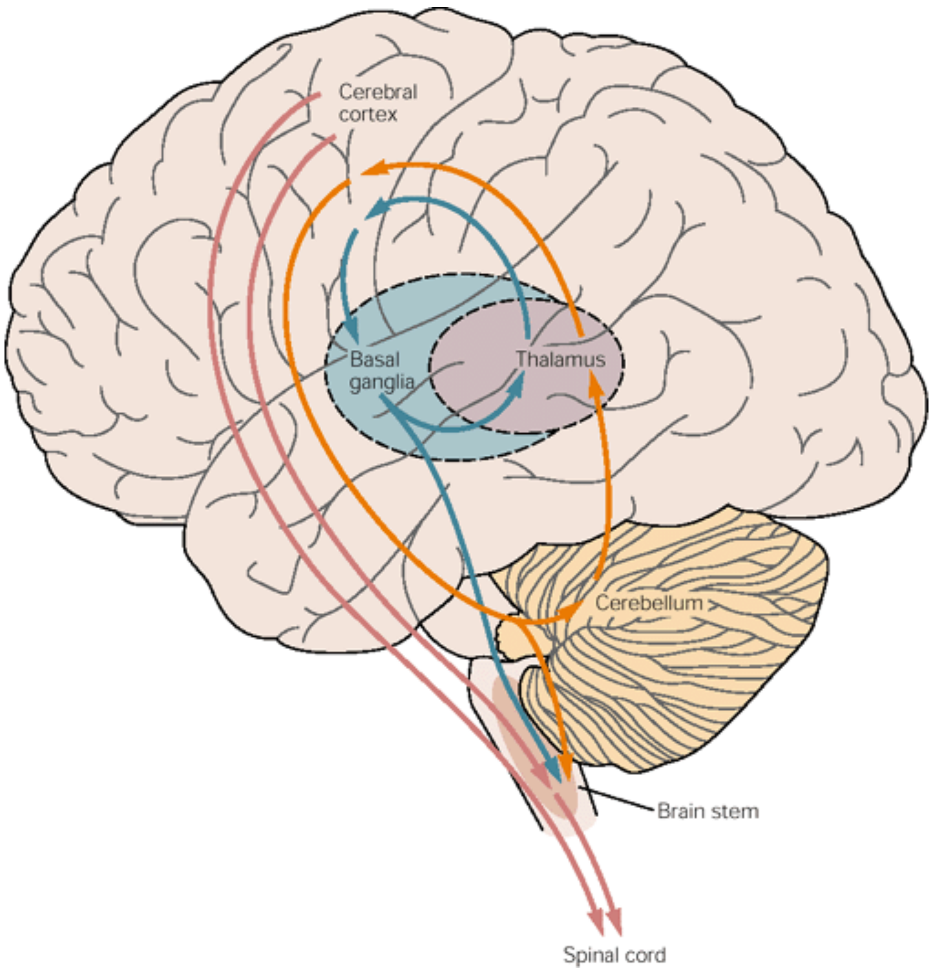
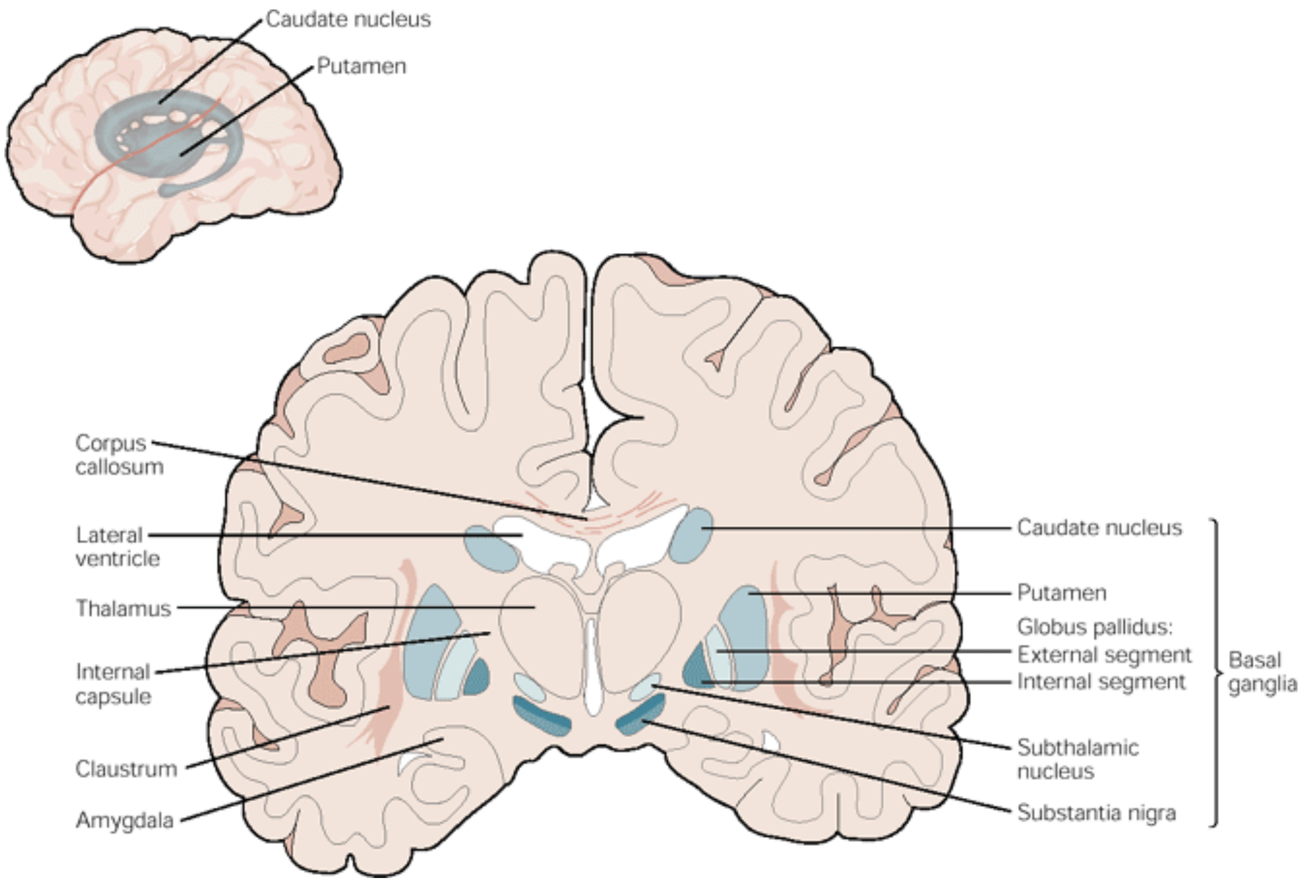
Basal ganglia



The basal ganglia and the cerebellum are involved in motor control. They are two parallel systems that receive input from and return their influences to the cerebral cortex through the thalamus. They also influence the brain stem and, ultimately, spinal mechanisms.

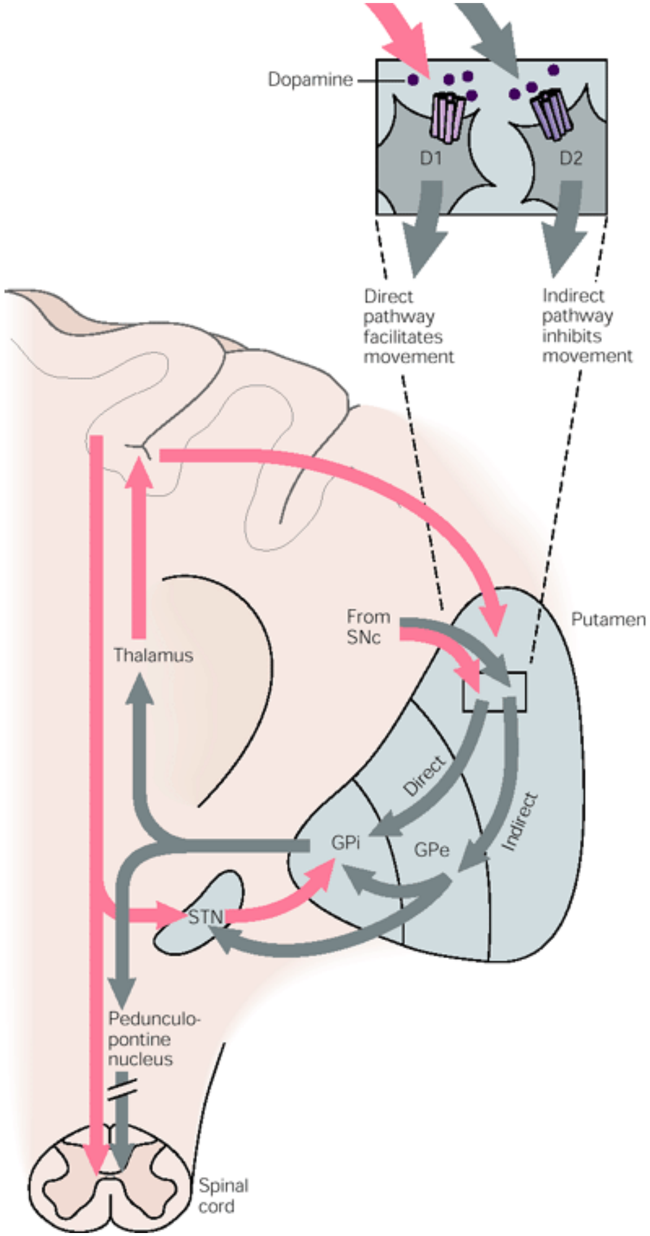
The basal ganglia inhibit a number of actions generated by the motor cortex. Release of this inhibition permits a motor system to become active. Therefore, the main role of basal ganglia is action selection. The 'decision making' of basal ganglia is influenced by inputs from the prefrontal cortex.

Basal ganglia



Basal ganglia is a group of different structures (nuclei). The four principal nuclei of the basal ganglia are (1) the striatum, (2) the globus pallidus (or pallidum), (3) the substantia nigra and (4) the subthalamic nucleus. The striatum consists of three important subdivisions: the caudate nucleus, the putamen, and the ventral striatum (which includes the nucleus accumbens and olfactory tubercle – not shown).

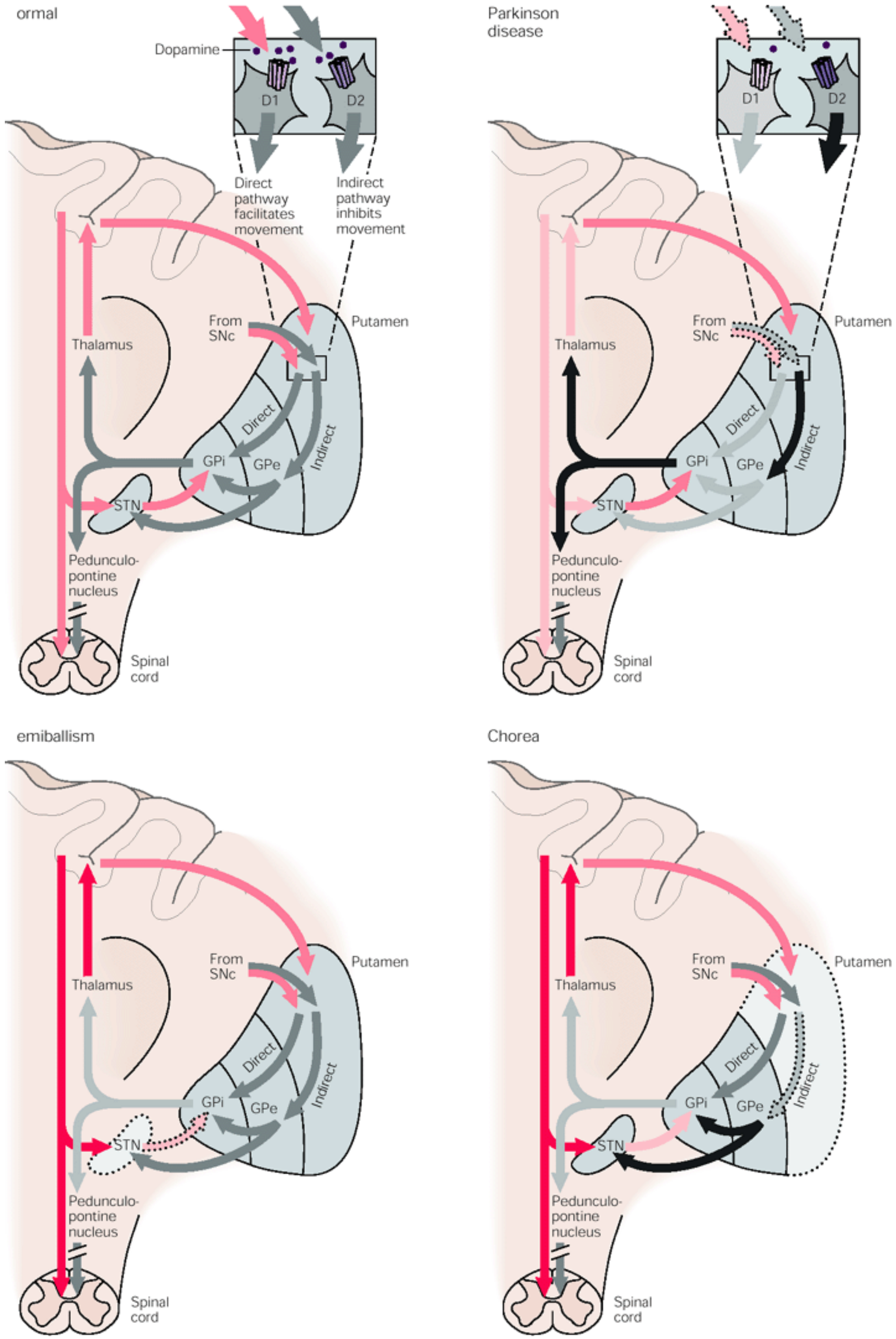
Basal ganglia-thalamocortical circuit



The anatomic connections of the basal ganglia-thalamocortical circuitry show the parallel direct and indirect pathways from the striatum to the basal ganglia output nuclei**.** Two types of dopamine receptors (**D1** and **D2**) are located on different sets of output neurons in the striatum that give rise to the direct and indirect pathways. Inhibitory pathways are shown as **gray arrows;** excitatory pathways, as **pink arrows**. **GPe** = external segment of the globus pallidus; **GPi** = internal segment of the globus pallidus; **SNc** = substantia nigra; **STN** = subthalamic nucleus.

The direct pathway provides *positive* feedback and the indirect pathway *negative* feedback in the circuit between the basal ganglia and the thalamus. Activation of the direct pathway disinhibits the thalamus, thereby increasing thalamocortical activity, whereas activation of the indirect pathway further inhibits thalamocortical neurons. As a result, activation of the direct pathway facilitates movement, whereas activation of the indirect pathway inhibits movement.

Movement disorders and the basal ganglia

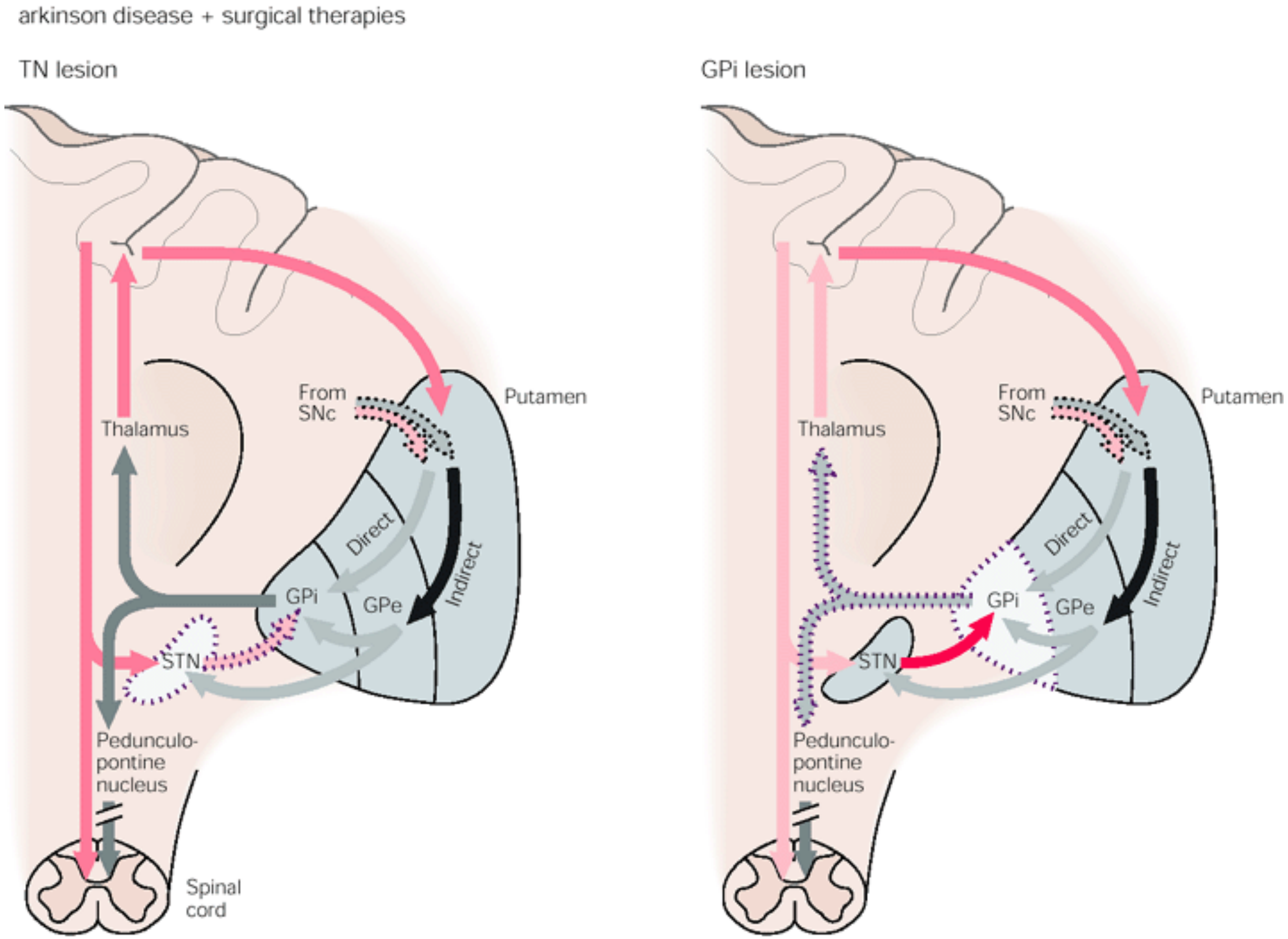


The basal ganglia-thalamocortical circuitry under normal conditions and in Parkinson's disease, hemiballism and chorea. Inhibitory connections are shown as gray and black arrows; excitatory connections, as pink and red.

Degeneration of the dopamine pathway in Parkinson's disease leads to differential changes in activity in the two striatopallidal projections, indicated by changes in the darkness of the connecting arrows (**darker arrows** indicate increased neuronal activity and **lighter arrows**, decreased activity). Basal ganglia inhibitory output to the thalamus is increased in Parkinson's disease and is decreased in hemiballism (undesired movements of the limbs) and chorea (involountary body movements that look coordinated).

Hemiballism:
https://www.youtube.com/watch?v=GzRV5HCyVl4

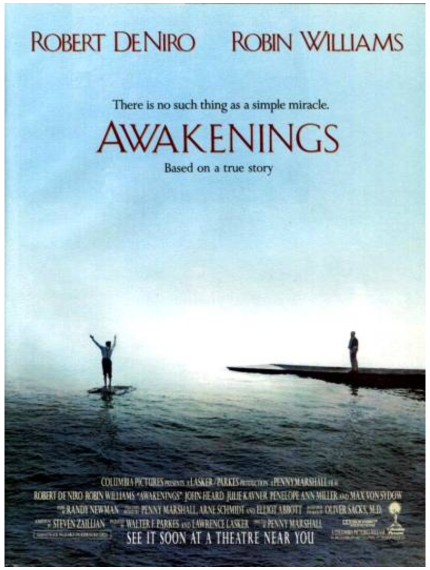
Parkinson's disease – surgical therapies



Lesions of the subthalamic nucleus (STN) (left) or internal segment of the globus pallidus (right) effectively reduce parkinsonian signs by respectively normalizating or eliminating abnormal and excessive inhibitory output from the internal pallidal segment.

Parkinson's disease – drug therapies

Parkinson's disease ilustration in *A Manual of Diseases of the Nervous System,* 1886



„Awakenings" movie based on Oliver Sacks book telling true story of a discovery of beneficial effects of then-new drug L-DOPA in catatonic patients, who survived epidemic of Encephalitis Lethargica.

L-DOPA is produced in the body from the amino acid L-tyrosine. L-DOPA crosses the protective blood–brain barrier, whereas dopamine itself cannot. In the central nervous system L-DOPA is converted to dopamine

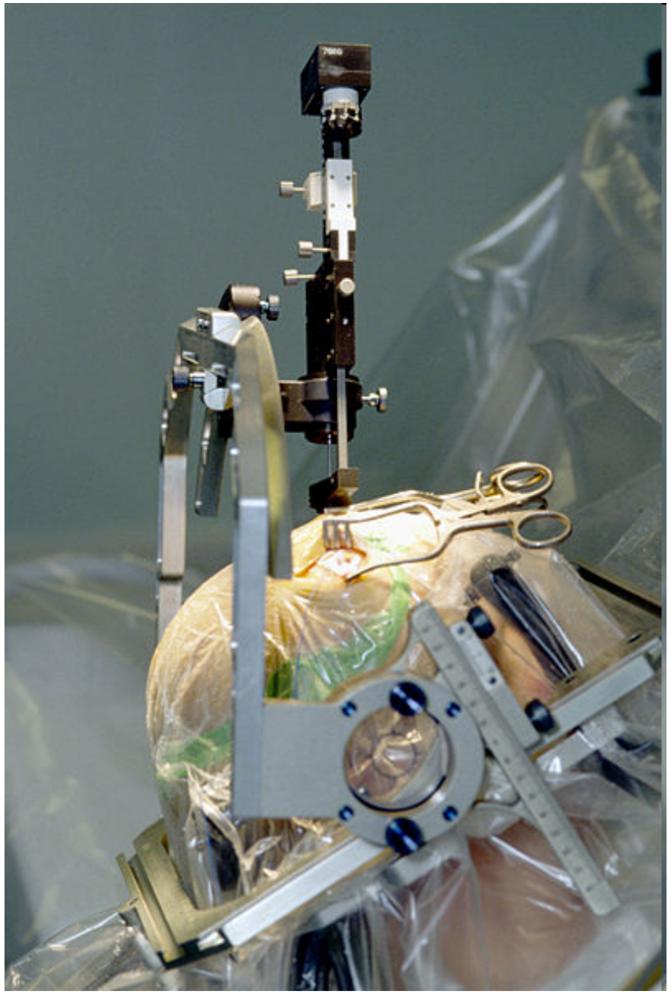
L-DOPA is used to increase dopamine concentrations in the treatment of Parkinson's disease.

L-DOPA is also converted into dopamine within the peripheral nervous system causing side effects (increased heart rate and blood pressure).

Therefore L-DOPA is administered with carbidopa and entacapon which prevent the peripheral synthesis of dopamine from L-DOPA.

L – levadopa, C – carbidopa, E - entacapon

Parkinson's disease – deep brain stimulation

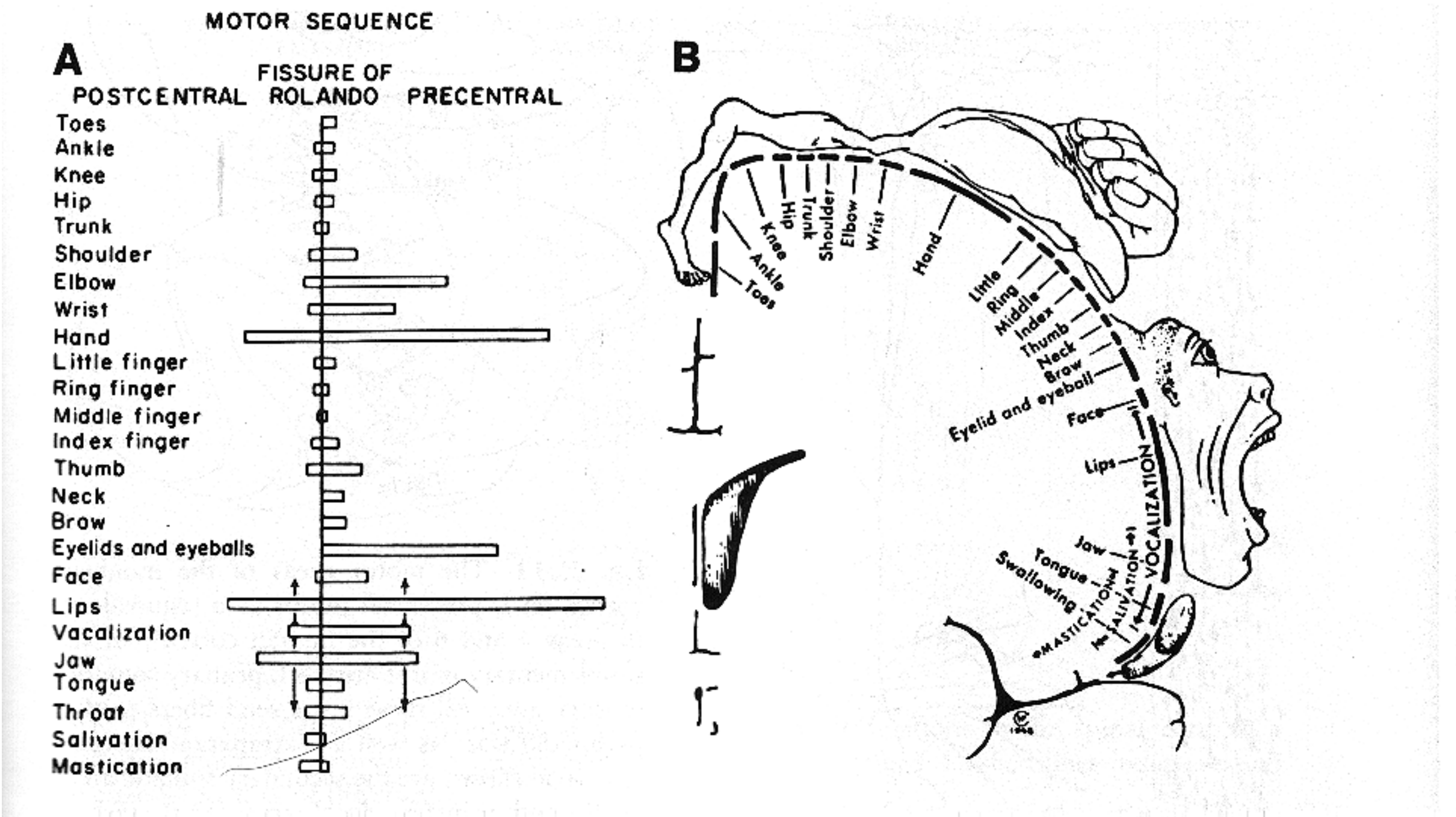


Implantation of electrode for deep brain stimulation. Globus pallidus interna (GPi) and subthalamic nucleus (STN) are the stimulation targets.

https://www.youtube.com/watch?v=uBh2LxTW0s0

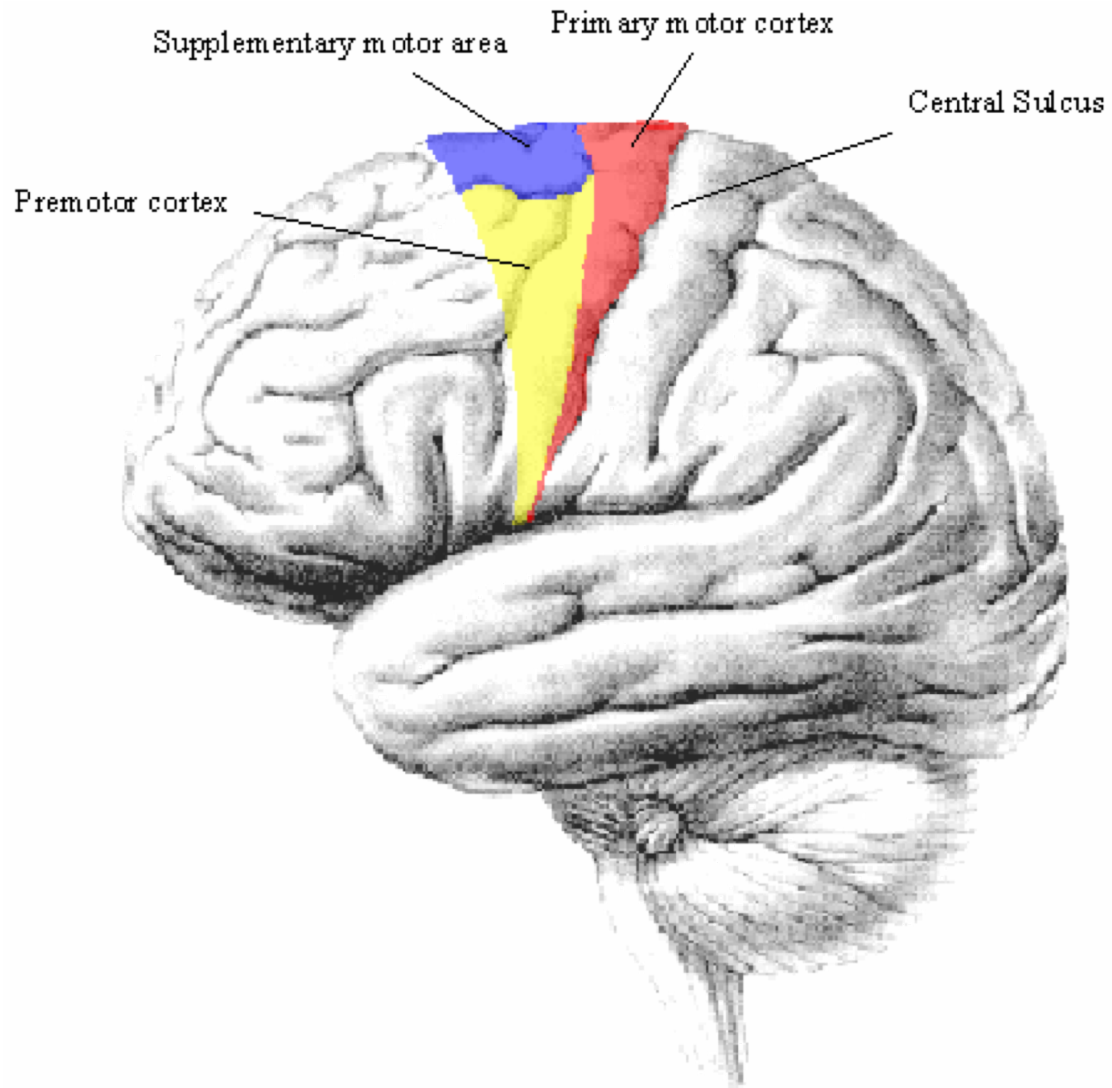
Motor cortex

It was discovered in 1870 that electrical stimulation of different parts of the frontal lobe (in monkey) produced movements of muscles. The area in which the lowest-intensity stimulation produced movements is now called the primary motor cortex. Motor cortex is involved in the planning, control, and execution of voluntary movements.



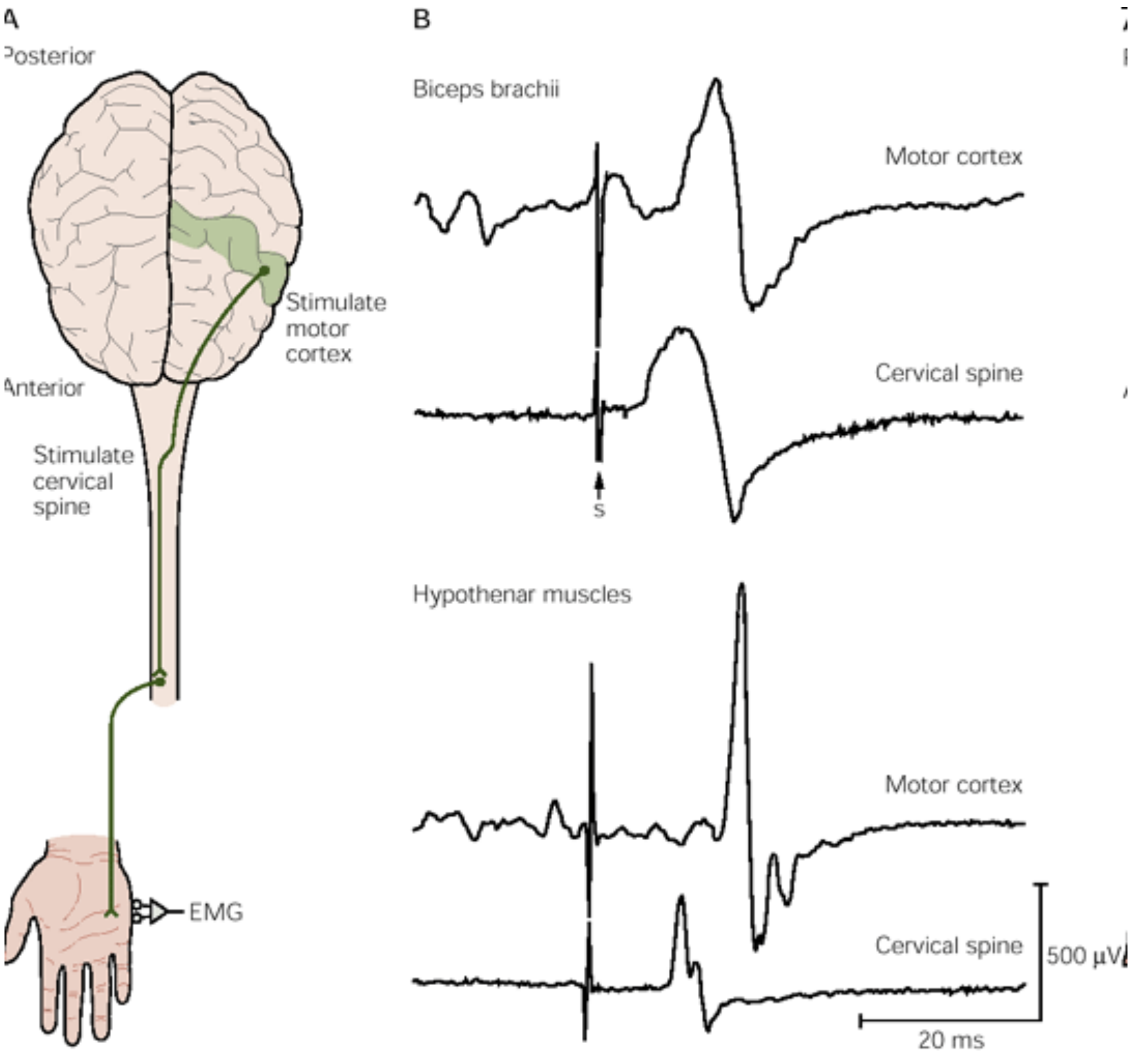
The motor homunculus of Penfield and Rasmussen (1950) obtained by electrical stimulation of the cortex. The relative proportions of movements elicited by stimulation anterior and posterior to the Rolandic sulcus, in a series of patients, is shown in A.

The motor areas



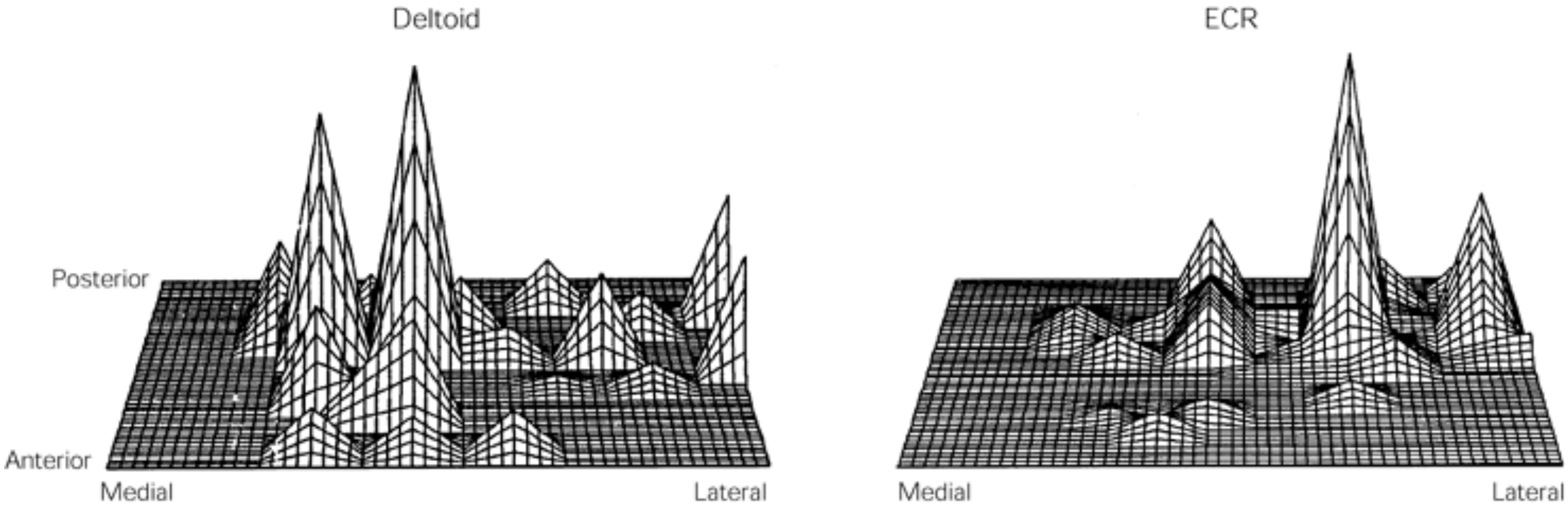
Motor cortex is located in the frontal lobe anterior to the Central sulcus (sometimes called Rolandic sulcus or fissure). The motor cortex can be divided into three main parts: the primary motor cortex (MI), the supplementary motor area (SMA) and the premotor cortex (PM). SMA and PM are together the secondary motor cortex (MII). Functionally, it means that there is multiple representation of a motor map in the cerebral cortex.

The primary motor cortex stimulation



A. Magnetic stimulation of the motor cortex or cervical spine activates the corticospinal fibers and produces a short-latency electromyographic (EMG) response in contralateral muscles. B. The traces show activation of arm and hand muscles when stimulation is applied over the cortex or the cervical spine. The peaks occur earlier from cervical stimulation because the corticospinal impulse has less distance to travel. The point marked **s** is a stimulus artifact. The primary motor cortex controls simple features of movement.

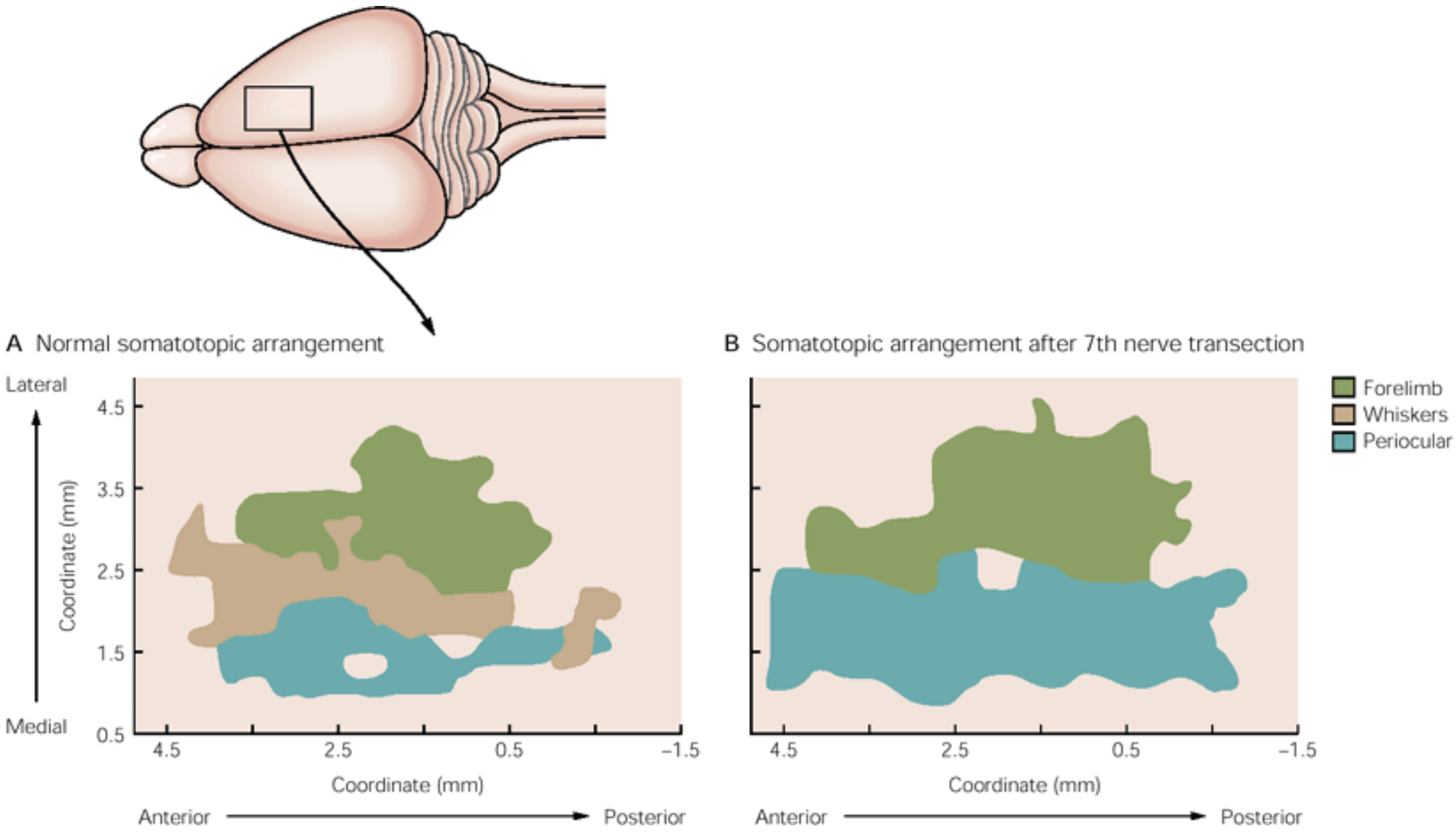
The primary motor cortex stimulation



More detailed studies, using microelectrodes inserted into the depths of the cortex (intracortical microstimulation or ICMS) to stimulate small groups of output neurons in MI showed that most stimuli activate several muscles and that the same muscles are activated from several separate sites.

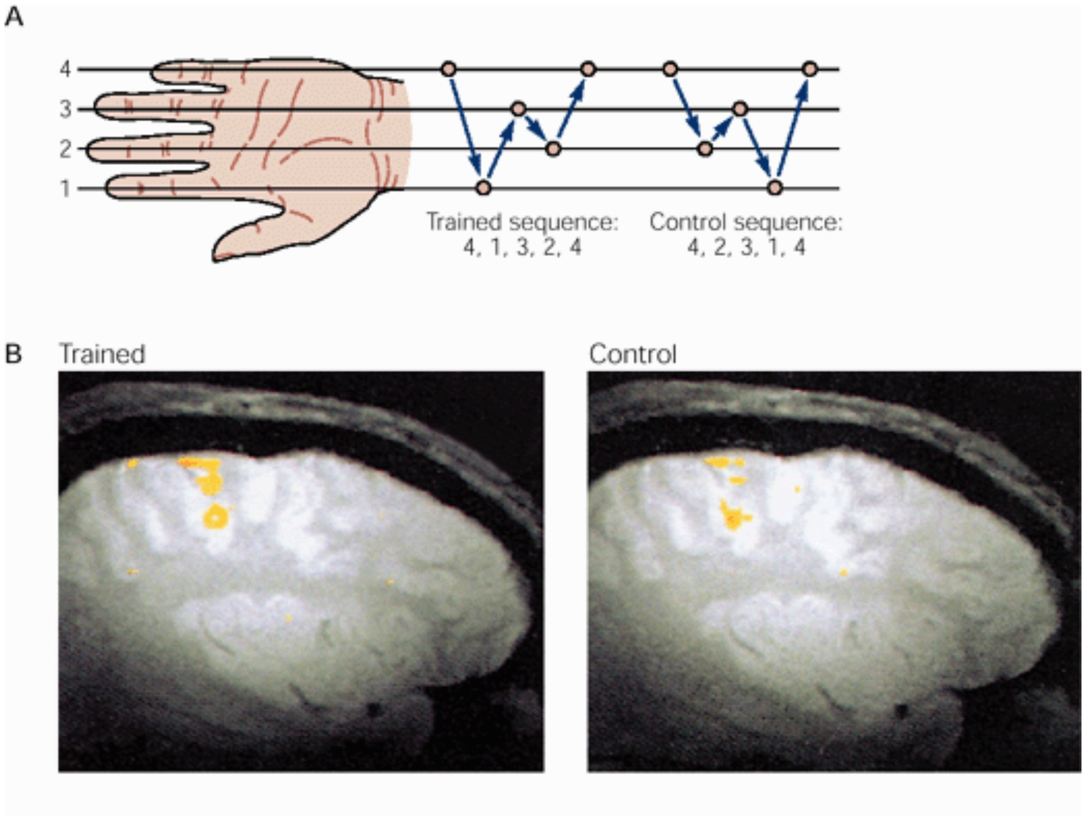
Topographic maps show sites in MI, stimulation of which, elicits EMG activation (indicating monosynaptic connections) in shoulder (deltoid muscle) and wrist muscles (extensor carpi radialis; ECR). The maps were constructed based on the inverse of the threshold (1/threshold) in microamperes. The maps show both redundancy and overlap of cortical representation. An implication of this redundancy in muscle representation is that inputs to motor cortex from other cortical areas can combine muscles in different ways in different tasks.

Plasticity in the somatotopic organization of the motor cortex



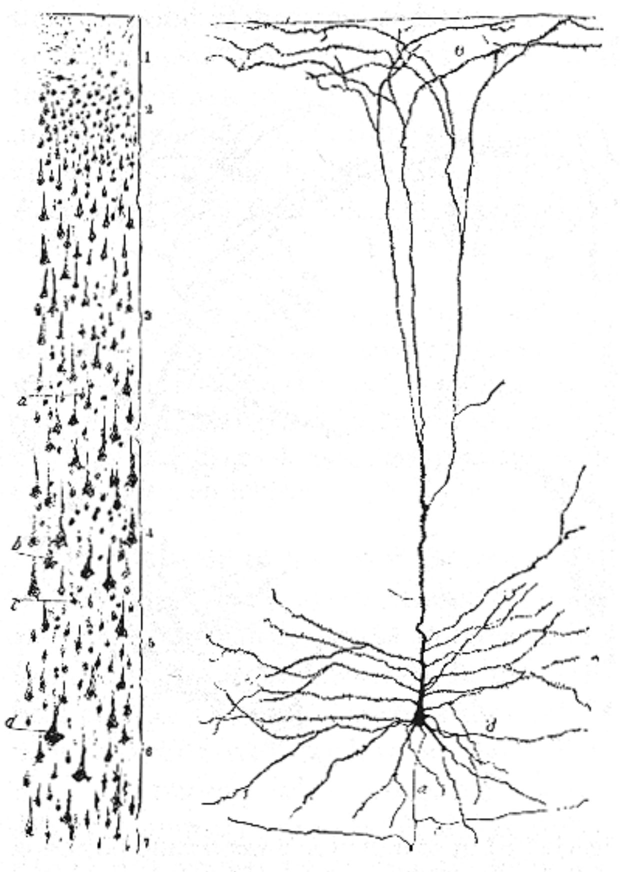
The somatotopic organization of the motor cortex is not fixed but can be altered during motor learning and following injury. A. Surface view of the rat frontal cortex shows the normal somatotopic arrangement of areas representing forelimb, whisker, and periocular muscles. B. Same view after transection of branches of the facial nerve. Areas of cortex devoted to forelimb and periocular control have increased, extending into the area previously devoted to whisker control. The change can take place in just a few hours. The loss of sensory inputs from the whiskers into the motor area is thought to trigger the reorganization.

Plasticity in the somatotopic organization of the motor cortex



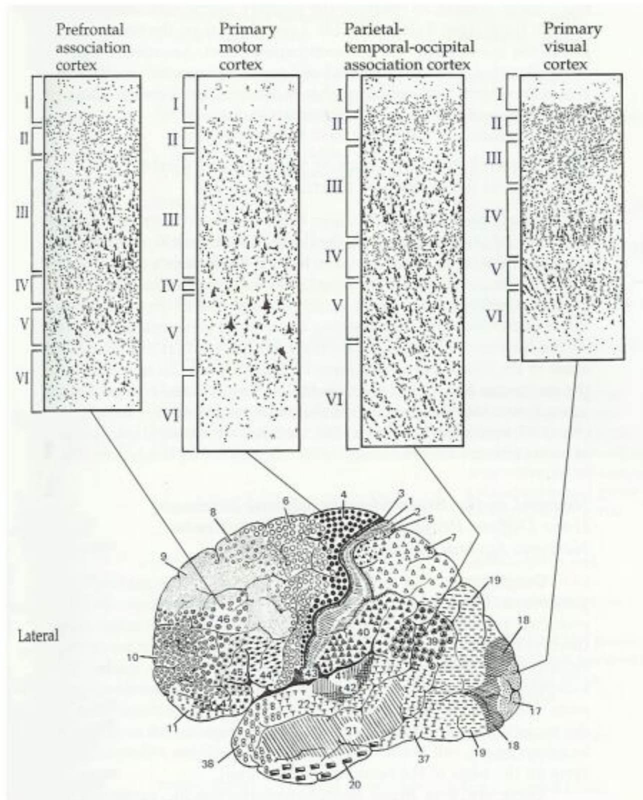
Voluntary movements improve with practice what may be associated with cortical reorganization.
A. Human subjects performed two finger-opposition tasks, touching the thumb to each fingertip in the sequences shown. Digits are numbered 1 through 4. Both the practiced and the novel sequence were performed at a fixed, slow rate of two component movements per second.
B. Functional MRI scans show the area in the primary motor cortex activated during the performance of a finger-opposition sequence that had been practiced daily for 3 weeks (Trained) followed by a novel sequence (Control - not trained). The area of activation is larger when the practiced sequence is performed. The experimenters interpret the increased area of metabolic activity as indicating that long-term practice results in a specific and more extensive representation of the trained sequence of movements in the primary motor cortex.

Neurons in cortical layer V give rise to corticospinal tract



Left: 7 cortical laminae of the human motor cortex. Only cell bodies have been stained. The laminae are identified on the basis of relative numbers of large cell bodies (pyramidal cells) and small cell bodies (pyramidal or stellate cells).

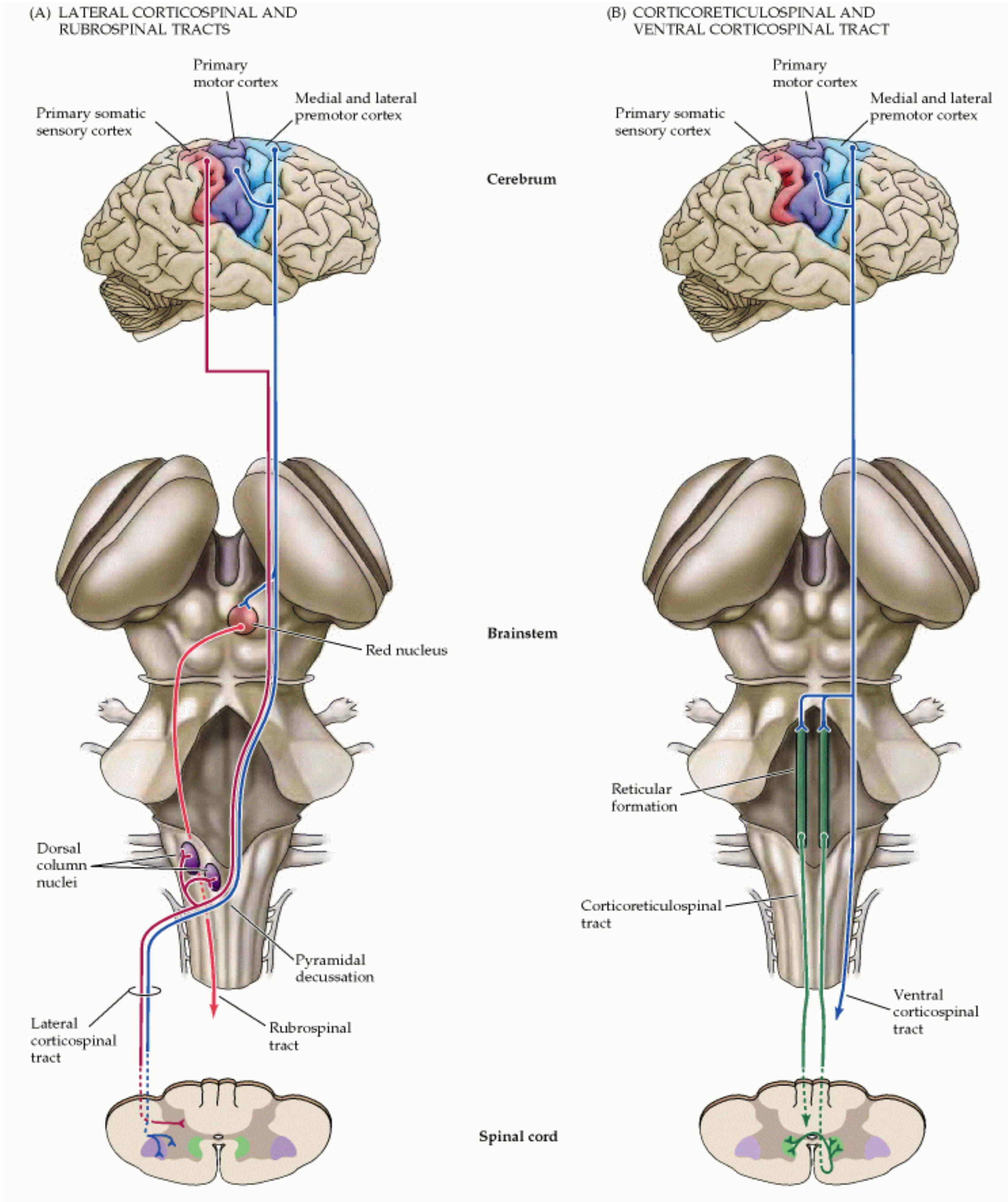
Right: Betz cell of the motor cortex impregnated by the Golgi method.



I. Molecular
II. External granular
III. External pyramidal
IV. Internal granular
V. Internal pyramidal
VI. Polymorphous

Comparison of cortical layers in different parts of the brain. In layer V of primary motor areas large cell bodies of Betz cells are visible. Betz cells are found mainly in the leg area.

Parallel motor pathways



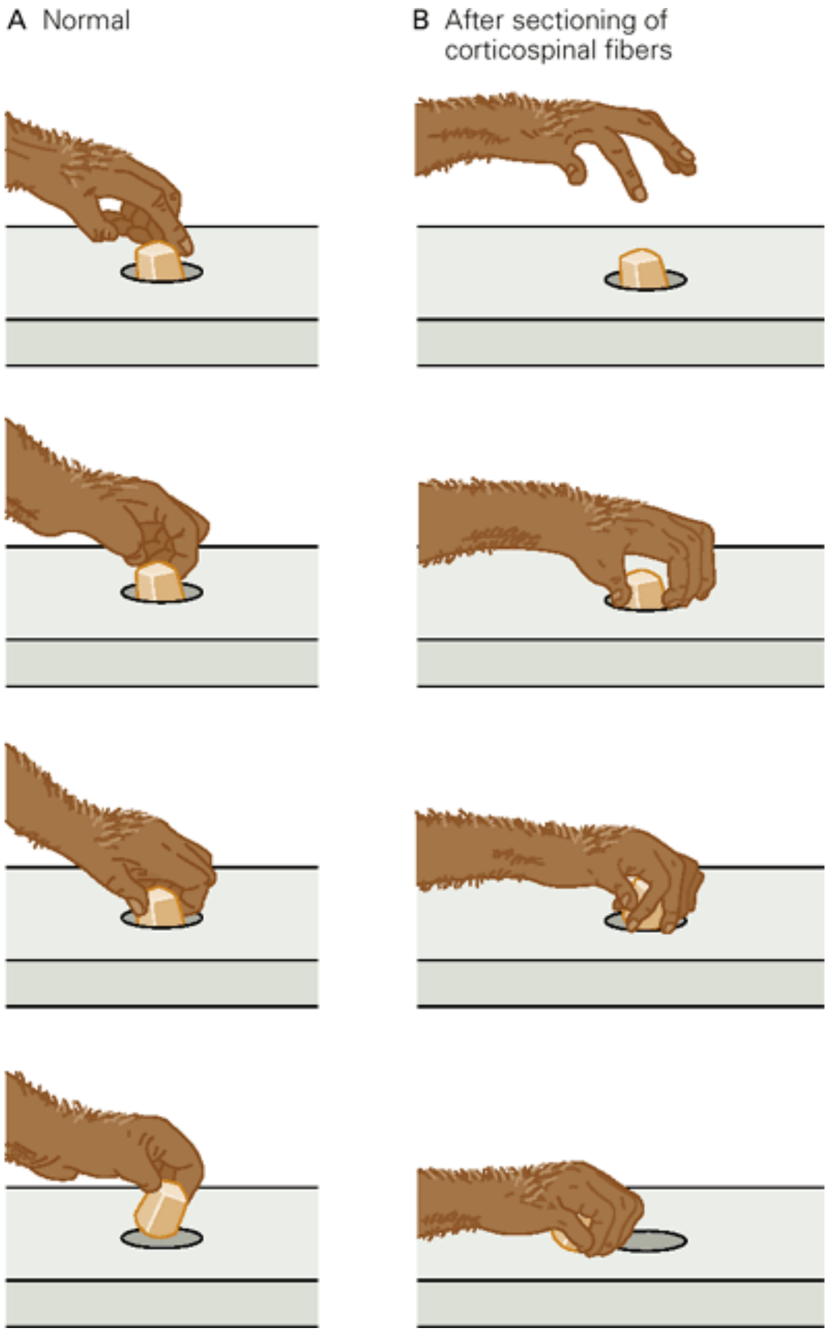
There are direct and indirect connections between the motor cortex and the spinal cord.

A. Direct pathway (pyramidal tract also called corticospinal tract) goes around pyramidal decussation and makes connections with motoneurons in the spinal cord. An indirect pathway from the cortex to the Red nucleus to the spinal cord is called the rubrospinal tract.

Just before entering the spinal cord, the pyramidal tract decussates. Fibres from the left hemisphere of the cortex cross over into the right lateral column of the spinal cord, and vice versa.

B. A second indirect pathway is composed of tracts that originate in various areas of the brainstem and contribute chiefly to postural control and certain reflex movements.

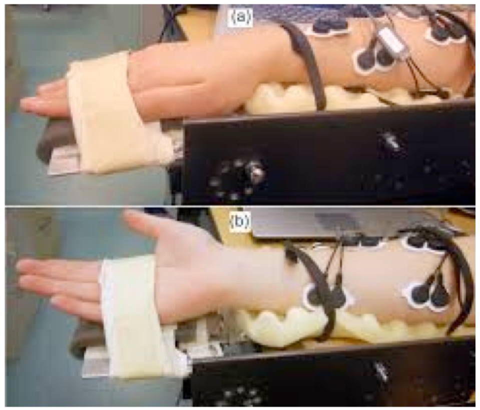
Direct corticospinal pathway is necessary for fine control of the digits.

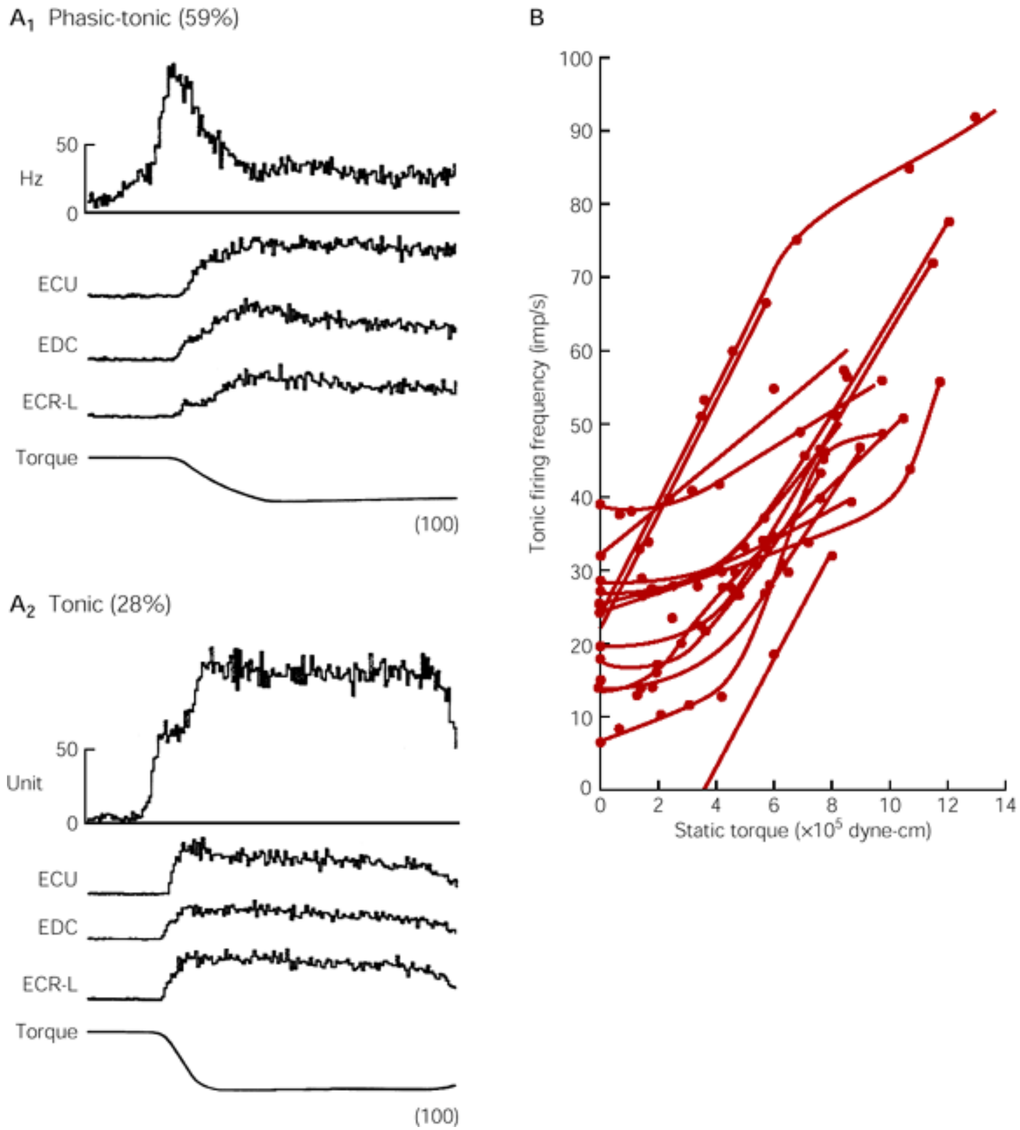


Sectioning the direct pathway produces contralateral weakness in monkeys. But the animals recover after a period of months, and they may climb, jump, and appear generally normal. Their partial recovery is possible because of the indirect pathway. However, some movements of the digits are lost permanently.

As shown on the picture, after bilateral sectioning of the corticospinal tract the monkey can only remove food from the well by grabbing with the whole hand.

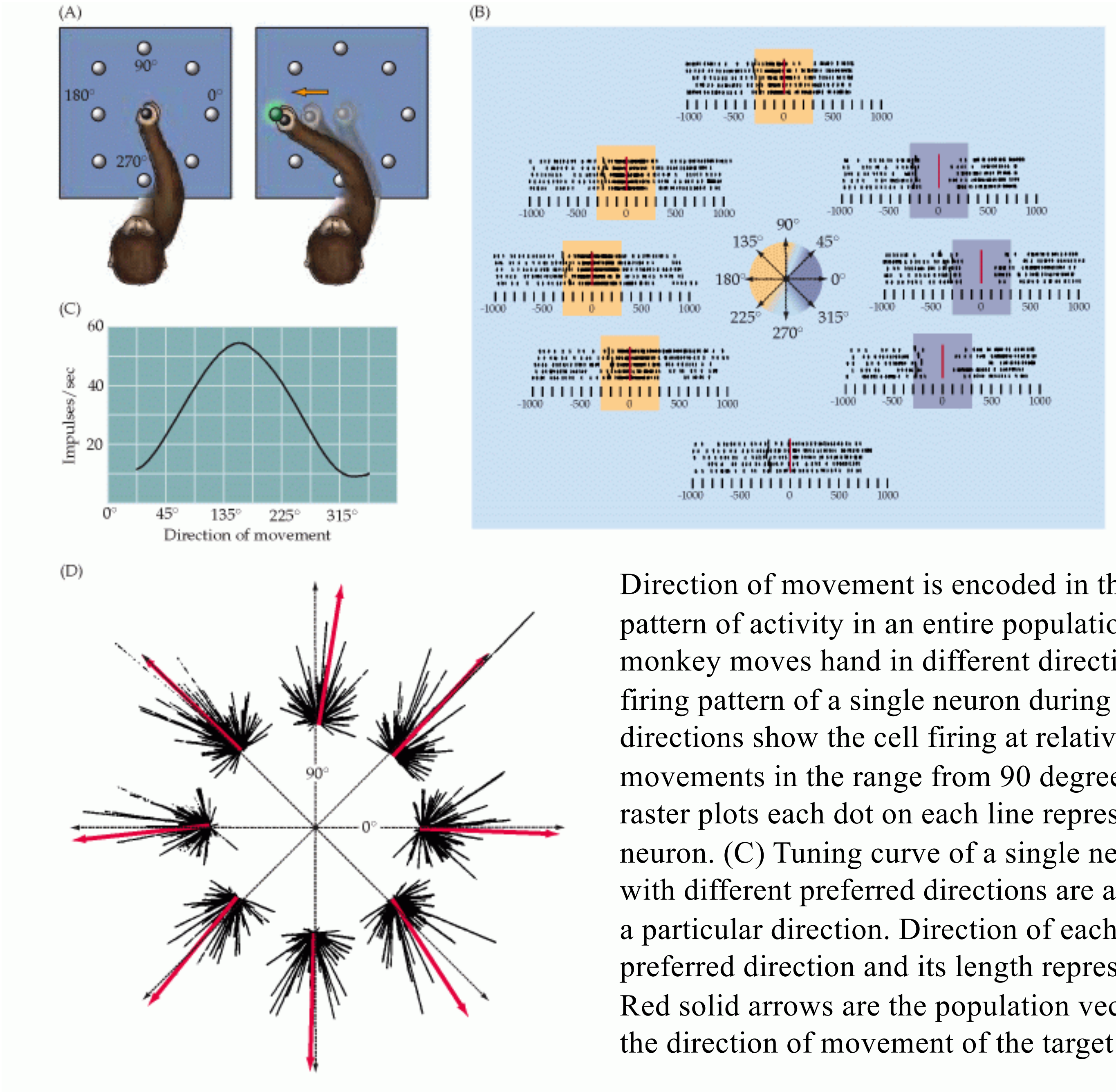
Muscle force is encoded in primary motor cortex activity





A1,2 Two types of characteristic response patterns in motor cortical neurons, phasic-tonic and tonic, during isometric wrist torques (picture) in which the torque level is reached and held. B. In both cell types activity increases with torque. The plot shows the relation between tonic firing rate (impulses per second) and static torque during wrist extension.

Direction of movement is encoded by populations of cortical neurons

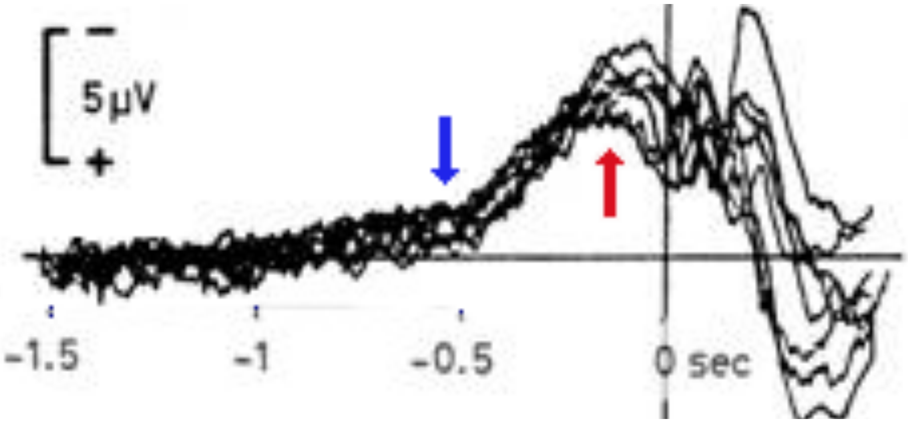


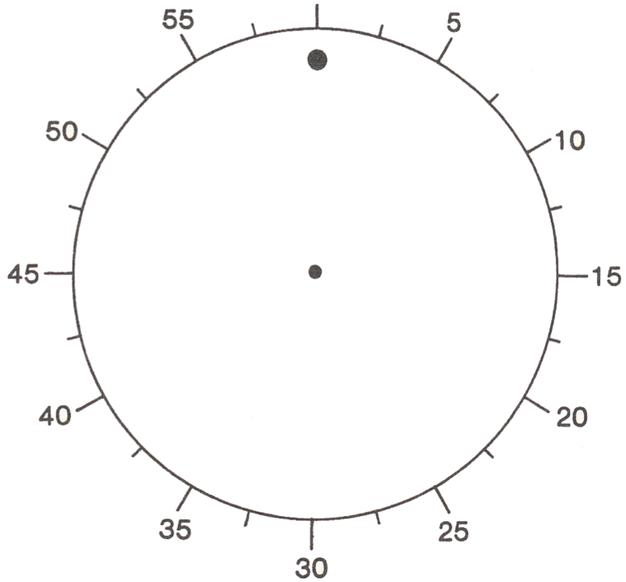
Direction of movement is encoded in the motor cortex by the pattern of activity in an entire population of cells. (A) Trained monkey moves hand in different directions. (B) Raster plots of the firing pattern of a single neuron during movement in eight directions show the cell firing at relatively higher rates during movements in the range from 90 degrees to 225 degrees. In the raster plots each dot on each line represents a spike in the recorded neuron. (C) Tuning curve of a single neuron. D. Cortical neurons with different preferred directions are all active during movement in a particular direction. Direction of each line represents the cell's preferred direction and its length represents the cell's firing rate. Red solid arrows are the population vectors; black thin arrows are the direction of movement of the target limb (Georgopoulos, 1982).

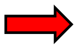
Libet's experiment and readiness potential

In voluntary movements the readiness potential RP (or germ. Bereitschaftspotential, BP) is observed in the EEG over supplementary motor area (SMA). In Benjamin Libet's experiment, it has been shown that the BP precedes by about 400 ms conscious decisions to perform volitional, spontaneous movements.

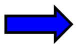
Libet's experiment (1983):





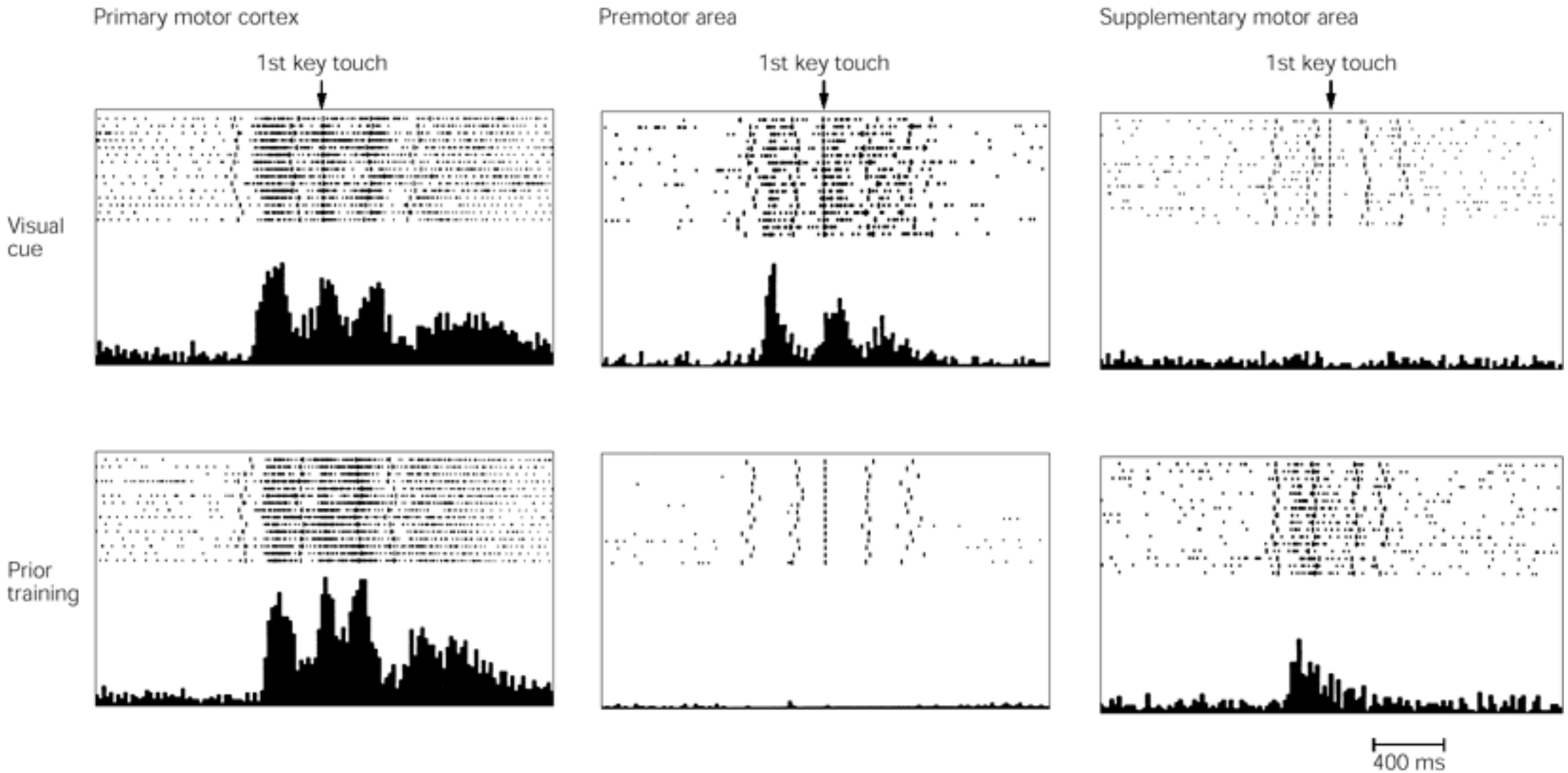


Conscious decision to move a finger



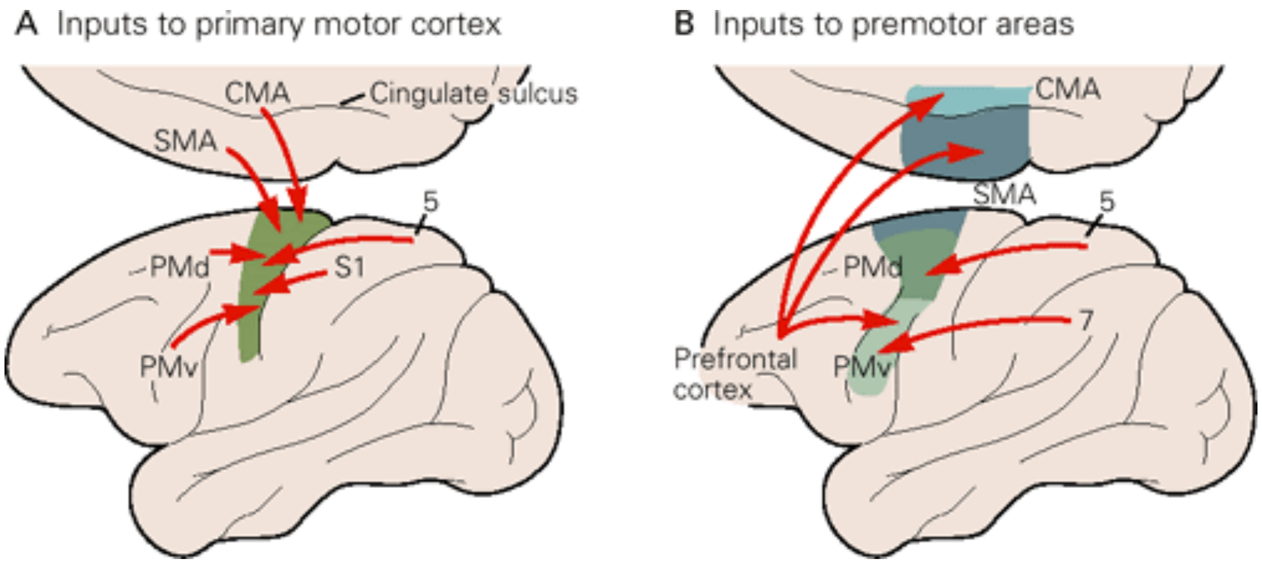
Beginning of readiness potential

Premotor areas - functions



Cell activity in the motor cortex depends on whether a sequence of movements is guided by visual cues or by prior training**.** Monkeys were required to press three buttons either in a sequence presented by lighting three panels or in a sequence they had learned previously. After being instructed to perform the observed sequence or the trained sequence, there was a delay before the animal was given a signal to initiate the movement. Raster plots represent cell discharge before and during movement on 16 trials, and the histogram shows the summed activity over all trials. Data are aligned to the onset of the first key touch. The cell in the primary cortex fired whether the sequence performed was the one learned in prior training or the one cued by lighted panels. The cell in the lateral premotor area (PM) fired only when the visually cued sequence was used, whereas the cell in the supplementary motor area (SMA) fired only when the trained sequence was used. Thus movements triggered by external sensory events involve the premotor areas. The supplementary motor area is involved in preparing movement sequences from memory in the absence of visual cues.

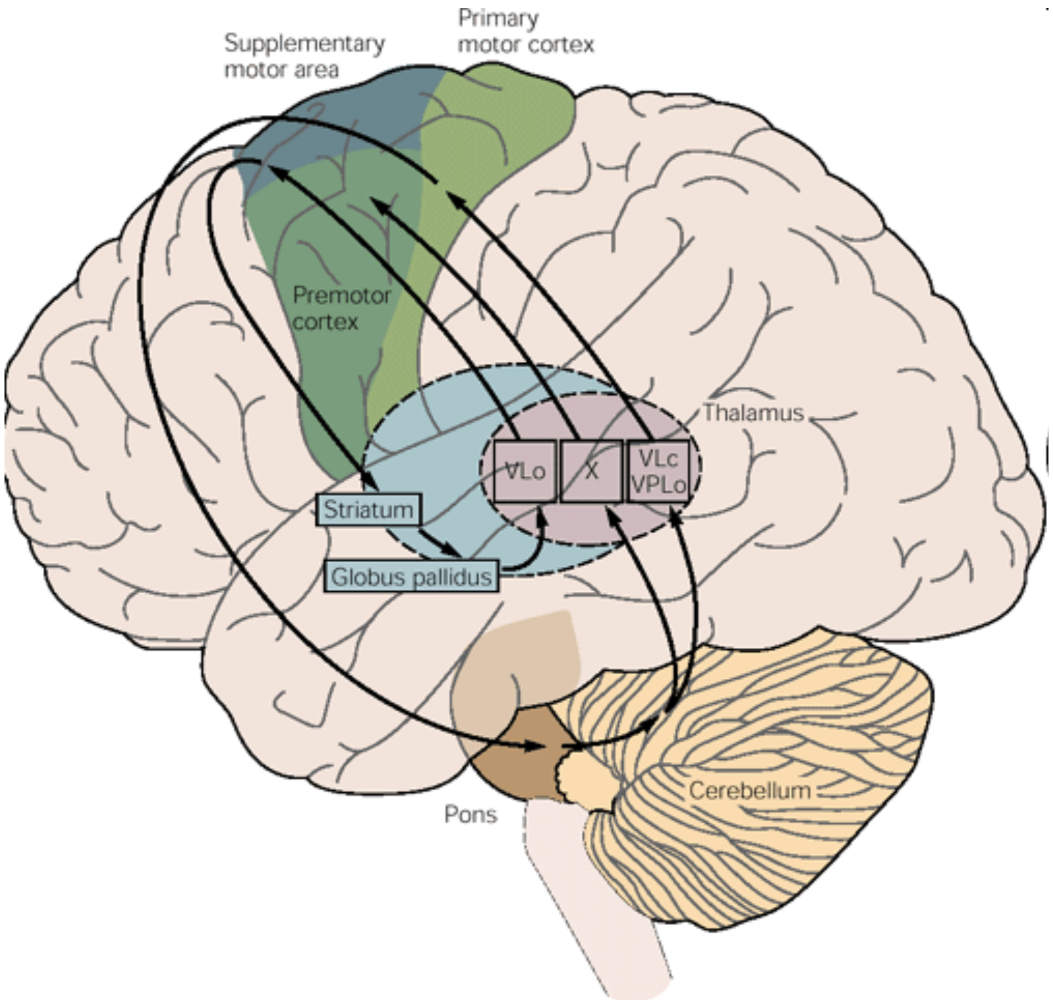
Cortical inputs to motor areas



A. The primary motor cortex receives inputs from: the primary somatosensory cortex (S1) and posterior parietal area 5 and premotor areas (PM).

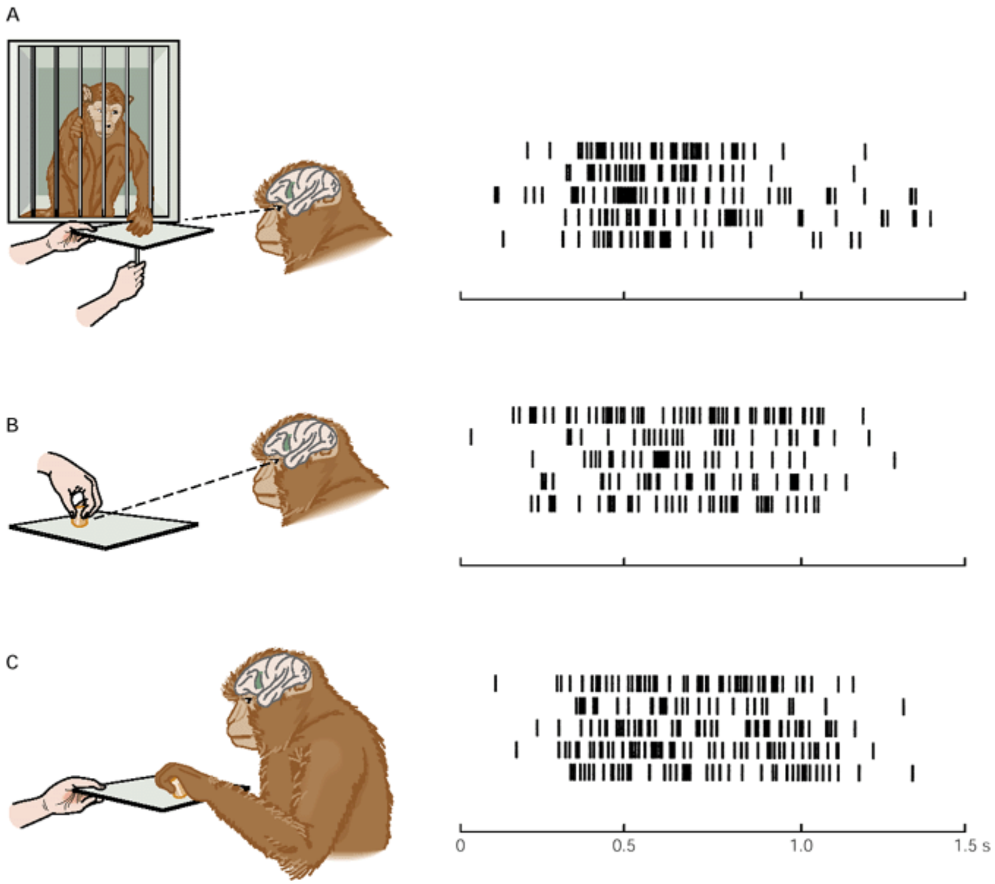
B. The premotor areas receive major inputs from areas 5 and 7 as well as from area 46 in the prefrontal cortex. Posterior parietal areas 5 and 7 are involved in integrating multiple sensory modalities for motor planning. Prefrontal cortex projects to the premotor area and to supplementary motor area and is important in working memory; it is thought to store information about the location of objects in space only long enough to guide a movement.

Subcortical inputs to the motor cortex



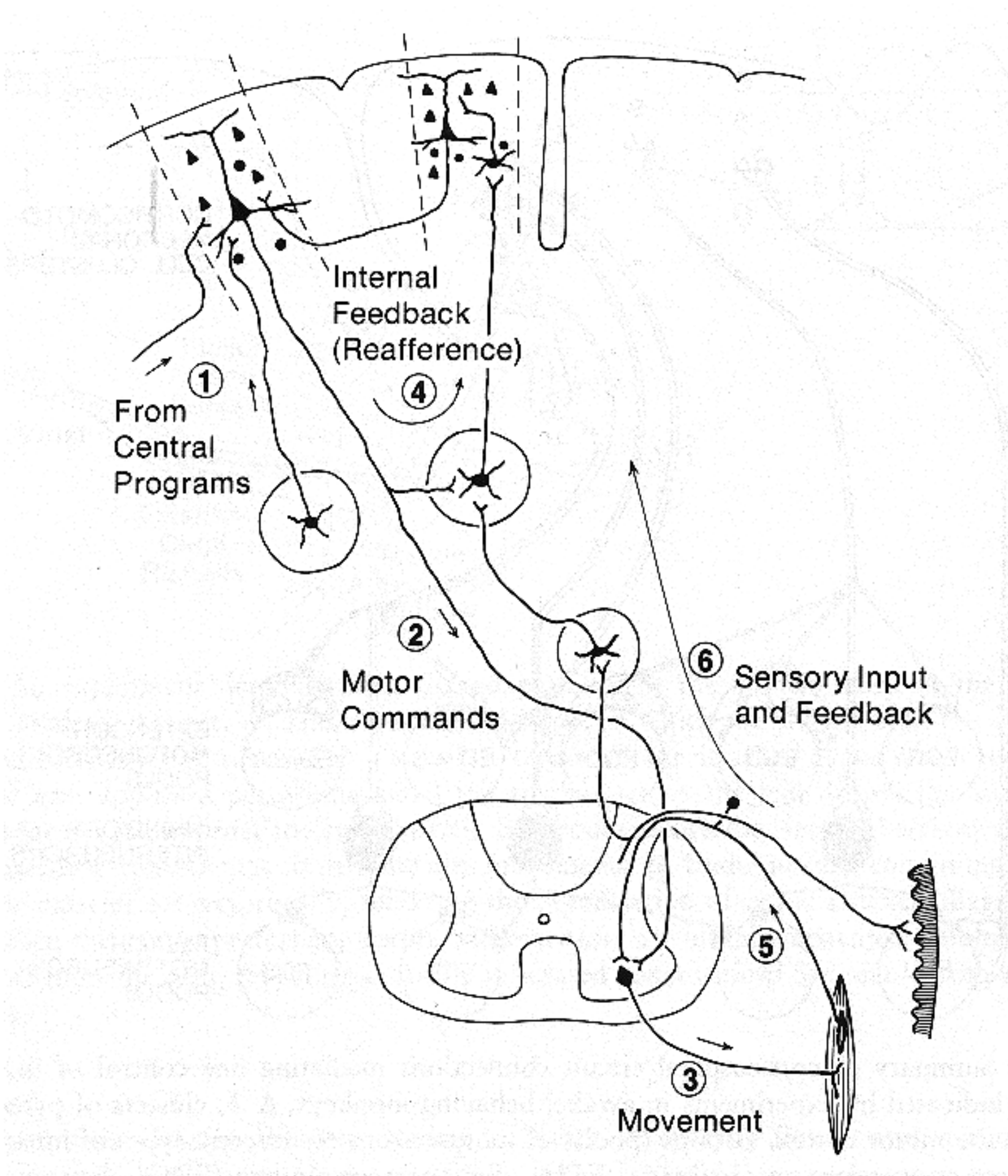
The premotor areas and primary motor cortex receive input from the basal ganglia and cerebellum via different sets of nuclei in the thalamus. The basal ganglia and cerebellum do not project directly to the spinal cord.

Mirror neurons



An individual cell in the premotor area is active whether the monkey performs a task or observes someone else perform the task. The fact that the same cell is active during action or observation suggests that it is involved in the abstract representation of the motor task. A. Activity in the neuron as the monkey observes another monkey make a precision grip. B. Activity in the same neuron as the monkey observes the human experimenter make the precision grip. C. Activity in the same neuron as the monkey itself performs a precision grip. (From Rizzolotti et al 1996.). These neurons have been called mirror neurons. Some researchers have argued that mirror neurons are the neural basis of the human capacity for emotions such as empathy.

Motor circuits - summary



1. Voluntary movements begin with central programs (prefrontal cortex) which activate, in appropriate pattern and sequence, the modules of the motor cortex.

2. The corticospinal fibers activate the motoneurons to the muscles.

3. Motoneurons elicit movements in the muscles.

4. Through collaterals, the corticospinal fibers also activate central sensory pathways and feed back the information to the cortex about the signals that have been sent.

5, 6 Sensory input from the muscles provides information about the state of contraction of the muscles and the extent of movement that has actually taken place.