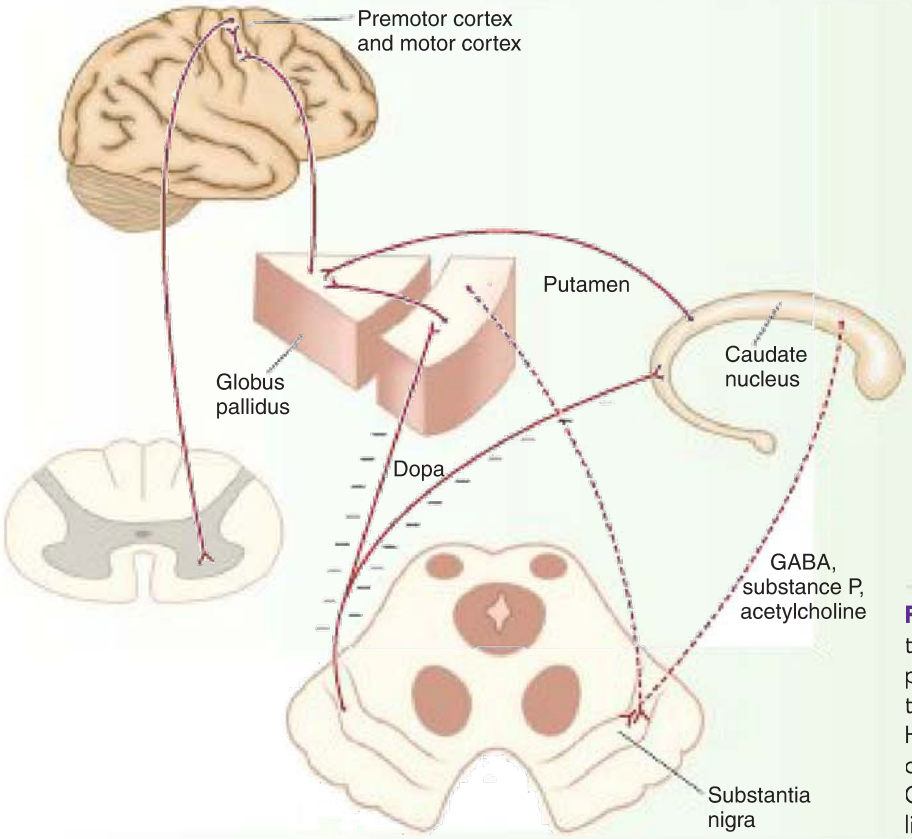


Figure 10-6 Diagram showing the degeneration of the inhibitory pathway between the corpus striatum and the substantia nigra seen in Huntington disease and the consequent reduction in the liberation of GABA, substance P, and acetylcholine in the substantia nigra.

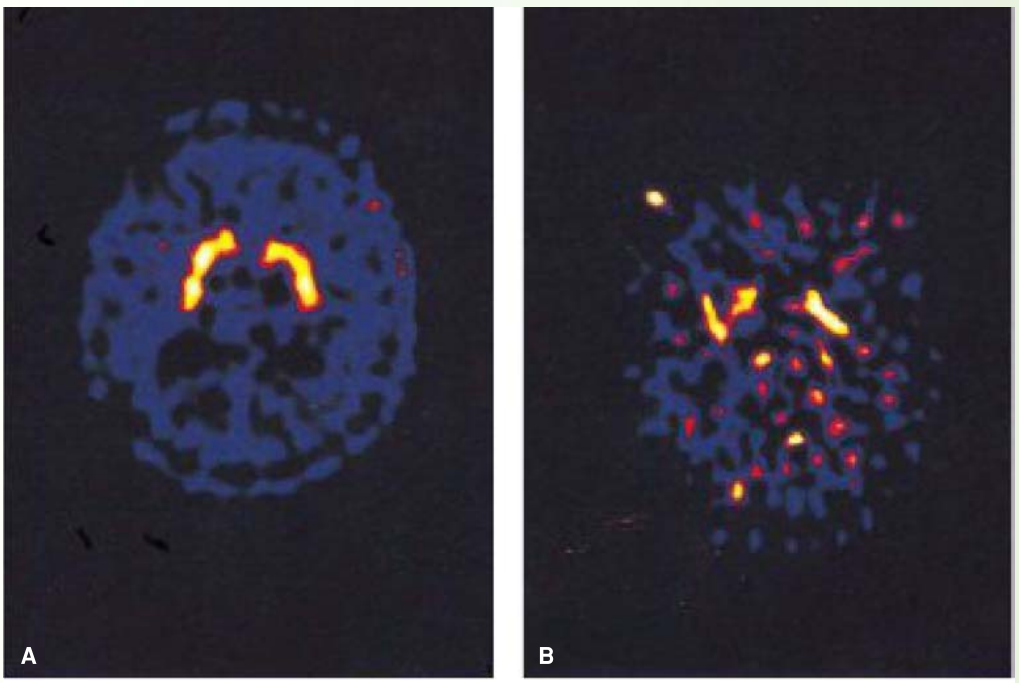


Figure 10-7 Axial (horizontal) positron emission tomography (PET) scans of a normal brain (**A**) and the brain of a patient with early Parkinson disease (**B**) following the injection of 18-F-fluorodopa. The normal brain image shows large amounts of the compound (yellow areas) distributed throughout the corpus striatum in both cerebral hemispheres. In the patient with Parkinson disease, the brain image shows that the total amount of the compound is low, and it is unevenly distributed in the corpus striatum. (Courtesy Dr. Holley Dey.)

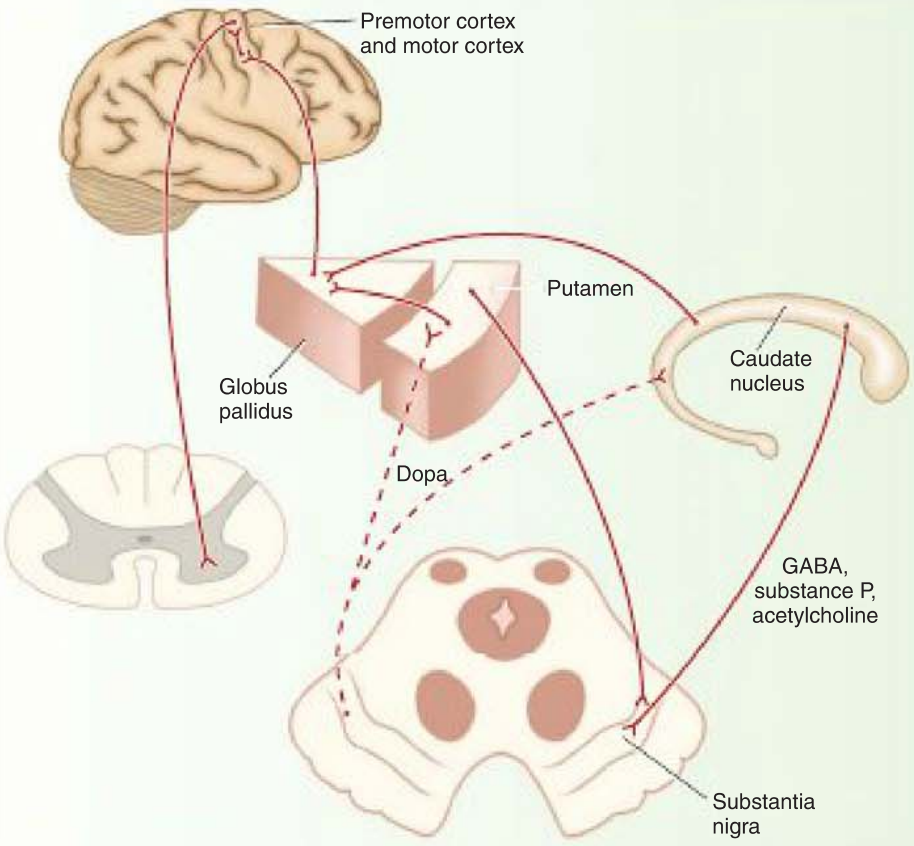


Figure 10-8 Diagram showing the degeneration of the inhibitory pathway between the substantia nigra and the corpus striatum in Parkinson disease and the consequent reduction in the release of the neurotransmitter dopamine in the striatum.

The degeneration of the neurons of the substantia nigra that send their axons to the corpus striatum results in a reduction in the release of the neurotransmitter dopamine within the corpus striatum (Figs. 10-7 and 10-8). This leads to hypersensitivity of the dopamine receptors in the postsynaptic neurons in the striatum.

Patients have the following characteristic signs and symptoms:

1. **Tremor.** This is the result of the alternating contraction of agonists and antagonists. The tremor is slow and occurs most obviously when the limbs are at rest. It disappears during sleep. It should be distinguished from the intention tremor seen in cerebellar disease, which only occurs when purposeful active movement is attempted.
2. **Rigidity.** This differs from the rigidity caused by lesions of the upper motor neurons in that it is present to an equal extent in opposing muscle groups. If the tremor is absent, the rigidity is felt as resistance to passive movement and is sometimes referred to as **plastic** rigidity. If the tremor is present, the muscle resistance is overcome as a series of jerks, called **cogwheel** rigidity.
3. **Bradykinesis.** Initiating (**akinesia**) and performing new movements is difficult. The movements are slow, the face is expressionless, and the voice is slurred and unmodulated. Swinging of the arms in walking is lost.
4. **Postural disturbances.** The patient stands with a stoop, and his or her arms are flexed. The patient walks by taking short steps and often is unable to stop. In fact, he or she may break into a shuffling run to maintain balance.
5. Neither loss of muscle power nor loss of sensibility occurs. Since the corticospinal tracts are normal, the superficial abdominal reflexes are normal, and no Babinski response is seen. The deep tendon reflexes are normal.

In a few types of Parkinson disease, the cause is known. **Postencephalitic** parkinsonism developed following the viral encephalitis outbreak of 1916 to 1917, in which damage occurred to the basal nuclei. **Iatrogenic** parkinsonism can be a side effect of antipsychotic drugs (e.g., phenothiazines). Meperidine analogues (used by drug addicts) and poisoning from carbon monoxide and manganese can also produce the symptoms of parkinsonism. **Atherosclerotic** parkinsonism can occur in elderly hypertensive patients.

Parkinson disease may be treated by elevating the brain dopamine level. Unfortunately, dopamine cannot cross the blood–brain barrier, but its immediate precursor L-dopa can and is used in its place. L-Dopa is taken up by the dopaminergic neurons in the basal nuclei and converted to dopamine. Selegiline, a drug that inhibits monoamine oxidase, which is responsible for destroying dopamine, is also of benefit in the treatment of the disease. Evidence shows that selegiline can slow the process of degeneration of the dopa-secreting neurons in the substantia nigra.

Transplantation of human embryonic dopamine-producing neurons into the caudate nucleus and putamen has been

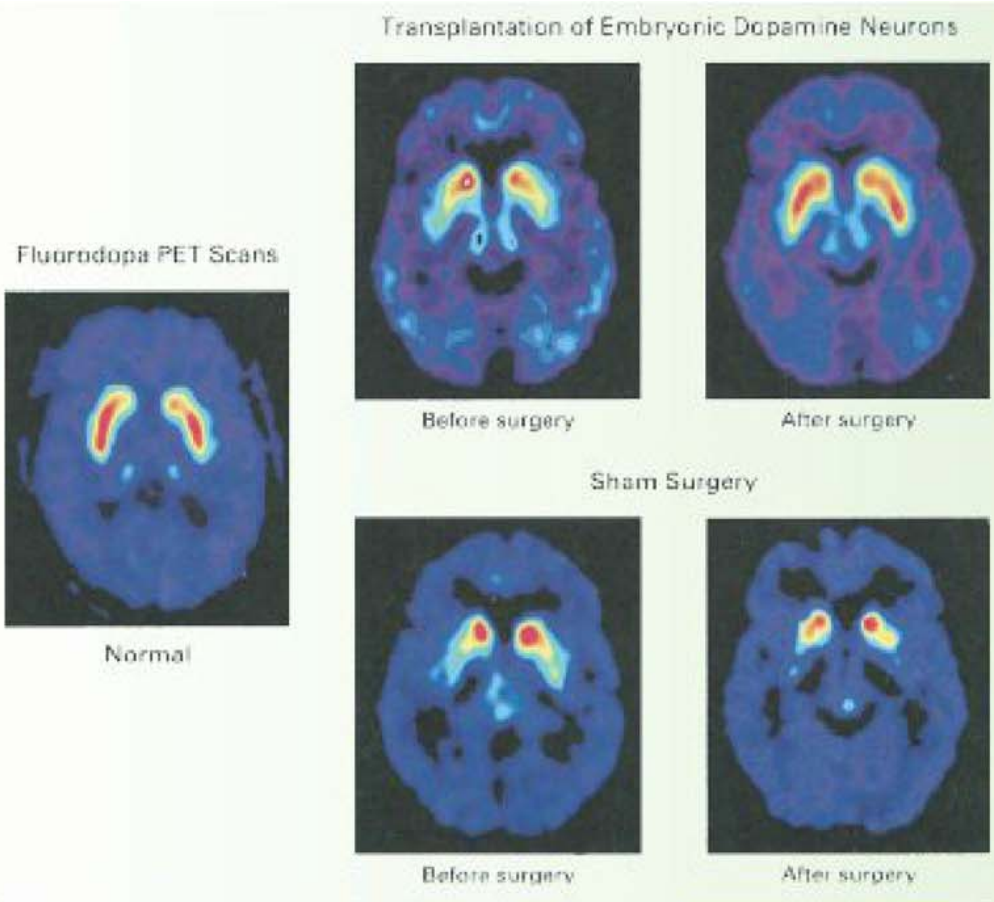


Figure 10-9 Change in 18-F-fluorodopa uptake in the brains of patients with Parkinson disease after transplantation, as shown in fluorodopa PET scans. In the panel on the far left, an axial (horizontal) section through the caudate nucleus and putamen of a normal subject shows intense uptake of 18-F-fluorodopa (red). On the right side, the upper panels show preoperative and 12-month postoperative scans in a patient in the transplantation group. Before surgery, the uptake of 18-F-fluorodopa was restricted to the region of the caudate nucleus. After transplantation, there was increased uptake of 18-F-fluorodopa in the putamen bilaterally. The lower panels show 18-F-fluorodopa scans in a patient in the sham-surgery group. There was no postoperative change in 18-F-fluorodopa uptake. (Courtesy of Freed, C. R., Greene, P. E., Breeze, R. E., et al. (2001). Transplantation of embryonic dopamine neurons for severe Parkinson's disease. *New England Journal of Medicine, 344*(10), 710–719.)

shown to lead to improvement in motor function in Parkinson disease (Fig. 10-9). Evidence shows that the grafts can survive, and synaptic contacts are made. Unfortunately, many of the grafted neurons do not survive, and in many cases, the clinical improvement is counteracted by the continuing degeneration of the patient's own dopa-producing neurons. Autotransplantation of suprarenal medullary cells can be a source of dopa-producing cells, but in the future, genetically engineered cells could be another source of dopa.

Since most of the symptoms of Parkinson disease are caused by an increased inhibitory output from the basal nuclei to the thalamus and the precentral motor cortex, surgical lesions in the globus pallidus (**pallidotomy**) have been shown to be effective in alleviating parkinsonian signs. At the present time, such procedures are restricted to patients who are no longer responding to medical treatment.

Drug-Induced Parkinsonism

Although Parkinson disease (primary parkinsonism) is the most common type of parkinsonism found in clinical practice, drug-induced parkinsonism is becoming very prevalent. Drugs that block striatal dopamine receptors (D2) are often given for psychotic behavior (e.g., phenothiazines and butyrophenones). Other drugs may deplete striatal dopamine (e.g., tetrabenazines). Drug-induced parkinsonism disappears once the agent is withdrawn.

Athetosis

Athetosis consists of slow, sinuous, writhing movements that most commonly involve the distal segments of the limbs. Degeneration of the globus pallidus occurs with a breakdown of the circuitry involving the basal nuclei and the cerebral cortex.

Key Concepts

- The corpus striatum comprises gray matter that sits lateral to the thalamus and is divided by the internal capsule into the caudate nucleus and lentiform nucleus.
- The caudate nucleus is a large C-shaped structure, forming the lateral wall and floor of the lateral ventricle, and is divided into a head, body, and tail. It terminates anteriorly in the amygdaloid nucleus.
- The lentiform nucleus consists of two nuclei, the putamen and globus pallidus. The paleness of the globus pallidus is due to the high concentration of myelinated nerve fibers.
- The corpus striatum, along with amygdaloid nucleus, substantia nigra, subthalamic nuclei, and claustrum, forms numerous complex afferent and efferent pathways.
- This circular process is initiated by motor information from the cortex, thalamus, and brainstem, processed by structures of the basal ganglia, and then channeled through the globus pallidus to influence muscular movements by returning and influencing the cerebral cortex.
- The basal nuclei not only influence the execution of a particular movement but also help prepare for movements (i.e., placing the trunk in the appropriate position in preparation for the movement by the lower limbs).

Clinical Problem Solving

1. A 10-year-old girl is seen by a neurologist because of the gradual development of involuntary movements. To begin with, the movements are regarded by her parents as general restlessness, but later, abnormal facial grimacing and jerking movements of the arms and legs occur. The child is now having difficulty in performing normal movements of the arms, and walking is becoming increasingly difficult. The abnormal movements appear to be worse in the upper limbs and are more exaggerated on the right side of the body. The movements are made worse when the child becomes excited but disappear completely when she sleeps. The child is recently treated for rheumatic fever. Is there any possible connection between this child's symptoms and the basal nuclei in the cerebral hemispheres?
2. A 40-year-old man complaining of rapid and jerky involuntary movements involving the upper and lower limbs is seen by his physician. The condition started about 6 months ago and is getting progressively worse. He says that he is extremely worried about his health because his father had developed similar symptoms 20 years ago and had died in a mental institution. His wife tells the physician that her husband also suffers from episodes of extreme depression and that she has noticed that he has periods of irritability and impulsive behavior. The physician makes the diagnosis of Huntington chorea. Using your knowledge of neuroanatomy, explain how this disease involves the basal nuclei.
3. A 61-year-old man suddenly develops uncoordinated movements of the trunk and right arm. The right upper limb will suddenly, vigorously, and aimlessly be thrown about, knocking over anything in its path. The patient is recovering from a right-sided hemiplegia, secondary to a cerebral hemorrhage. What is the name given to this clinical sign? Does this condition involve the basal nuclei?

Answers and Explanations to Clinical Problem Solving

1. This child is suffering from Sydenham chorea (see p. 315). This condition occurs, in the majority of cases, in female children between the ages of 5 and 15 years. It is characterized by the presence of rapid, irregular, involuntary movements that are purposeless. The disease is associated with rheumatic fever, and complete recovery is the rule.
2. Huntington chorea is a progressive inherited disease that usually appears between the ages of 30 and