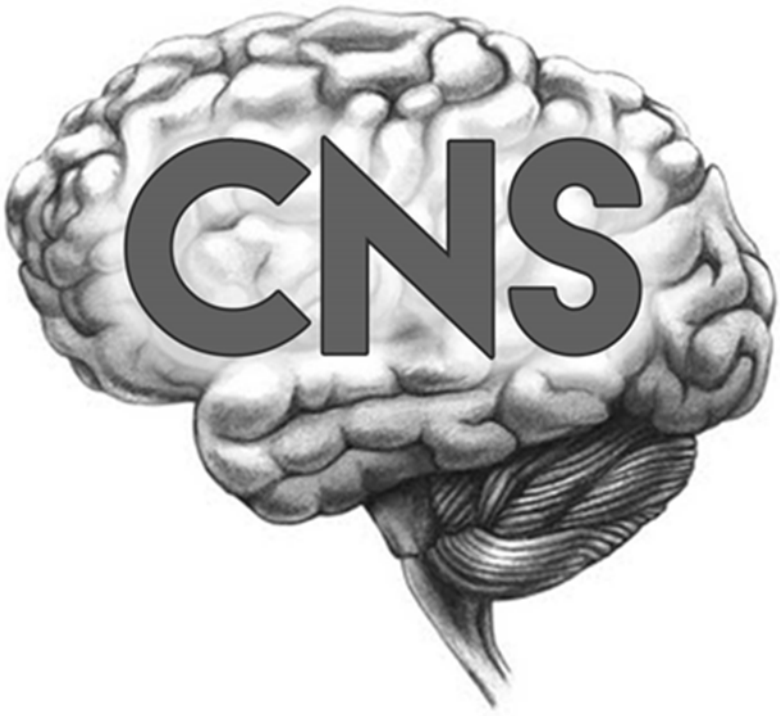

PHYSIOLOGY

☑ Sheet ○ Slide ○ Handout

Number

8

Subject

Basal ganglia and spinal cord

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Price:

Basal ganglia and motor functions of spinal cord

Overview of basal ganglia physiology. There are two pathways within the basal ganglia : (1) *direct pathway* which facilitates the movement. (2) *indirect pathway* which inhibits the movement. In addition, there is a balance between these two pathways.

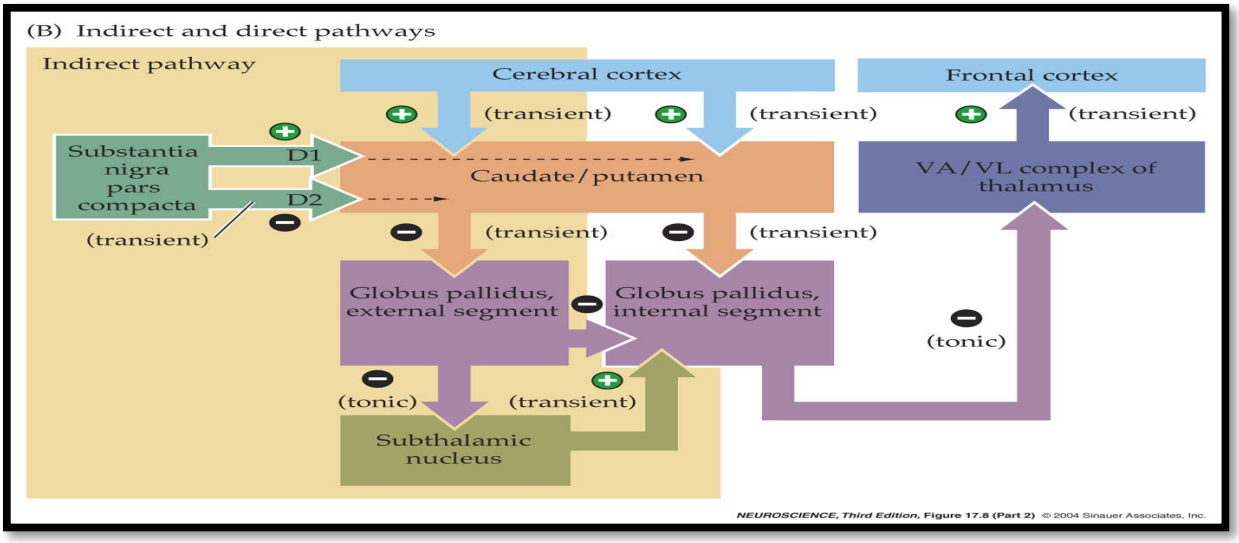
In direct pathway, *the striatum* (putamen and caudate) receives excitatory inputs from the cerebral cortex which are mediated by glutamate, then inhibitory GABAergic projection from the striatum goes to *the internal segment of globus pallidus* that is tonically active with high intrinsic rate of firing. Inhibitory GABAergic neurons emerge from the globus pallidus internus to synapse in the nuclei of *the thalamus* which in turn sends excitatory signals to the motor cortex.

So **activation** of this pathway results in inhibition of inhibitory pallidal output neurons and hence *disinhibition* of the thalamic neurons and consequently excitatory signals will be transmitted to the motor cortex facilitating the movement.

In indirect pathway, the cerebral cortex sends excitatory signals to the striatum giving inhibitory GABAergic neurons that project *to the external segment of the globus pallidus* and inhibit an inhibitory GABAergic projection from the globus pallidus externus to the *subthalamic nucleus*, from which excitatory neurons project to the globus pallidus internus providing excitatory effect to the inhibitory GABAergic *pallidothalamic output* neurons, consequently inhibition of the thalamus occurs and less excitatory signals go to the motor cortex.

So **activation** of this pathway results in disfacilitation of the motor cortical neurons and inhibition of the movement.

Dopamine is released from *pars compacta of substantia nigra* and in striatum there are two different receptors for dopamine ; (1) *D1receptors* which exert an **excitatory action** on the striatal neurons that *control the direct pathway*. (2) *D2 recptors* which exert an **inhibitory action** on the striatal neurons that *control the indirect pathway.* Refer to figure (8-1).



Figure(8-1): represents a summary for the flow and processing of cortical signals within the basal ganglia involving direct and indirect pathways.

Abnormalities in basal ganglia. Hypokinetic disorders result from insufficient direct pathway output and excess indirect pathway output while Hyperkinetic disorders result from excess direct pathway output and insufficient indirect pathway output. In addition, there are lesions of basal ganglia which includes:

(1) Lesions in *globus pallidus* resulting in **athetosis** in which *contralateral* spontaneous writhing movements of the hand, arm, neck, and face occur and the patient exhibits a snake-like involuntary movement and this condition happens when part of globus pallidus is destroyed then when the command reaches to a certain area of globus pallidus the neural circuit is directed to another area resulting in involuntary movement**.

(2) Lesions in *putamen* results in **chorea** in which involuntary flicking movements of the distal muscles occur *especially in the hands* but it may also occur in face ,leg, eye or in shoulders.

(3) Lesions in *substantia nigra* that means loss of dopaminergic inputs to putamen and caudate and consequently **parkinson's disease** which characterized by rigidity, resting tremor and akinesia (bradykinesia). **Akinesia or bradykinesia** is due to the fact that the basal ganglia is involved in initiation the movement and when there is no initiation, the movement tends to be slower and the patient thinks before each movement he(she) wants to do. On the other hand, **rigidity** happens because normally basal ganglia inhibit the tone thus when the basal ganglia are impaired, the tone will increase resulting in rigidity***.

Also, **resting tremor** happens because of disinhibition of the thalamus and consequently more excitatory signals are transmitted to motor cortex and finally, resting (pill-rolling) tremor occurs****.

(4) Lesions in *subthalamus*; sudden flailing movement of entire limb (hemiballismus) contralaterally and if the lesion is in both sides then it is ballismus.

(5) Huntington's chorea is autosomal dominant disease results from loss of GABAcontaining neurons projecting from straitum to globus pallidus and substantia nigra. It is unlike rheumatic fever associated chorea which is reversible once you treat rheumatic fever.

Pathogenesis and symptoms of parkinson's disease. In parkinson's disease, there is degeneration of substantia nigra, so dopamine secretion will decrease which means less excitation of striatum (direct pathway), less inhibition of *globus pallidus internus(overactive)* and finally, less activity to thalamus which in turn will send less excitatory signals to motor cortex resulting in bradykinesia (Akinesia). On the other hand, decreased dopamine secretion will lead to less inhibition of striatum(indirect pathway), more inhibition to globus pallidus externus, disinhibition of subthalamic nucleus, *overactive globus pallidus internus* and finally less activity to thalamus resulting in less excitation of motor cortex ending with hypokinesia(bradykinesia).

The symptoms include : (1) motoric such as resting tremor, bradykinesia, rigidity and loss of postural reflexes. Association circuit which is mediated mainly by caudate nucleus is involved in cognitive function, so when is subjected to damage *later during the course of the disease* the cognitive function will be impaired, also *later in the disease*, the patient will be(2) depressed, the behavior will change and (3)dementia occurs.

In page2**; according to Dr.faraj, athetosis is due to lesion in putamen not in globus pallidus.

In page2***; according to Dr.faraj, *overactive globus pallidus internus* inhibits midbrain extrapyramidal area resulting in disinhibition of pontine reticulospinal tract and gamma motoneurons leading to hypertonia of axial and proximal extensors(mainly)also disinhibition of rubrospinal tract and gamma motoneurons increasing the tone of proximal and distal flexors , so hypertonia in the flexors and extensors in the same limb means rigidity.

In page 3****; dr. faisal explained tremor assuming that there is disinhibition of thalamus (although we said that in parkinson's disease the thalamus receives more inhibitory signals from globus internus) but Dr. faraj related the tremor to *overactive globus palliuds internus.*

Also , patients with parkinson's disease are *monotonous* with monotone voice and show slow response and slow emotions .

Integration of motor control. *(1)Spinal cord level*: preprogramming of patterns of movement of all **muscles** (i.e., withdrawal reflex, walking movements, etc.). (2) *Brainstem level:* maintains equilibrium by adjusting **axial tone**. *(3) Cortical level:* **issues commands** to set into motion the patterns available in the spinal cord and controls the intensity and modifies the timing. *(4) Cerebellum:* functions with all levels of control to **adjust motor activity**, equilibrium, and planning of motor activity. *(5) Basal ganglia:* function to assist cortex in executing subconscious but **learned patterns of movement**, and to plan sequential patterns to accomplish a purposeful task. Refer to figure (8-2).

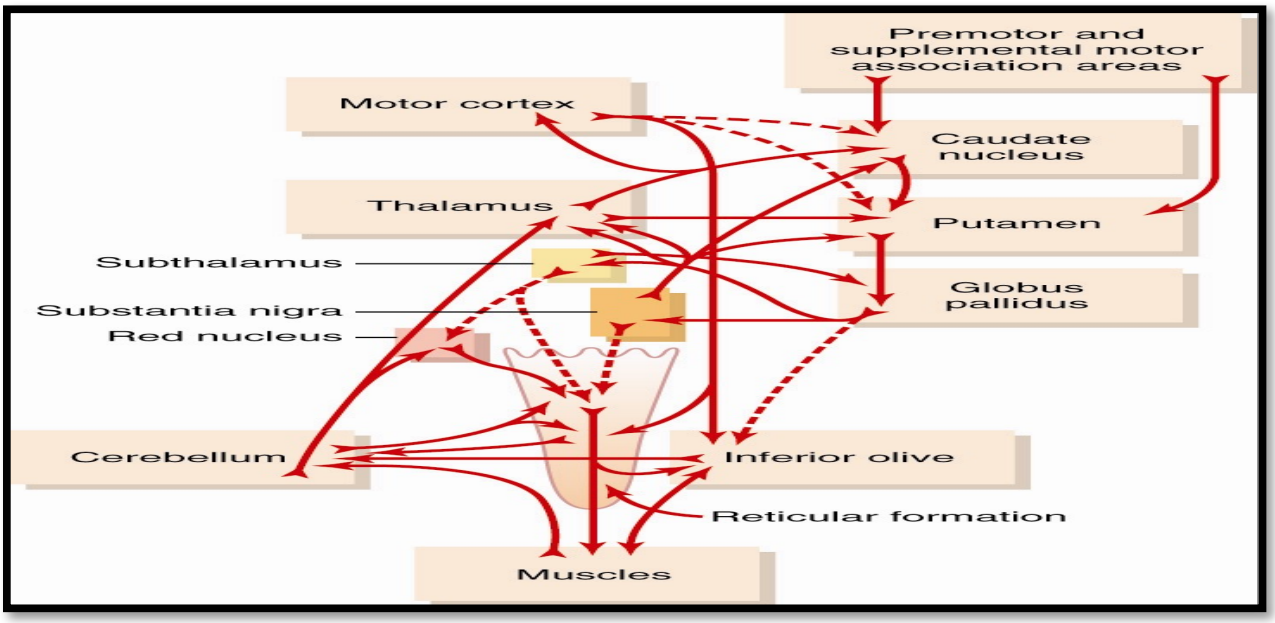


Figure (8-2): represents the integration of motor control illustrating the medial motor system controlling axial and proximal (antigravity muscles or the extensors) and lateral motor system controlling distal muscles(or the flexors) and part of the proximal receiving signals from motor cortex, also motor command reaches the basal ganglia and through direct and indirect pathways assist cortex in executing subconscious learned patterns of movement, further more cerebellum aids in coordination of the movement and planning of rapid ballistic movements involving three parts: vestibulocerebellum, spinocerebellum and cerebrocerebellum.

Pay attention that dr.faisal considers *the distal muscles as flexors* and *the proximal muscles as extensors.*

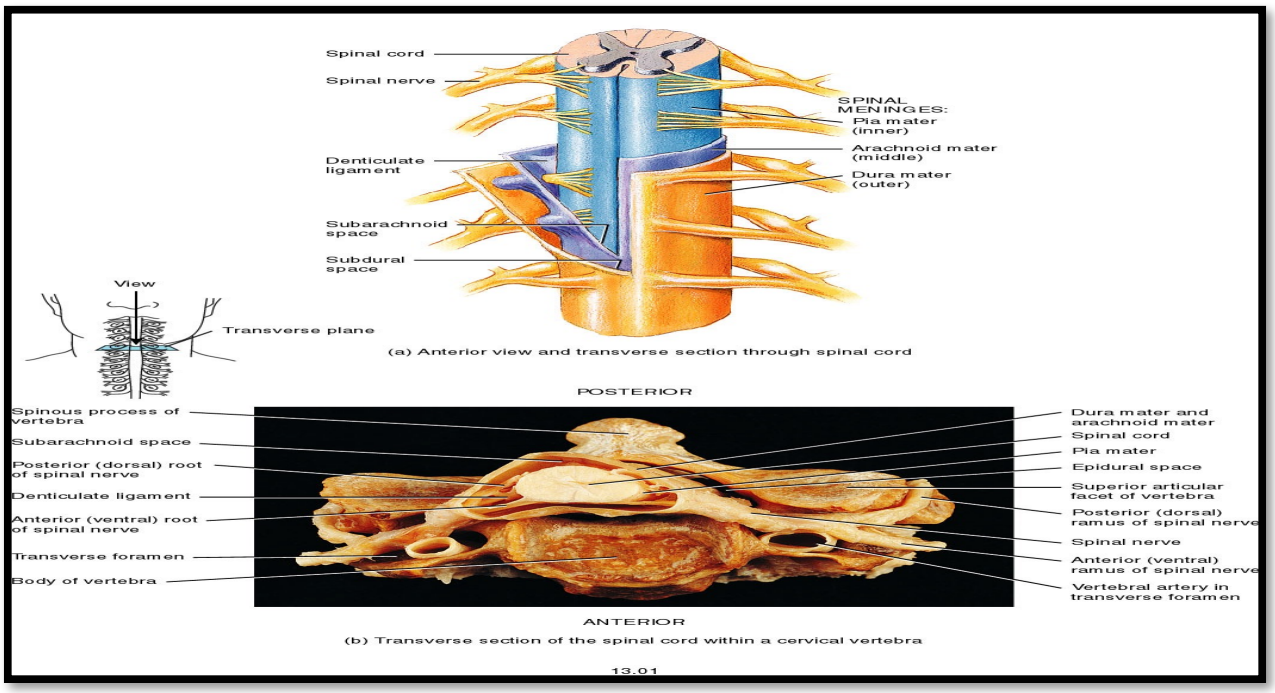
Stimulation of cortex may end with contraction of single muscle fiber but along with basal ganglia and cerebellum, complex movements occur.

Motor functions of the spinal cord. Motor functions of the spinal cord is related to *muscle spindle and Golgi tendon organs* because from them the cerebellum receives feedback through posterior(dorsal) spinocerebellar tract.

Testing *spinal cord reflexes* is important to test the integrity of the spinal cord, and when there is impairment in the spinal cord, the neural circuit of the reflex is impaired and the circuit for the reflex is the same for walking, running, etc, actually it is the same for all movements that are mediated by a certain muscles. So testing the reflex gives me an indication about the integrity of neural circuits through which different movements are performed, and consequently the integrity of the spinal cord.

Neuronal circuits for walking and various reflexes are contained within the spinal cord and higher brain centers activate and command these circuits.

Anatomy of the spinal cord. The spinal cord is located in bony structure which is the vertebral column and the spinal cord is surrounded by meninges from outside to inside: dura mater, arachnoid mater and pia mater. The spinal cord is composed of 31 segments: 8 cervical, 12 thoracic, 5 lumbar, 5 sacral and 1 coccygeal .Refer to figure (8-3).



Figure(8-3): represents the structure of the spinal cord and the surrounding meninges and between the arachnoid and pia mater, subarachnoid space containing cerebrospinal fluid(CSF) is present. CSF is important in nutrition.

Blood brain barrier (BBB). It is a highly selective semipermeable membrane barrier that separates the circulating blood from the brain extracellular fluid in CNS, it is formed by the brain endothelial cells of microvasculature capillaries which are *continuous* by tight junctions, so patient with meningitis, it is more favorably to give the antibiotic *intrathecally* not orally to reach CSF since it is difficult to pass through BBB.

Spinal cord segments. The segment is composed of *grey matter (H-shaped)* which is subdivided into *anterior (motor)horn and posterior(sensory) horn which are present in all segments* but the *lateral horn* is present in some segments (T1-L2; thoracolumbar) from which preganglionic autonomic *(sympathetic)* fibers emerge to synapse in autonomic ganglion giving postganglionic nerve fibers and *the lateral horn* is also present in (S2-S4) giving preganglionic *parasympathetic* nerve fibers. (Notice that the origin of parasympathetic is craniosacral while the sympathetic is thoracolumbar) . In addition to grey matter, the segment is composed of *white matter*. Refer to figure (8-4).

In the center of grey matter, there is *central canal* which is a continuation of the fourth ventricle thus **CSF** passes from the fourth ventricle to central canal. In **syringomyelia**, the central canal is enlarged compressing the surrounding neurons resulting in symptoms.

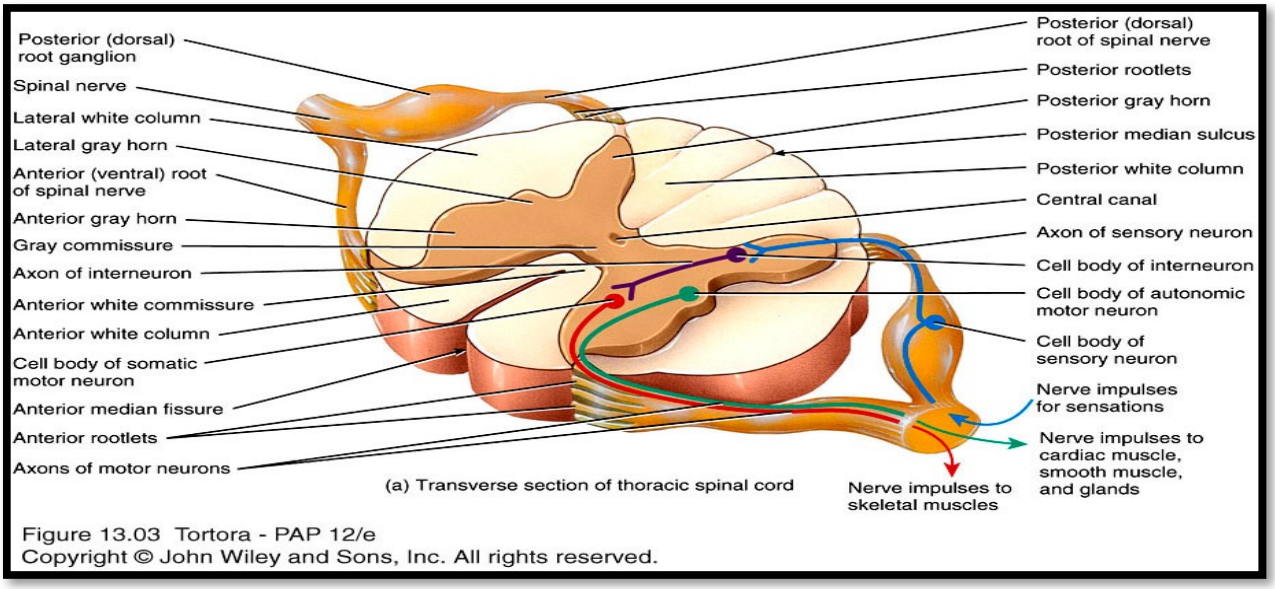


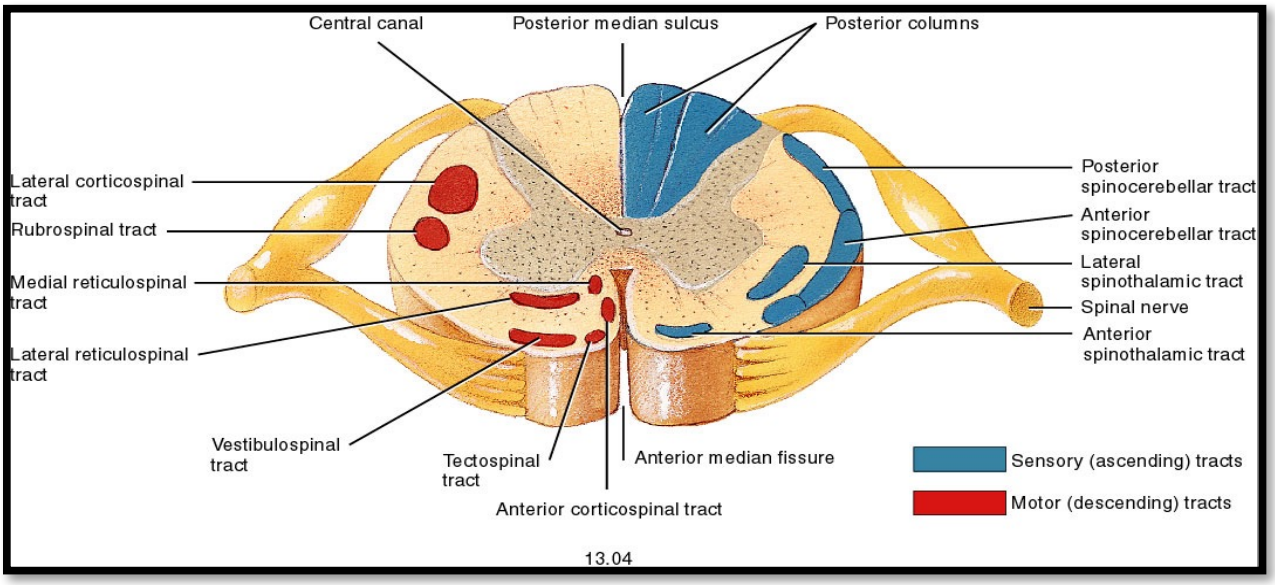
Figure (8-4): represents the spinal cord segment in which sensory nerve fibers enter the dorsal horn through the dorsal root and synapse in the interneurons, then the interneurons synapse in motor nerve fibers in the anterior horn which leave the segment through the ventral root and finally to the muscles. Actually, the number of interneurons is much more than the number of motor and sensory neurons in the segment.

Topographical organization in the spinal cord segments and motor tracts. Proximal muscles (extensors) are presented in the medial aspect of the anterior horn while the distal muscles (the flexors) are presented in the lateral aspect of the anterior horn. White matter of the segment is composed of dorsal column, lateral column and anterior (medial) column; in the lateral column the following tracts **(lateral system)** are located: (1) lateral corticospinal tract. (2) rubrospinal tract, but in the medial (anterior) column, the following tracts**(medial system)** are located: (1) lateral (medullary) and medial(pontine) reticuolspinal tracts. (2) lateral and medial vestibulospinal tracts. (3)tectospinal tract. (4) ventral corticospinal tract. refer to figure (8-5).

Pay attention that also we classify the tracts into the medial system because it ends in the medial part of lamina 9 of anterior horn and into lateral system because it ends in the lateral part of lamina 9 of anterior horn.

Linking the topographical organization with the motor tracts, we find that the medial system controls the proximal(extensors) and the lateral system controls the distal (flexors).

Even though that lateral (medullary) reticulospinal tract is located in the medial(anterior) column (anatomically), it is considered as a part of lateral system functionally.*****



Figure(8-5): represents the location of motor and sensory tracts in the spinal cord segment.

*****: this is according to Dr.Faisal, but according to Dr.Faraj; he considers that lateral reticulospinal tract as a part of the medial system.

Classification of the neurons.We classify the neurons into: **(A) fibers** which are myelinated fibers and subdivided into: (1) A alpha. (2) A beta. (3) A gamma. (4) A delta which is the smallest myelinated nerve fiber such as pain fibers and **(C) fibers** which are unmyelinated .
Also, the neurons are classified into: I (myelinated) fibers, II (myelinated) fibers, III (myelinated) fibers and IV (unmyelinated) fibers.

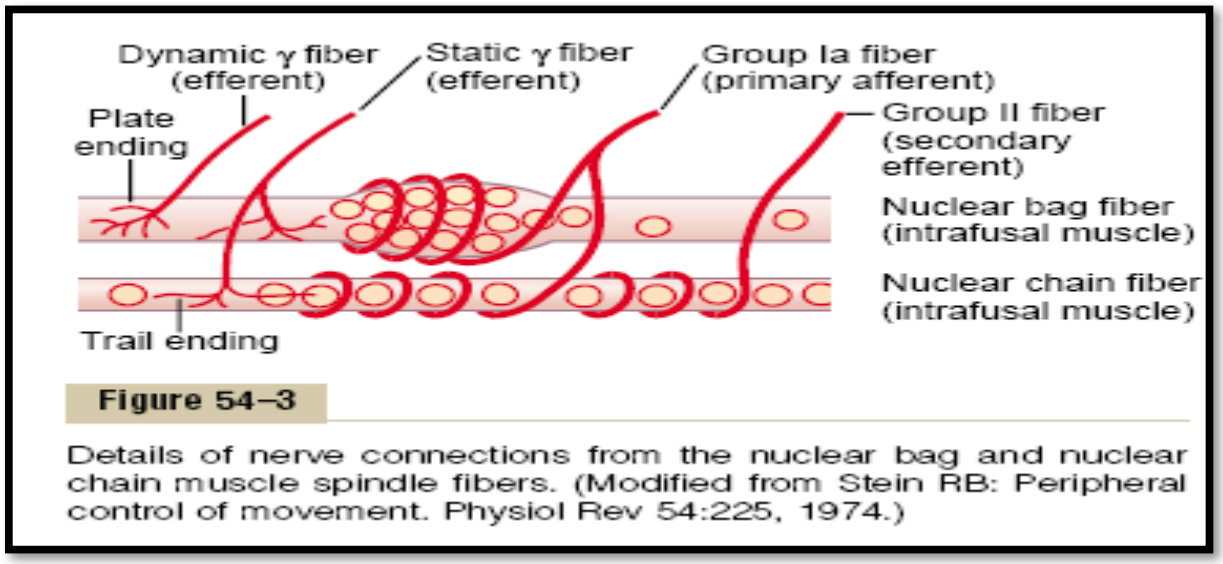
Anterior Motor Neurons.(*1)Alpha motor neurons* give rise to large type A alpha fibers that can excite **extrafusal** muscle fibers collectively called a motor unit. (2) *Gamma motor neurons* give rise to smaller type A gamma fibers that can excite **intrafusal fibers**, a special type of sensory receptor.

(**Hint**: *extrafusal fibers* are the fibers that make up the large mass of skeletal muscle and are responsible of the contraction of the muscle while *intrafusal fibers* are a special type of sensory receptors (*muscle spindles)* which are found inside the muscle; the muscle spindle is composed of **(1) a central sensory area** innervated by sensory afferent fibers (Ia and II) and at the periphery of the central area, **(2)contractile elements** are present and these elements are innervated by gamma motor neurons. Muscle spindles are the receptors that are responsible of the *stretch reflex)*.

Interneurons and propriospinal fibers. Interneurons are 30 times as many as anterior motor neurons, small and very excitable and comprise the neural circuitry for the motor reflexes, while Propriospinal fibers travel up and down the cord for 1 - 2 segments especially for pain sensation providing pathways for multisegmental reflexes.

Sensory receptors of the muscle. (1*) muscle spindles* sense the length of the muscle and change in the length. (2) *Golgi tendon organ* sense tendon tension and change in tension.

Structure and innervations of muscle spindle. Muscle spindle consists of a central non-contractile part called the receptor area from which sensory nerve endings arise and a peripheral contractile part that is innervated by gamma motoneurons. There are two types of intrafusal muscle fibers (muscle spindle): *(1) nuclear bag fibers. (2) nuclear chain fibers*. **Afferent fibers** (sensory nerve endings) arise from 2 types: (1*) primary or annulospiral endings or Ia afferent* fibers which encircle the central parts of the receptor areas of both nuclear bag and nuclear chain. (2*) secondary or flower spray endings or group II afferent* fibers which lie on both sides of the primary endings and encircle the peripheral parts of the receptor areas of only the nuclear chain fibers. On the other hand, **efferent fibers** arise from the gamma motoneurons which are in 2 types: (1) *dynamic fibers* that supply the nuclear bag fibers. (2) *static fibers* that supply the nuclear chain fibers. Refer to figure (8-6).



Figure(8-6): represents the structure and innervations of muscle spindle.******

******: you may pay attention to the figure to notice that group II fiber is secondary efferent which is wrong it should be afferent instead of efferent and the static gamma fibers supply both nuclear bag and nuclear chain, but this is not a critical point, JUST UNDERSTAND THE PRINCIPLE.

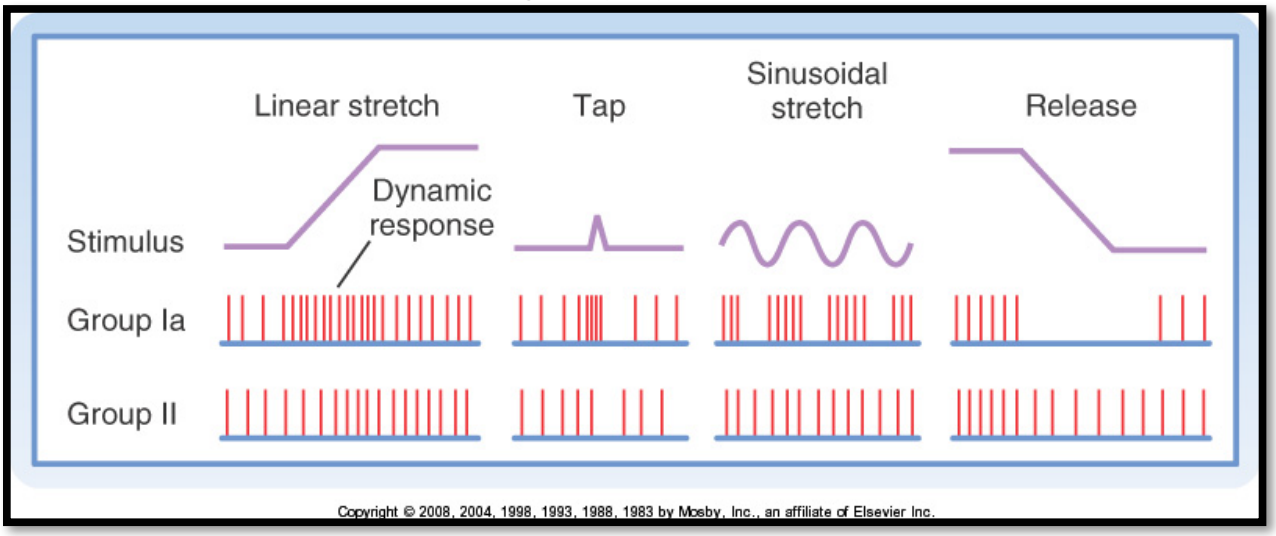
How and why the muscle spindle works. Muscle spindle is a stretch receptor, so it responds to stretch. So, when the central sensory area of the spindle is stretched, sensory signals are carried through afferent fibers to synapse directly in alpha motoneurons which in turn stimulate the extrafusal fibers to contract and this is called **stretch reflex**. But when the muscle is contracted, the contraction is inward (medially) which means decrease in the stretch of receptor sensory area, so less impulses go through afferent fibers and less activation of alpha motoneurons and finally the contraction of extrafusal fibers is inhibited. In other words, the stimulation of muscle spindle is mediated through stretching the central sensory area.

There are two ways to stimulate the muscle spindle: (1) stimulation of the gamma efferent fibers from supraspinal centers; when gamma efferent fibers are stimulated from supraspinal centers , they stimulate the peripheral contractile part of muscle spindle to contract outward(laterally) **stretching** the sensory receptor area giving sensory signals carried through **secondary afferent fibers** to synapse directly **in alpha motoneurons** stimulating the extrafusal muscle to contract and as long as the gamma fibers receive from higher center in the brain(tonically active), the muscle contraction is maintained and this is the basis of t**he muscle tone** of your muscles that is very important to initiate any movement. So muscle tone is due to *alpha-gamma co-activation*, actually this requires that the afferent fibers to be **slowly adapted to cope with the maintained contraction** and this what is found in the secondary afferent fibers. (2) stretching of the whole muscle laterally increases the stretch of the receptor area stimulating the muscle spindle discharging impulses carried through **primary afferent fibers** to synapse directly in alpha motoneurons stimulating extrafusal muscle to contract. Stretching the muscle can be induced by hitting the tendon of a muscle (patellar tendon of quadriceps muscle for example; **knee jerk*******) and the movement that results from **tendon jerks** is rapid and not maintained, so the afferent fibers must be **rapidly adapting** and this what is found in primary afferent fibers**.**

:*******In physics, jerk is *the rate of change* of acceleration with respect to time; that is, the derivative of acceleration with respect to time, and as such the second derivative of velocity, or the third derivative of position.

The responses of a primary and secondary endings to various types of muscle lengths. *Primary endings* are *rapidly-adapting receptors*, so when the muscle spindle is stretched, the rate of discharge of impulses from these receptors initially increases, but it rapidly declines to the original level when the stretching force is maintained and the length of the muscle stops to increase. Since the primary afferent fibers are stimulated only during the stretching movement like in **tendon jerk**, their response has been called *the dynamic response* which informs the Nervous System about *the rate of change in the length* of the stretched muscle; as the rate increases, the number of impulses increases and when the rate decreases, the number of impulses decreases.

On the other hand, *the secondary endings are slowly-adapting receptors*, so when the muscle spindle is stretched, the number of impulses discharged from these endings increases in *proportion to the degree of the stretch.* But when the stretching force is maintained, these receptors continue to discharge at fast rate for a long period of time, as long as the muscle stretch is maintained. Therefore, this response has been called *the static response* which explains **the skeletal muscle tone.** The static response informs the nervous system continuously about the length of the stretched muscle. Refer to figure (8-7).



Figure(8-7): represents the dynamic response through group Ia and the static response through group II.

The density of muscle spindles. The number of muscle spindles in muscles is *not homogenous* hence the number of muscle spindles in muscles used too much like muscles involved in posture(antigravity muscles which are used always) have a higher number of muscle spindles in comparison with muscles not used too much. So, the density of muscle spindles in axial and extensors is higher than that found in flexors.

Golgi tendon organ. Impulses from Golgi tendon organs travel via Ib nerve fibers. In the spinal cord, they project upon inhibitory neurons which in turn will inhibit alpha motoneurons supplying the muscle under the tension.

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- Q constant = $2.4912*10^{-6}$ m/s.$(Qaswal)^2$.
- Qaswal photonic shift.