Higher motor control

Motor cortex

1. Primary motor cortex (M I; Brodmann’s area 4):
   A. there is topographical representation of different muscle area of the body.
   B. the cortical representation of body part is proportionate in size to the skill with which the part is used.
   This is why more than half of entire primary motor cortex is concerned with controlling the hand and speech.
   C. stimulation of particular area in the motor cortex causes contraction of group of muscles not a single
      and this is due to overlapping in representation.
   D. the facial area is represented bilaterally, but the rest of the representation is unilateral.
   E. the cortical motor area controlling the muscular of the opposite side of the body
   F. cortical area representation of muscles may increase in size when motor learning is involving this is
      called cortical plasticity. This is why motor cortex map may change with experience.
   G. Cerebral cortex contains six layers of neurons.
   H. Vertical column found in ① somato-sensory cortex, ② visual cortex, and ③ motor cortex cells

Function:
① Exerts a continual tonic stimulatory effect on motor neurons
Execution of skill movements
Determines the direction, force and velocity of movements

Lesion:
1. Pure MI lesions are rare.
2. Lesion causes muscle hypotonia (weakness) not spasticity
3. Lesion affecting muscle contralateral (the opposite side of the body) side
4. Lesion affecting distal muscles (hand and finger)
5. Lesion causes loss ability to control fine movements

The vertical columns characterized by:
1. They have diameter ranges between 0.3 to 0.5 mm and contain about 10,000 cells bodies of neurons.
2. They functions as a unit, usually stimulating a group of synergistic muscles, but sometimes stimulating just a single muscle.
3. Each column contains 6 distinct layers of the cortex. They give rise to the corticospinal fibers all lie in the fifth layer of cells from the cortical surface. Conversely, the input signals all enter by way of layers 2 through 4. And the sixth layer gives rise mainly to fibers that communicate with other regions of the cerebral cortex itself.

4. The neurons of each column operate as an integrative system, using information from multiple inputs sources to determine the output responses.
5. Each column can functions as an amplifying system to stimulate large numbers of pyramidal fibers to the same muscles.
6. Each column of cells excites two populations of pyramidal cell neurons
   - Dynamic neurons: excessively excited for a short period at the beginning of a contraction, causing the initial rapid development of force
   - Static neuron: fire at a much slower rate, but they continue firing at this slow rate to maintain the force of contraction as long as the contraction is required i.e. maintains force

Secondary or Pre-motor cortex (M II):
Pre-motor cortex contains a somatotopic map
Pre-motor cortex receives input from sensory regions of the parietal cortex (Sensory guidance of movements)
Pre-motor cortex project to M-I, spinal cord and brain stem reticular formation (extrapyramidal pathway).
Pre-motor cortex and supplementary motor cortex share area 6.
Pre-motor cortex is more extensive than primary motor cortex.
Pre-motor cortex has the following features (although its functions are still incompletely understood):
Nerve signals generated in the premotor area cause much more complex “patterns” of movement than the
discrete patterns generated in the primary motor cortex.
a. Pre-motor cortex play role in setting posture at rest of planning movements so that the individual is
prepared to move
b. Pre-motor cortex is involved in control of proximal limb muscle thereby orienting the body for
movements
For instance, the pattern may be to position the shoulders and arms so that the hands are properly
oriented to perform specific tasks.
c. Pre-motor cortex are intimately involved in selecting a specific movement or sequence of movements
from the repertoire of possible movements
F. Lesion
Lesion of supplementary cortex may result in apraxia (impaired ability to develop strategy for movements)
Lesion results in re-emergence of suckling and grasp reflex in adults
Lesion do not causes paralysis but only slowing of the complex limb movements
Lesion may result in loss of short-term or working memory.
A special class of neurons called mirror neurons (found in pre-motor area) becomes active when a person
performs a specific motor task or when he or she observes the same task performed by others. Thus, the
activity of these neurons “mirrors” the behavior of another person as though the observer was performing
the specific motor task. Brain imaging studies indicate that these neurons transform sensory
representation of acts that are heard or seen into motor representation of these acts.

3. Supplementary motor area (M-III):
Supplementary motor area control the primary and pre-motor cortex
Supplementary motor area has topographical organization for the control of motor function, but it is less
precise than in primary motor cortex.
Supplementary motor area contraction often bilateral rather unilateral.
The functions of this area are:
A. Supplementary motor area appears to be involved primarily in programming motor sequence.
Supplementary motor area functions in mental rehearsal of movements before performing complex motor
function.

Supplementary motor area with premotor cortex translates the desire to perform a motor task into series of
motor commands that will do the task

The commands will be transfer primary motor are to be executed
B. Supplementary motor area activated before movement and prior to activation of the secondary and
primary motor areas, because Supplementary motor area is especially concerned with preparing the
hands, arms, and body to move
C. Supplementary motor area becomes active simultaneously with the intention to move
D. Supplementary motor area is involved in voluntary movements when the movements being performed
are complex and involve planning.
Supplementary motor area functions in concert with the premotor area to provide body-wide attitudinal movements, fixation movements of the different segments of the body, positional movements of the head and eyes, and so forth, as background for the finer motor control of the arms and hands by the premotor area and primary motor cortex. Lesions of this area in monkeys produce awkwardness in performing complex activities and difficulty with bimanual coordination.

4. Specialized area of motor control found in human motor cortex:
   A. Broca’s area "word formation" area 44, 45:
      Coordinate movements of tongue and vocal cord for word formation
      Damage to this area does not prevent vocalization but it makes it impossible for the person to speak whole word.
   B. Voluntary eye movement field:
      Damage to this area prevents a person from voluntarily moving the eye toward different objects and eyelid movements such as blinking
   C. Head rotation:
      This area is closely associated with the eye movement field; it directs the head toward different objects.
   D. Area for hand skills:
      Destruction in this area, the hand movement become uncoordinated and no purposeful a condition called (motor apraxia).

5. Posterior parietal cortex:
   Lesions of the posterior parietal cortex (Brodman’s area 5, 7) cause defects in motor performance that are characterized by inability to execute learned sequences of movements such as eating with a knife and fork. Some of the neurons in area 5 are concerned with aiming the hands toward an object and manipulating it, whereas some of the neurons in area 7 are concerned with hand–eye coordination.

Voluntary movements: simplified linear sequence of events:
Command must be organized by the brain:
1. Identify target is space:
   a. objective is identified in posterior parietal cortex (area 5,7) which receives input from somatosensory, visual, vestibular and auditory systems
   b. Sense of body position in relation to target also required
2. Information transmitted to supplementary and premotor area where the motor plan is developed
3. Motor plan transmitted to primary motor cortex and down descending pathway to interneurons and motor neurons.

Accessory motor system
It includes cerebellum and basal ganglia, where neither of these structures can control muscle function by itself. Instead, these structures always function in association with other systems of motor control.

The basal ganglia and cerebellum are large collections of nuclei that modify movement on a minute-to-minute basis. Impulses generated at the primary motor strip are sent via the extrapyramidal fibers to both, and both structures send information right back to cortex via the thalamus. (Remember, to get to cortex you must go through thalamus.) The output of the cerebellum is excitatory, while the basal ganglia are inhibitory. The balance between these two systems allows for smooth, coordinated movement, and a disturbance in either system will show up as movement disorders.

The basal ganglia
Functionally, the basal ganglia and their interconnections and neurotransmitters form the extrapyramidal system.

Anatomical structure:
1. Caudate nucleus.
2. Putamen.
4. Subthalamic nucleus.
5. Substania nigra.

Caudate nucleus + Putamen = Striatum
Globus pallidus + Putamen = Leticular nucleus.
substantia nigra is divided into a pars compacta and a pars reticulate. Globus pallidus is divided into external and internal segment.

**Metabolic consideration of basal ganglia:**
1. It has high oxygen consumption.
2. The copper content of the substantia nigra is particularly high.

**The functions of the basal ganglia:**
One of the principal roles of the basal ganglia in motor control is to function in association with the corticospinal system to control complex patterns of motor activity.

An example is the writing of letters of the alphabet, cutting paper with scissors, hammering nails, shooting a basketball through a hoop, most aspects of vocalization, controlled movements of the eyes, and virtually any other of our skilled movements, most of them performed subconsciously.

**Basic characteristic function of basal ganglia**
1. The basal ganglia are involved with subconscious control of skeletal muscle
2. The basal ganglia has the ability of “action selection” (i.e. it decide which loop to excite)
3. Under normal conditions, basal ganglia do not initiate particular movements
4. Primitive cortex for voluntary muscular activity

**Functions of Basal Ganglia**
1. Planning of movements
2. Control of complex & reflexive movements
3. Characteristics of movements: Timing of movements, Speed of movements and Scale the intensity of movements

For instance, a person may write the letter “a” slowly or rapidly. Also, he or she may write a small “a” on a piece of paper or a large “A” on a chalkboard. Regardless of the choice, the proportional characteristics of the letter remain nearly the same. In patients with severe lesions of the basal ganglia, these timing and scaling functions are poor (in fact, sometimes they are nonexistent).

4. Sequencing of multiple successive movements

5. Postural control (righting reflex, Sequencing of multiple parallel movements (Producing of automatic associated movement) Example Swing of arm while walking)

6. Help cortex to execute subconscious but learned patterns

7. Inhibition of motor tone

8. Control the group movements for emotional expression

9. Checks abnormal involuntary movements

10. Control of reflex muscular activity (Has inhibitory effect on spinal reflexes)

Neuronal circuitry of the Basal Ganglia:

Motor Loop:
First: executive loop
A. The putamen circuit
The putamen circuit is executive pattern of motor activity

The putamen circuit has two circuits:
a. Direct Pathway (Excitatory):
It is named as direct because it passes directly from Putamen to Globus pallidus (internal portion)
Indirect Pathway (inhibitory):
It is named as indirect because it passes indirectly from Putamen to Globus pallidus (external portion)

1. Cortex → Putamen → Globus pallidus (external portion) → sub-thalamic nucleus

Examples of functions:
- Cortical inputs excite via glutamate the putamen
- Putamen releases GABA to globus pallidus externa (GPe), decreasing activity of GPe
- Decreased activity of GPe leads to less inhibition via GABA of the thalamus
- Less inhibition of the thalamus means more excitation via glutamate of the motor cortex
- Motor cortex excited = Increase in movement
The putamen circuits has its inputs mainly from the parts of the brain adjacent to the primary motor cortex (mainly in the premotor and supplementary areas of the motor cortex and in the somatosensory areas of the sensory cortex) but not much from the primary motor cortex itself. Then its outputs do go mainly back to the primary motor cortex or closely associated premotor and supplementary cortex.

**Abnormal Function in the Putamen Circuit:**

1. Athetosis caused by lesions in the globus pallidus
2. Hemiballismus caused by lesion in the subthalamus
3. Chorea

C. Hyper-direct pathway: The cortico-subthalamo-pallidal (inhibitory):

Hyper-direct pathway conveys powerful excitatory effects from the motor-related cortical areas to the globus pallidus, bypassing the striatum, with shorter conduction time than effects conveyed through the striatum and connects the cortex directly to the subthalamic nucleus, which then sends excitatory projections to the globus pallidus internal segment. The pathway is therefore the fastest routes to influence basal ganglia output.

The three pathway will cooperate with each other to selected the desired movements where the three pathways will act on globus pallidus internal segment the desired movement will be stimulated by direct pathway and undesired movement inhibited (fast by hyper direct pathway and slow by indirect pathway).

Hemiballismus can be seen as a defect in action of both the hyperdirect and indirect pathways.

B. The nigrostriatal pathway

Nigrostriatal projection from the substantia nigra pars compacta to the striatum
There is a population of cholinergic neurons in the striatum whose axons do not leave the striatum (called striatal cholinergic interneurons or local circuit neurons). These cholinergic interneurons

a. The cholinergic actions INHIBIT striatal cells of the Direct pathway. 
Dopaminergic neuron type 1 receptors (D1) to the direct pathway is excitatory
b. The cholinergic actions EXCITE striatal cells of the Indirect pathway. 
Dopaminergic neuron type 2 receptors (D2) to indirect pathway is inhibitory

In other words, the direct pathway (which turns up motor activity) is excited by dopamine while the indirect pathway (which turns down motor activity) is inhibited. Both of these effects lead to increases thalamocortical activity and excite the sensimotor cortex, and facilitate movement activity. Thus the effects of cholinergic neurons are OPPOSITE the effects of dopamine on the direct and indirect pathways so the striatum effects on motor activity are opposite those of dopamine.

Disorders of the Basal Ganglia:

The histological hallmark of Parkinson's disease (PD) is the presence of fibrillar aggregates called Lewy bodies. Lewy body formation has been considered to be a marker for neuronal degeneration, because neuronal loss is found in the predilection sites for Lewy bodies. To date, more than 70 molecules have been identified in Lewy bodies, in which alpha-synuclein is a major constituent of Lewy bodies' fibrils.

Pathophysiology of Parkinson's disease
Direct Pathway:
\[ \downarrow \text{Dopamine effect (excitatory)} \quad \blacktriangleleft \quad \uparrow \text{Acetylcholine effect (inhibitory)} \quad \blacktriangleright \quad \text{inhibit direct pathway} \]
\[ \blacktriangleleft \text{motor activity (hypokinetic symptoms)} \]

Indirect Pathway:
\[ \downarrow \text{Dopamine effect (inhibitory)} \quad \blacktriangleleft \quad \uparrow \text{Acetylcholine effect (excitatory)} \quad \blacktriangleright \quad \text{stimulate indirect pathway} \]
\[ \blacktriangleleft \text{motor activity (hypokinetic symptoms)} \]

Normally there is balance between the effect of dopamine and acetylcholine but in Parkinson’s disease where there is decrease in dopamine this balance is disturbed so solve the problem of Parkinson’s disease we can either rising dopamine level (by dopamine supply or remove enzyme inhibitory effect) or lowering acetylcholine level in striatum (anticholinergic drug).

Both treatments increase activity in the Direct Pathway (the “turning up” system) and decrease activity in the Indirect Pathway (the “turning down” system)

Clinical Presentation:
Damage to the basal ganglia causes two different classes of syndromes, one characterized by an increase in movement (hyperkinetic) and the other characterized by decreased movement (hypokinetiic).
The hypokinesia (reduced movement) is the hallmark of Parkinson’s disease, three other signs (rigidity, tremor and loss of postural reflexes) accompany this decrease in movement.

1. Rigidity

Rigidity resistance to passive movement
Rigidity is present in all muscle groups, both flexor and extensor

Rigidity is of two types:

a. lead-pipe rigidity: resistance to passive movement is intense and consistent through the entire range of motion

b. cog-wheeling rigidity: resistance to passive movement is intermittent change in tone to passive movement of joint

Unlike the spasticity linked to upper motor neuron lesions (altered skeletal muscle performance with a combination of paralysis, increased tendon reflex activity (hyper-reflexia) and hypertonia)

When one limb is engaged in voluntary active movement, the other limb is often stiff.

Stiffness of the limbs, face, and posture are typical and may cause shoulder pain early in the disease. Because rigidity inhibits the alternating contraction and relaxation of muscles, movement is often slow and jerky.
The tremor is often the first symptom. The tremor is more noticeable at rest and tends to increase with walking, concentration, and feelings of anxiety. About 75% of patients have unilateral resting tremor on diagnosis. The tremor may involve "pill rolling" movement of forefinger and thumb or pronation-supination (slow turning) of the forearm. The tremor may involve the diaphragm, tongue, lips, and jaw, but tremor of the head rarely occurs. The tremor may be noticeable with handwriting. Some develop micrographia (small, cramped handwriting).

Postural instability
The gradual change in posture can include:
- flexion of the head (the head bent forward)
- stooping (hunched shoulders and upper body)
- leaning forward
- an inability to maintain an upright trunk position when sitting or standing.
- There is a tendency to hold arms in a flexed position when walking.
- People with more advanced Parkinson's disease have difficulty making postural adjustments, or righting themselves, if they begin leaning or falling.
As the reflexes needed to maintain upright posture are gradually lost, there is an increased risk of falls and injury.

Gait disturbances (bradykinesia)
- Rigidity and postural instability
- walking with
  - shuffling gait (small steps followed by the need for quicker steps to maintain balance)
  - festinating gait: appear to be walking up stairs, unable to walk on heels, imbalance and short steps that tend to accelerate in an effort to "catch up" with the body's center of gravity. This stumbling run creates a potential risk of falling.
  - decreased arm swing are used to help maintain upright posture when walking.
There is also a tendency to turn "en bloc," all together - as a whole, with neck and trunk rigid, taking many small steps to turn.

In more advanced disease, there may be gait "freezing" episodes, a sudden inability to move feet and legs, lasting a few seconds or longer. It may occur at the onset of walking (start hesitation), or when changing directions, or when walking through a narrow space like a doorway.

http://www.neuroanatomy.wisc.edu/coursebook/motor2.pdf
http://www.indiana.edu/~m131/lectures/BGb%20C%202016.pdf

Second: cognitive loop
The caudate circuit:
The caudate nucleus plays a major role in this cognitive control of motor activity
Cognitive process
The term (cognition) means the thinking processes of the brain, using both the sensory input to the brain and the information already stored in memory. Most of our actions occur as a consequence of thoughts generated in the mind, process called (cognitive control of motor activity). The caudate nucleus plays a major role in this cognitive control of motor activity. Thus, cognitive control of motor activity determines sub-consciously which patterns of movement will be used together and in which sequence to achieve a complex goal.

The caudate nucleus receives large amounts of its input from the association areas of the cerebral cortex overlying the caudate nucleus, mainly areas that also integrate the different types of sensory and motor information into usable thought patterns. The returning signals go to the accessory motor regions in the premotor and supplementary motor areas that are concerned with putting together sequential patterns of movement.

Cerebral cortex ➤ caudate nucleus ➤ internal Globus Pallidus ➤ thalamus

A good example of this phenomenon would be a person seeing a lion approach and then responding instantaneously and automatically by
(1) turning away from the lion, (2) beginning to run, and (3) even attempting to climb a tree.
Without the cognitive functions, the person might not have the instinctive knowledge, without thinking for too long a time, to respond quickly and appropriately. Thus, cognitive control of motor activity determines subconsciously, and within seconds, which patterns of movement will be used together to achieve a complex goal that might itself last for many seconds.

One especially important cortical area is the posterior parietal cortex, which is the locus of the spatial coordinates for motor control of all parts of the body, as well as for the relation of the body and its parts to all its surroundings.

Damage to posterior parietal cortex produce

1. **Agnosia**: inability to recognize sensory inputs such as light, sound, and touch
2. **Personal neglect syndrome**

**Non-motor Loop:**

A. **Limbic loop:**
   It is involved in giving motor expression to emotions like smiling, aggressive or submissive posture

B. **Occulomotor loop:**
   It is concerned with voluntary eye movements (saccadic movements)

C. **Prefrontal loop**
   It may regulate the initiation and termination of cognitive processes such as planning, working memory, and attention.
The cerebellum
The cerebellum plays major roles in:
a. the timing of motor activities
b. in rapid, smooth progression from one muscle movement to the next.
c. in the intensity of muscle contraction when the muscle load changes
d. in controls the necessary instantaneous interplay between agonist and antagonist muscle groups.
The cerebellum helps in:
a. sequence the motor activities
b. monitors the motor activities
c. makes corrective adjustments in the body’s motor activities while they are being executed so that they will conform to the motor signals directed by the cerebral motor cortex and other parts of the brain.

Afferent Pathways from Other Parts of the Brain.
1. the corticopontocerebellar pathway
2. afferent tracts originate in each side of the brain stem
   a. olivocerebellar tract
   b. vestibulocerebellar fibers
   c. reticulocerebellar fibers
Afferent Pathways from the Periphery.

A. spinocerebellar tract
The spinocerebellar pathways can transmit impulses at velocities up to 120 m/sec, which is the most rapid conduction in any pathway in the central nervous system.

The dorsal spinocerebellar tract
The signals transmitted in the dorsal spinocerebellar tracts come mainly from the muscle spindles and to a lesser extent from other somatic receptors throughout the body, such as Golgi tendon organs, large tactile receptors of the skin, and joint receptors. All these signals apprise the cerebellum of the momentary status of (a) muscle contraction, (b) degree of tension on the muscle tendons, (c) positions and rates of movement of the parts of the body, and (d) forces acting on the surfaces of the body.

The ventral spinocerebellar tract.
The ventral spinocerebellar tracts receive from anterior horns of the spinal cord from (1) the brain through the corticospinal and rubrospinal tracts and (2) the internal motor pattern generators in the cord itself. Thus, this ventral fiber pathway tells the cerebellum which motor signals have arrived at the anterior horns; this feedback is called the “efference copy” of the anterior horn motor drive.

B. spinoreticular pathway & spino-olivary pathway
the movements and positions of all parts of the body even though it is operating at a subconscious level

Spinal cord

The spinoreticular pathway to the reticular formation of the brain stem and also through the spino-olivary pathway to the inferior olivary nucleus

Cerebellum

Deep Cerebellar Nuclei and the Efferent Pathways.
Located deep in the cerebellar mass on each side are three deep cerebellar nuclei: the dentate (سمن, interposed (The emboliform and globose nuclei are known collectively as the nucleus interpositus) وسط، and fastigial (The vestibular nuclei in the medulla also function in some respects as if they were deep cerebellar nuclei because of their direct connections with the cortex of the flocculonodular lobe.)

Each time an input signal arrives in the cerebellum, it divides and goes in two directions:
(1) directly to one of the cerebellar deep nuclei
(2) to a corresponding area of the cerebellar cortex overlying the deep nucleus.

Then, a fraction of a second later, the cerebellar cortex relays an inhibitory output signal to the deep nucleus.

Thus, all input signals that enter the cerebellum eventually end in the deep nuclei in the form of initial excitatory signals followed a fraction of a second later by inhibitory signals.

From the deep nuclei, output signals leave the cerebellum and are distributed to other parts of the brain.

The three major layers of the cerebellar cortex are:
① The molecular layer (close to the surface): contains a. Dendrites of Purkinje cell and Golgi type cell b. Granular cell T-fibers or Parallel fibers c. stellate cell d. Basket cell
② Purkinje cell layer: a. Purkinje cell b. Astrocytes
Granule cell layer: a. Granular cell b. Golgi type cell
Beneath these cortical layers, in the center of the cerebellar mass, are the deep cerebellar nuclei that send output signals to other parts of the nervous system.

**Functional Unit of the Cerebellar Cortex (canonical circuit):**
The cerebellum has about 30 million nearly identical functional units.
The cerebellum functional unit centers
1. on a single, very large Purkinje cell
2. on a corresponding deep nuclear cell

The histology of cerebellar cortex neuronal cells:

a. The Purkinje cells:
The Purkinje cells are among the biggest neurons in the body.
The Purkinje cells have very extensive dendritic arbors that extend throughout the molecular layer.

b. The granule cells
The granule cells, which receive input from the mossy fibers and innervate the Purkinje cells.
The granule cells have their cell bodies in the granular layer.
The granule cells send an axon to the molecular layer, where the axon bifurcates to form a T.
The granule cells' branches of the T are straight and run long distances.
The granule cells' branches of the T are called parallel fibers.
The dendritic trees of the Purkinje cells are markedly flattened and oriented at right angles to the parallel fibers. The parallel fibers thus make synaptic contact with the dendrites of many Purkinje cells, and the parallel fibers and Purkinje dendritic trees form a grid of remarkably regular proportions (receive >150,000 parallel fiber synaptic inputs).

c. The other three types of neurons in the cerebellar cortex are in effect inhibitory interneurons.
   1. Basket cells
   Basket cells are located in the molecular layer.
Basket cells receive input from the parallel fibers and each projects to many Purkinje cells. Basket cells axons form a basket around the cell body and axon hillock of each Purkinje cell they innervate.

2. Stellate cells
Stellate cells are similar to the basket cells but more superficial in location.

3. Golgi cells
Golgi cells are located in the granular layer. Golgi cells dendrites, which project into the molecular layer, receive input from the parallel fibers. Golgi cells cell bodies receive input via collaterals from the incoming mossy fibers and the Purkinje cells. Golgi cells axons project to the dendrites of the granule cells.

Four of the five cell types are inhibitory, including Golgi cells, stellate cells, basket cells, and Purkinje cells; where the neurotransmitter is GABA. The fifth type, granular cells, represent the only excitatory cells in the cerebellar cortex.

The main inputs to the cerebellar cortex (Afferent pathway to cerebellar cortex circulatory neurons):

a. The climbing fibers
Climbing fiber come from a single source, the inferior olivary nuclei of the medulla. Climbing fiber inputs exert a strong excitatory effect on single Purkinje cells. There is only one climbing fiber per Purkinje cell (each climbing fiber only goes to one to three Purkinje cells).

This climbing fiber is distinguished by the fact that a single impulse in it will always cause a single, prolonged (up to 1 second), peculiar type of action potential in each Purkinje cell with which it connects, beginning with a strong spike and followed by a trail of weakening secondary spikes. This action potential is called the complex spike.

b. The mossy fibers
Mossy fibers come from Reticular nuclei, Vestibular nuclei, pontine nuclei and spino-cerebellar tract. The mossy fibers provide direct proprioceptive input from all parts of the body plus input from the cerebral cortex via the pontine nuclei to the cerebellar cortex. The mossy fibers input exert weak excitatory input on many Purkinje cells via granule cells. The mossy fibers end on the dendrites of granule cells in complex synaptic groupings called glomeruli. The glomeruli also contain the inhibitory endings of the Golgi cells.
The climbing fibers and the mossy fibers are excitatory; release excitatory neurotransmitter, glutamate in the case of the mossy fibers and aspartate in the case of climbing fibers.

The main outputs to the cerebellar cortex (Efferent pathway to cerebellar cortex circulatory neurons):
The Purkinje cell output is the only output to deep Cerebellar Nuclei.

Deep Cerebellar Nuclei receives
1. Two excitatory stimuli from climbing fibers and mossy fibers
2. One inhibitory stimuli from Purkinje cells

One characteristic of both Purkinje cells and deep nuclear cells is that normally both of them fire continuously; the Purkinje cell fires at about 50 to 100 action potentials per second, and the deep nuclear cells fire at much higher rates. Furthermore, the output activity of both these cells can be modulated upward or downward.

the deep cerebellar nuclei first excited by signal from the cerebral motor cortex or brain stem through climbing fibers and mossy fibers► increases deep nuclear cell excitation► enhance the motor movement► (after few milliseconds) inhibitory signal from Purkinje cells to stop the muscle movement from overshooting its mark. Otherwise, oscillation of the movement would occur

It is interesting, the inhibitory Purkinje cell input to deep cerebellar nuclei but the output of deep cerebellar nuclei to the brain stem and thalamus is always excitatory.

1. fastigial nuclei (control extensor muscles)► reticular formation and vestibular nuclei
2. interposed nuclei (control flexor muscles)► red nuclei and thalamus
3. dentate nuclei (coordination)► red nuclei and thalamus

The neuronal circuit through cerebellar cortex
First: Consider first the flow of information through the cerebellar cortex after stimulation of the mossy fiber system. Mossy fibers excite granule cells, which, in turn, excite Purkinje cells

A. granular cell and Golgi cell
Granule cell, which can be inhibited in two ways.
1. Feed-forward inhibition (inhibition of the output=feed-forward)
   Mossy fibers (+) ► granule cell (+) ► parallel fiber ► Golgi cell (+) ► granule cell (-)
2. Feedback inhibition (inhibition of the input=feedback)
   Mossy fiber [+ ] ► Golgi cell [- ] ► granule cell [- ]

B. parallel fiber
Granule cell (+) ► parallel fiber ► stellate cells (+), basket cells (+) and Purkinje cell (+)

C. stellate cells and basket cells
i. Stellate cells ► Purkinje cell (-) inhibition of the output=feed-forward inhibition
ii. Basket cells ► Purkinje cell (-) inhibition of the output=feed-forward inhibition

Both cells cause lateral inhibition of adjacent Purkinje cells, thus sharpening the signal

The mossy fiber input to the Purkinje cell synaptic connections are weak, so large numbers of mossy fibers must be stimulated simultaneously to excite the Purkinje cell called a simple spike

ملاحظة: عندما يكون (parallel fiber عبر وسط هو (inhibition) فانه يكون (feed-forward inhibition) و (feedback inhibition) عندما لا يكون هناك وسط فانه يكون (feed-forward inhibition)
Function of the cerebellum in overall motor control:
The nervous system uses the cerebellum to coordinate motor control functions at three levels:

1. The vestibulocerebellum (or flocculonodular lobe).

   Structures: flocculo-nodular lobe (flocculus and nodulus)

   In people with vestibulocerebellar dysfunction, balance (equilibrium) is far more disturbed during performance of rapid motions than during stasis, especially when these movements involve changes in direction of movement, posture and muscle tone, coordination of gait, eye movements and stimulate the semicircular ducts.

   This phenomenon suggests that the vestibulocerebellum is important in controlling balance between agonist and antagonist muscle contractions of the spine, hips, and shoulders during rapid changes in body positions as required by the vestibular apparatus.

   One of the major problems in controlling balance is the amount of time required to transmit position signals and velocity of movement signals from the different parts of the body to the brain.

   To solve this problem is “anticipatory correction”

\[
\begin{array}{|c|c|c|c|}
\hline
\text{Neuron} & \text{Action on} & \text{Action} & \text{Neurotransmitter} \\
\hline
\text{Climbing fibers} & \text{Purkinje cells and} & \text{Excitation} & \text{Aspartate} \\
& \text{Cerebellar nuclei} & & \\
\hline
\text{Mossy fibers} & \text{Granule cells} & \text{Excitation} & \text{Glutamate} \\
& \text{Golgi cells and} & & \\
& \text{Cerebellar nuclei} & & \\
\hline
\text{Granule cells} & \text{Purkinje cells} & \text{Excitation} & \text{Glutamate/Aspartate} \\
& \text{Stellate cells} & & \\
& \text{Basket cells} & & \\
\hline
\text{Stellate cells} & \text{Purkinje cells} & \text{Inhibition} & \text{GABA} \\
\hline
\text{Basket cells} & \text{Purkinje cells} & \text{Inhibition} & \text{GABA} \\
\hline
\text{Golgi cells} & \text{Granule cells} & \text{Inhibition} & \text{GABA} \\
\hline
\text{Purkinje cells} & \text{Cerebellar nuclei} & \text{Inhibition} & \text{GABA} \\
& \text{Vestibular nuclei} & & \\
\hline
\end{array}
\]
The signals from the periphery tell the brain how rapidly and in which directions the body parts are moving. It is then the function of the vestibulocerebellum to calculate in advance from these rates and directions where the different parts will be during the next few milliseconds. The results of these calculations are the key to the brain’s progression to the next sequential movement.

2. The spinocerebellum (because it receive information from spinal cord)

Structures: vermis and intermediate zone of the cerebellar hemispheres (para-vermis) the intermediate zone of each cerebellar hemisphere receives two types of information when a movement is performed:

1. Information from the cerebral motor cortex and from the midbrain red nucleus (cortico-ponto-cerebellar tract) telling the cerebellum the intended sequential plan of movement for the next few fractions of a second,
2. feedback information from the peripheral parts of the body, especially from the distal proprioceptors of the limbs (the dorsal spinocerebellar tract), telling the cerebellum what actual movements result.

After the intermediate zone of the cerebellum (also inferior olivary complex) has compared the intended movements with the actual movements, the deep nuclear cells of the interposed nucleus send corrective output signals back.
(1) to the cerebral motor cortex through relay nuclei in the thalamus and
(2) to the magnocellular portion (the lower portion) of the red nucleus that gives rise to the
rubrospinal tract.
The rubrospinal tract in turn joins the corticospinal tract in innervating the lateral-most motor neurons
in the anterior horns of the spinal cord gray matter, the neurons that control the distal parts of the
limbs, particularly the hands and fingers.
This part of the cerebellar motor control system
(1) Provides smooth, coordinated movements of the agonist and antagonist muscles of the distal
limbs for performing acute purposeful patterned movements.
(2) Cerebellar learning mechanisms, eventually corrects the motions until they perform the desired
function.

3. The cerebro-cerebellum
Structures: lateral cerebellar hemispheres
experimental studies suggest that these portions of the cerebellum are concerned with two important
but indirect aspects of motor control:
(1) the planning of sequential movement (ability to progress smoothly from one movement to the
next in orderly succession)
(2) the “timing” of the sequential movements.
Destruction of the lateral zones of the cerebellar hemispheres, along with their deep nuclei, the
dentate nuclei, can lead to extreme incoordination of complex purposeful movements of the hands,
fingers, and feet and of the speech apparatus.
In human beings, the lateral zones of the two cerebellar hemispheres are highly developed and
greatly enlarged. This characteristic goes along with human abilities to plan and perform intricate
sequential patterns of movement, especially with the hands and fingers, and to speak. Yet,
(1) The large lateral zones of the cerebellar hemispheres have no direct input of information from the
peripheral parts of the body.
(2) Almost all communication between these lateral cerebellar areas and the cerebral cortex is not
with the primary cerebral motor cortex but instead with the premotor area and primary and
association somatosensory areas.
Functions of cerebellum
① Planning of sequential movements
It seems that the “plan” of sequential movements actually begins in the sensory and premotor areas
of the cerebral cortex, and from there the plan is transmitted to the lateral zones of the cerebellar
hemispheres (involved not with what movement is happening at a given moment but with what will
be happening during the next sequential movement a fraction of a second or perhaps even seconds
later. Then, amidst much two-way traffic between cerebellum and cerebral cortex, appropriate
motor signals provide transition from one sequence of movements to the next.
② Timing function.
A. The lateral zones of the cerebellar hemispheres is to provide appropriate timing for each
succeeding movement.
In the absence of these cerebellar zones, one loses
a. the subconscious ability to predict ahead of time how far the different parts of the body will move
in a given time.
b. the person becomes unable to determine when the next sequential movement needs to begin.
As a result, the succeeding movement may begin too early or, more likely, too late.
B. the large lateral lobes helps to “time” events other than movements of the body. For instance, the rates of progression of both auditory and visual phenomena can be predicted by the brain, but both of these require cerebellar participation. As an example, a person can predict from the changing visual scene how rapidly he or she is approaching an object.

3 Prevent Overshoot and to “Damp” Movements

action tremor or intention tremor.

If the cerebellum is intact, appropriate learned, subconscious signals stop the movement precisely at the intended point, thereby preventing

1. the overshoot
2. the tremor (action tremor or intention tremor).

This activity is the basic characteristic of a damping system.

All control systems regulating pendular elements that have inertia must have damping circuits built into the mechanisms. For motor control by the nervous system, the cerebellum provides most of this damping function.

4 Cerebellar Control of Ballistic Movements

Ballistic movement is muscle contractions that exhibit maximum velocities and accelerations over a very short period of time. They exhibit high firing rates, high force production, and very brief contraction times. Example fingers in typing, saccadic movements of the eyes these movement are fast so no time for feedback information about muscle during action but the entire movement is preplanned

When the cerebellum is removed, three major changes occur:

(1) The movements are slow to develop and do not have the extra onset surge
(2) the force developed is weak,
(3) the movements are slow to turn off, usually allowing the movement to go well beyond the intended mark.

Therefore, in the absence of the cerebellar circuit, the motor cortex has to think extra hard to turn ballistic movements on and again has to think hard and take extra time to turn the movement off. Thus, the automatism of ballistic movements is lost.

5 The Purkinje cells “Learn” to correct motor error (Role of the Climbing Fibers)

Under resting conditions the climbing fibers fire about once per second

\[ \text{extreme depolarization of the entire dendritic tree of the Purkinje cell, lasting for up to a second, each time they fire.} \]

the Purkinje cell fires (complex spike)

When a person performs a new movement for the first time, feedback signals from the muscle and joint proprioceptors will usually denote to the cerebellum how much the actual movement fails to match the intended movement, and the climbing fiber signals alter the long-term sensitivity of the Purkinje cells in some way. Over a period, this change in sensitivity, along with other possible “learning” functions of the cerebellum, is believed to make the timing and other aspects of cerebellar
control of movements approach perfection. When this state has been achieved, the climbing fibers no longer need to send “error” signals to the cerebellum to cause further change.

**Turn-On/Turn-Off (agonist muscle) and Turn-Off/Turn-On (antagonist muscle)**

**Output Signals from the Cerebellum**

The typical function of the cerebellum is to help provide rapid turn-on signals for the agonist muscles and simultaneous reciprocal turn-off signals for the antagonist muscles at the onset of a movement. Then, upon approaching termination of the movement, the cerebellum is mainly responsible for timing and executing the turn-off signals to the agonists and the turn-on signals to the antagonists.

### Clinical Abnormalities of the Cerebellum

<table>
<thead>
<tr>
<th>Vestibulocerebellum</th>
<th>A. Eye movement disorder:</th>
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<tbody>
<tr>
<td></td>
<td>1. Nystagmus</td>
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<td></td>
<td>2. Vestibulo-ocular reflex</td>
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<tr>
<td>spinocerebellum.</td>
<td>Truncal or gait ataxia</td>
</tr>
<tr>
<td>cerebrocerebellum</td>
<td>A. Limb or appendicular ataxia</td>
</tr>
<tr>
<td></td>
<td>1. Dysmetria</td>
</tr>
<tr>
<td></td>
<td>i. hypometria</td>
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<tr>
<td></td>
<td>ii. hypermetria or past pointing</td>
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<tr>
<td></td>
<td>2. Dysdiadocho-kinesia</td>
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<td></td>
<td>B. Dysarthria</td>
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<td></td>
<td>C. Hypotonia</td>
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<td>D. intention tremor</td>
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Typical defects observed in cerebellar diseases.

A. A lesion in the left cerebellar hemisphere delays the initiation of movement. The patient is told to clench both hands at the same time on a “go” signal. The left hand is clenched later than the right, as is evident in the recordings from a pressure bulb transducer squeezed by the patient.

B. A patient moving his arm from a raised position to touch the tip of his nose exhibits inaccuracy in range and direction (dysmetria) and moves his shoulder and elbow separately (decomposition of movement). Tremor increases as the finger approaches the nose.

C. A subject was asked to alternately pronate and supinate the forearm while flexing and extending at the elbow as rapidly as possible. Position traces of the hand and forearm show the normal pattern of alternating movements and the irregular pattern (dysdiadochokinesia) typical of cerebellar disorder.