CHAPTER 9

THE BASAL GANGLIA

The basal ganglia (BG) are subcortical masses of gray matter that include the following nuclei (figure 55) :

(1) The caudate nucleus.

(2) The lentiform (or lenticular) nucleus : This consists of 2 parts **(a)** An outer part called the **putamen (b)** An inner part called the **globus pallidas**, which is further divided into *external and internal segments*.

Both the *caudate nucleus and putamen* are called the **corpus striatum.**

(3) The subthalamic nucleus (= *subthalamus or body of Luys*).

(4) The substantia nigra (in the midbrain).

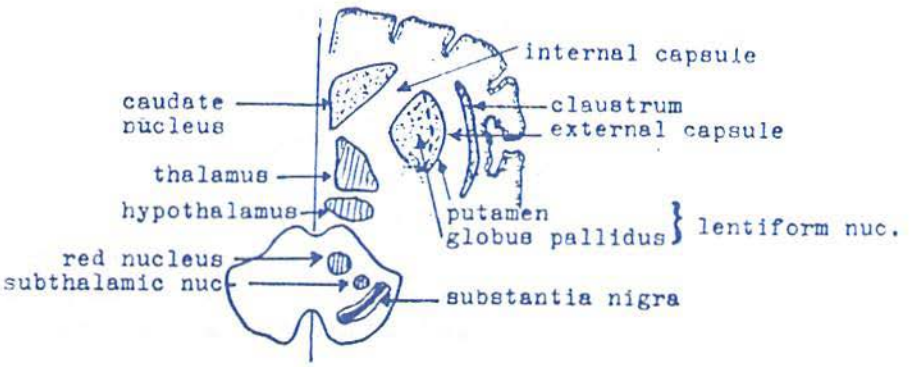

Figure 55 : The basal ganglia (BG).

CONNECTIONS OF THE BASAL GANGLIA

The BG constitute a basic part of the ***extrapyramidal system***. *Their afferent (input) fibres are derived mainly from the cerebral cortex to the corpus striatum, while their efferent (output) fibres originate mainly from the globus pallidus*. Their connections can generally be divided into **3 parts :**

(A) Cortical connections of the basal ganglia

(1) Putamen circuit (figure 56) **:** Fibres start from the cortical motor areas and end at the **putamen,** from which new fibres arise and end at the ***internal globus pallidus***. From the latter, fibres arise and relay at the ***thalamic ventrolateral nucleus***, from which fibres arise and finally end at the cortical motor areas, specially ***the primary motor area (area 4)***.

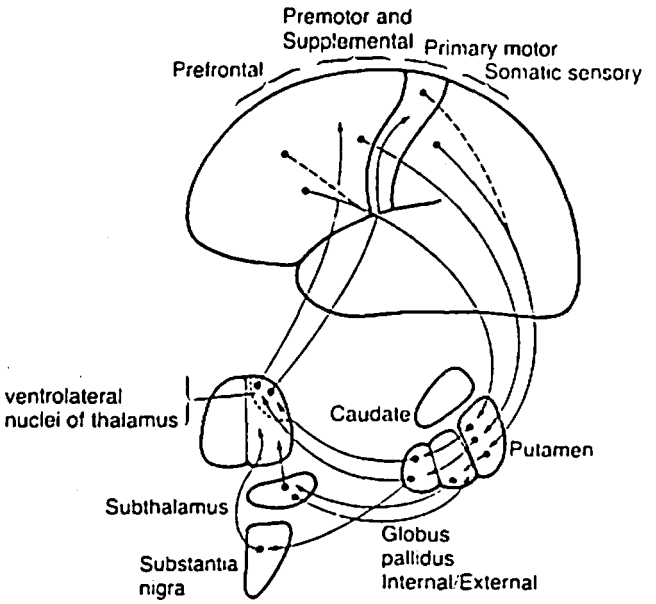

Figure 56 : The putamen circuit.

** There are other circuits that are closely associated with the putamen circuit and involve the ***subthalamus and substantia nigra*** (figure 56).

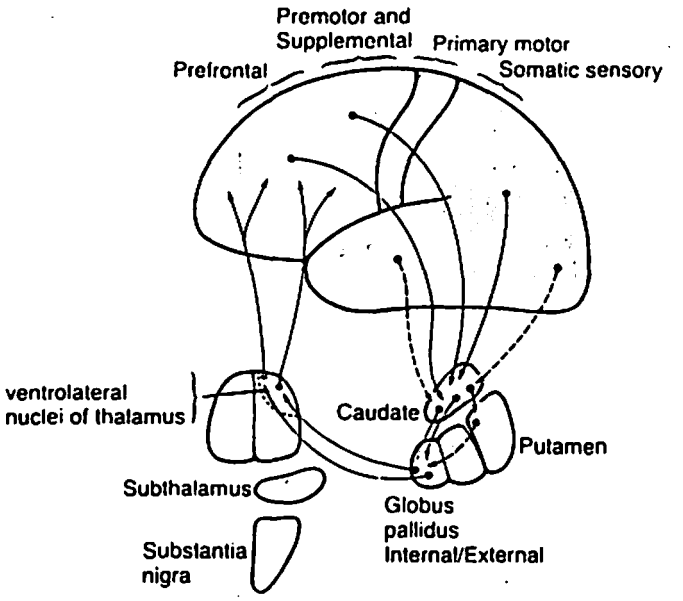

Figure 57 : The caudate circuit.

(2) Caudate circuit (figure 57) : Fibres start from both the ***cortical motor and sensory association areas*** and end at the **caudate nucleus**, from which new fibres arise and end at the ***internal globus pallidus***. From the latter, fibres arise and relay at the ***thalamic ventrolateral nucleus***, from which fibres arise and finally ***end at the cortical motor association areas***.

(B) Interconnections of the basal ganglia

(1) A negative feedback interconnection between the external part of the globus pallidus and the subthalamus (figure 56).

(2) Dopaminergic ***nigro-striatal connection*** (figure 58).

(3) GABA-ergic ***striato-nigral & striato-pallidal projections*** (figure 58).

(C) Brain stem connections of the basal ganglia

Fibres from the globus pallidus project to **(a)** ***The reticular formation*** **(b)** ***The red nucleus*** **(c)** ***The vestibular nucleus*** **(d)** ***The inferior olivary nucleus***. Signals from the BG are transmitted *through such connections to the spinal centres via the extrapyramidal tracts.*

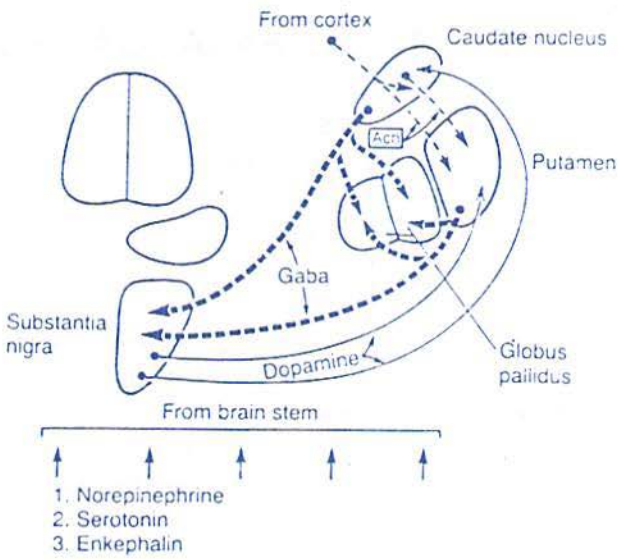

Figure 58 : Neurotransmitters in the basal ganglia.

NEUROTRANSMITTERS IN THE BASAL GANGLIA

These are multiple and include the following (figure 58) :

1. ***Acetylcholine*** (mainly from *intra-striatal neurons*).
2. ***Dopamine*** (from the *nigro-striatal neurons*).
3. ***GABA*** (from the *striato-nigral and striato-pallidal neurons*).

4. ***Norepinephrine, serotonin and enkephalin*** (from the neurons that project from various centres in the brain stem to the basal ganglia).
5. ***Glutamate*** (from the cortico-striatal and subthalamic neurons).

Acetylcholine, glutamate and norepinephrine are ***excitatory transmitters***, while ***all the remaining transmitters are inhibitory***, and the balance between inhibition and excitation in the BG maintains normal motor function. Normally, ***the inhibitory effect predominates*** (which decreases the excitatory discharge of the BG) and in addition, the *discharge of the BG to the thalamus is mainly inhibitory via GABA-ergic nerve fibres*. These factors *decrease the excitatory discharge from the thalamus to the cortical motor areas*.

** The predominance of inhibitory neurons in the BG makes the circuits described above (specially the putamen circuit and its associated circuits) to act as ***negative feedback loops*** that stabilize the motor control system, and prevent excessive and undesirable movements.

** Excessive deposition of copper in the liver and BG occurs in ***Wilson's disease*** resulting in their damage (= ***hepatolenticular degeneration***). Also, if the bile pigments blood level increases markedly, they *cross the blood brain barrier* and deposit in the BG leading to their damage (= ***kernicterus***).

FUNCTIONS OF THE BASAL GANGLIA

The functions of the BG are ***purely motor*** and include the following :

(A) Control of the muscle tone

The **lentiform nucleus decreases the muscle tone** by inhibiting the vestibular nucleus and activating the inhibitory reticular formation (page 72). On the other hand, ***the caudate nucleus increases the muscle tone*** by stimulating the facilitatory reticular formation as well as the vestibular and inferior olivary nuclei (page 71).

However, generalized stimulation of the BG decreases the muscle tone (indicating predominance of the inhibitory effect of the lentiform nucleus).

(B) Control of voluntary movements

(1) The BG discharge ***before the movements start,*** and are concerned with ***planning and programming of movements*** as follows **(a)** The **putamen circuit** *is concerned with execution of learned patterns of movement* **(b)** The **caudate circuit** *is concerned with converting thoughts into motor actions* (*a function known as the* ***cognitive control of motor activity***). This involves determination of **(i)** The pattern of movements to be used and their sequence **(ii)** The timing and rapidity of performing the movements **(iii)** The scale (intensity) of movements. An example for such function is what happens to a person on seeing a lion (he automatically and rapidly turns away, begin to run and even attempt to climb a tree).

(2) As a part of the extrapyramidal system, the BG initiate subconscious automatic movements (e.g. swinging of the arms during walking).

DISEASES OF THE BASAL GANGLIA

(1) CHOREA

Chorea means ***"dance"***, and it is 2 main types :

(a) Huntington's chorea : This is a hereditary disease, and its onset is usually at 30-50 years of age.

(b) Sydenham's chorea : This occurs in young ages (5-15 years) commonly as a complication of ***rheumatic fever***.

Chorea is due to lesions of the corpus striatum, specially the ***caudate nucleus***. It is associated with ***degeneration of both cholinergic and GABA-ergic neurons,*** and is characterized by the following symptoms :

(1) Hyperkinetic features in the form of rapid purposeless involuntary ***dancing movements*** that occur suddenly ***during rest*** and superimpose on voluntary movements. Their cause is ***release of the globus pallidus and substantia nigra from inhibition*** (due to GABA deficiency), which allows spontaneous discharge of excitatory signals to the cortical motor centres, resulting in such movements.

(2) Hypotonia due to loss of the facilitatory effect of the caudate nucleus on the stretch reflex. It is associated with ***pendular knee jerk*** (page 69).

(3) Dementia (decreased memory and cognitive function) due to loss of the acetylcholine-secreting neurons.

(2) ATHETOSIS

This is due to lesions of the ***globus pallidus***. It is characterized by ***hyperkinetic features*** in the form of involuntary ***slow writhing movements*** (= twisting snake-like movements) specially in the face, the distal parts of the upper limbs and the hands

(3) HEMIBALLISMUS

This is due to lesions of the ***subthalamic nucleus***. It is characterized by ***hyperkinetic features*** in the form of ***sudden, rapid and violent involuntary movements*** e.g. sudden flexion of the lower limb.

(4) PARKINSON'S DISEASE (PARALYSIS AGITANS)

This is due to lesions of the ***substantia nigra,*** which leads to ***degeneration of the dopaminergic nigro-striatal fibres (resulting in marked reduction of the dopamine content in the BG)***.It occurs more in old age (because there is normally a steady loss of the dopaminergic neurons and receptors in the BG with progress of age) and is hastened by ***atherosclerosis and prolonged use of phenothiazine tranquilizers*** (*which block the D_2 receptors*).

Manifestations of Parkinson's disease (Parkinsonism)

Pakinsonism is characterized by both *hyperkinetic features* (***rigidity and static tremors***) and *hypokinetic features* (***akinesia and bradykinesia***).

(1) MUSCLE RIGIDITY

This occurs in all muscles (but the ***tendon jerks are usually not exaggerated***). When the limbs are passively moved, it is either continuous (= ***lead-pipe rigidity***) or interrupted (= ***cogwheel rigidity***). It is primarily an **alpha rigidity** (page 73) that occurs as a result of a ***release phenomenon***. Destruction of the dopaminergic neurons releases the corpus striatum from the inhibitory effect of dopamine, and this leads to increased output of excitatory signals to the cortical motor areas, which consequently discharge excess excitatory signals to the spinal alpha motor neurons via the corticospinal tract resulting in rigidity.

(2) AKINESIA OR HYPOKINESIA (LACK OF MOVEMENTS)

This is associated with **bradykinesia** (= slow movements), and is manifested by **(a)** *Marked difficulty in initiating voluntary movements* **(b)** ***Mask face*** due to lack of facial expression **(c)** ***Slow, monotonous and low-volume speech*** **(d)** ***Shuffling gait*** i.e. walking rapidly in short steps without lifting the legs from the ground **(e)** ***Absence of the associated movements*** e.g. swinging of the arms during walking..

The real cause of akinesia is unknown. However, recently it was found that ***dopamine is also decreased in the limbic system***, and this might greatly reduce the psychic drive for motor activity which leads to akinesia.

(3) STATIC TREMOR

This is a tremor that appears **during rest** and disappears during sleep and on doing voluntary movements. It occurs at a rate of *3-6 or 8 cycles per second* due to regular alternating contraction of the antagonistic muscles (probably as a result of *oscillation of activity in the feedback circuits after loss of their inhibition caused by dopamine deficiency*). It is marked in the upper limbs, and in the hands it often appears as ***pill-rolling movements***.

Treatment of Parkinsonism

The main disorder in Parkinsonism is the ***imbalance between the inhibitory and excitatory influences in the BG, with predomination of the latter***. Accordingly, the symptoms of this disease can be relieved by one or more of the following **:**

(1) Anticholinergic drugs (which decrease the excitability effect of acetylcholine). However, these drugs have proved not very effective.

(2) Increasing the dopamine content of the BG by either *:*

(a) L-Dopa : This drug ***can cross the blood-brain barrier*** and is converted to dopamine in the brain (***dopamine itself is useless*** *because it fails to cross the blood-brain barrier*). However, its effect disappears after prolonged use.

(b) L-Deprenyl : This is a drug that ***inhibits the monoamine oxidase enzyme*** (which destroys dopamine), so it increases the dopamine content in the basal ganglia.

(c) Implantation of dopamine-secreting tissue *in or near* the basal ganglia (the best was found to be ***from a fetal corpus striatum***).

(3) Blocking the feedback circuits between the basal ganglia and the cortical motor areas : This has been tried surgically by **destruction** of either **(a)** The ventrolateral nucleus of the thalamus **(b)** The interenal segment of the globus pallidus (= ***pallidotomy***) **(c)** The subthalamic nucleus.

EFFECTS OF EXTENSIVE LESIONS OF THE BASAL GANGLIA

In addition to the changes in muscle tone and the hyperkinetic or hypokinetic features that occur in the above diseases, extensive lesions of the BG also lead to the following :

(1) ***Apraxia*** (= *inability to perform familiar motor acts in absence of muscle paralysis*). This specially occurs in lesions of the ***putamen circuit*** which is *concerned with execution of the learned patterns of movement.*

(2) ***Failure of organizing movements to perform a complex action, slow performance of the movements, and drawing figures with disproportionate scales*** (page 123 & figure 73 right). This is associated with a dysarthric form of aphasia, and specially occurs in lesions of the ***caudate circuit*** (page 100).

THE RELEASE PHENOMENA IN THE CNS

Lesions and diseases of the CNS are frequently associated with exaggerated activity in certain nervous centres. In some cases, this phenomenon is due to ***denervation hypersensitivity***. However, more commmonly it is due to ***release of these centres from an inhibitory effect*** that was exerted by the affected areas. This is illustrated in the following examples :

(1) The gamma rigidity that occurs in decerebrate animals (page 72).

(2) The gamma spasticity that occurs in UMNL (page 80).

(3) Recovery of the spinal reflex activity and the ***mass reflex*** that follows complete spinal cord transection (page 85).

(4) Thalamic hyperpathia (page 90).

(5) Release of the feeding centre from the inhibitory effect of the satiety centre in cases of hypoglycemia (page 92).

(6) The sham rage reaction (page 93).

(7) The static tremors and alpha rigidity that occur in Parkinsonism (page 102)as well as the hyperkinetic features in other diseases of the basal ganglia

(8) Miosis due to release of the Edinger-Westphal nucleus from cortical inhibition in the 3rd (surgical) stage of anesthesia (refer to special senses).