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HUMAN ANATOMY STUDY GUIDE.
THE REFLEX ARC.
THE NEURAL PATHWAYS
(AFFERENT AND EFFERENT TRACTS)

Issue 260

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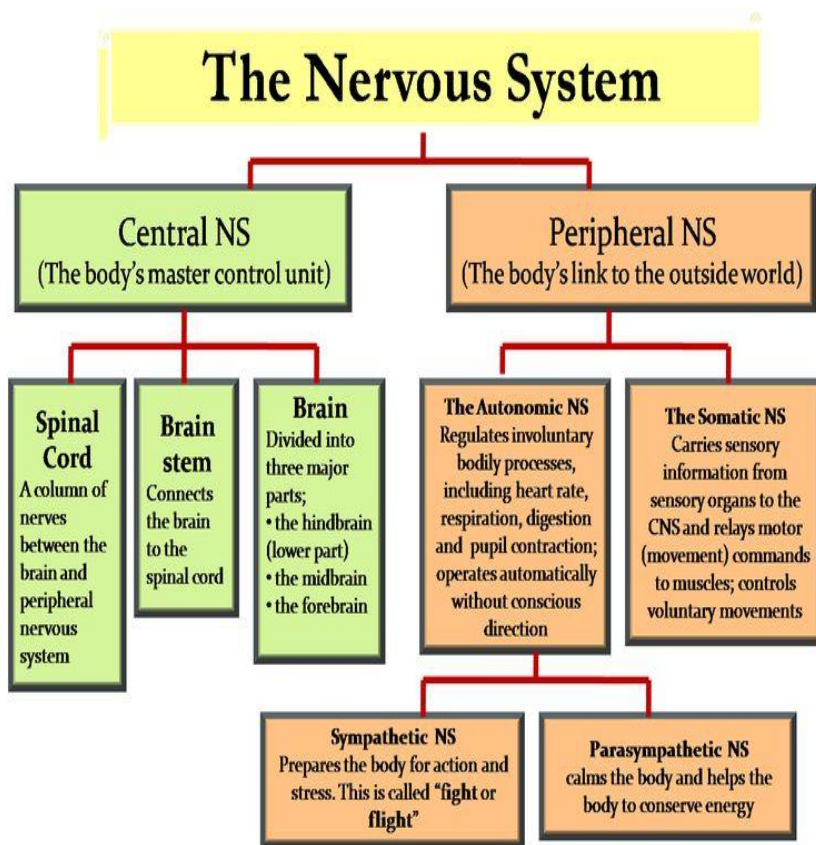
This study guide is recommended for the first-year students (specialty 222 «Medicine», field of knowledge 22 «Health care», educational qualification «Master of Medicine», and professional qualification «Doctor of Medicine») to facilitate their studying of the neural system. The study guide is divided into two parts: the reflex arc, the neural pathways.

The Nervous System

Central NS
(The body's master control unit)

Peripheral NS
(The body's link to the outside world)

Spinal Cord
A column of nerves between the brain and peripheral nervous system

Brain stem
Connects the brain to the spinal cord

Brain
Divided into three major parts;
• the hindbrain (lower part)
• the midbrain
• the forebrain

The Autonomic NS
Regulates involuntary bodily processes, including heart rate, respiration, digestion and pupil contraction; operates automatically without conscious direction

The Somatic NS
Carries sensory information from sensory organs to the CNS and relays motor (movement) commands to muscles; controls voluntary movements

Sympathetic NS
Prepares the body for action and stress. This is called "fight or flight"

Parasympathetic NS
calms the body and helps the body to conserve energy

The nervous system **(NS)** is the mechanism concerned with the correlation and integration of various bodily processes, the reactions and adjustments of the organism to its environment, and with conscious life. It may be divided into two parts. The central nervous system **(CNS)** consists of the brain or *encephalon,* contained within the cranium, and the spinal cord or *medulla spinalis.* The peripheral nervous system **(PNS)** consists of a series of nerves by which the central nervous system is connected with the various tissues of the body. These nerves may be arranged in two groups, *cranial (12 pairs) and spinal (31 pairs). Also PNS has: 31 pairs of spinal and 12 pairs of cranial ganglions, nervous plexus and trunks, peripheral nerves with branches and receptors.* The two groups are intimately connected and closely intermingled. Some basic anatomical concepts of the

nervous tissue find in the book author is V. G. Koveshnikov «Human anatomy».

Sometimes our body can react in a split second, faster than it could take to send the information to the brain for processing. These reflexes are the subject of this lesson. We'll cover what a reflex arc is, as well as the cells involved and why they are needed.

What Is a Reflex Arc?

Have you ever been cooking and accidentally bumped your hand against a hot pan? Likely, before you could even register what happened, you jerked your hand away, maybe even clutching your hot skin. When something like this happens, it feels like you simply react to the situation automatically, without thinking. Although biologically this might seem impossible, it's exactly what really happens in your nervous system.

Although we think of the brain as being the boss of all of our actions and thoughts, some actions actually take place without the brain's input. These reactions are called **reflexes.** However, very few reactions are actually true reflexes. People usually think catching an object flying at their head, like a baseball, is a reflex, but it is not. The information goes to your brain for processing before you actually respond. Thus, some of us are much better at catching the baseball than others.

A true **reflex arc** involves only a few neurons, or cells of the nervous system, and the information goes only from your body to your spinal cord, not your brain. Let's look at the cells that make up the reflex arc and how they work.

Reflex Arc Components.

Most reflex arcs have five main components: receptors, sensory neurons, interneurons, motor neurons and muscles. However, not all reflexes use interneurons. Some connect sensory neurons directly to motor neurons and do not use interneurons. Let's go through each of these components.

Throughout your body, neurons have special proteins in their membrane called **receptors.** Receptors respond to signals in the environment. Some receptors respond to pressure. When the cell is compressed, the receptors are activated, letting your brain know something is pressing on your skin or organs. Other receptors respond to pain or to chemical stimuli, like smells or tastes. Sensory receptors in your ears respond to vibrations in the air that we interpret as sound, and receptors in your eyes respond to light.

Sensory neurons are the cells that contain sensory receptors. They send information from the body to the central nervous system, the brain and spinal cord. These cells are activated when the receptor gets a signal from

the environment. The activated sensory neuron extends into the spinal cord, sending an electrical signal all the way to another neuron, the interneuron.

Interneurons are like the middleman of the nervous system. They connect sensory input to other cells that are required for action. The interneuron relays that signal to next neuron, a motor neuron.

Motor neurons connected with interneurons and send electric messages from anterior horn to target organ (muscles).

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THE STRUCTURES OF A CROSS-SECTION
OF THE SPINAL CORD

A cross-section of the spinal cord includes grey and white matter. The grey matter is a collection of neural body cells (the darkest color of a cross-section). There are large and small multipolar cells here. The white matter contains axons and dendrites (fibers) of neural cells (Fig. 1).
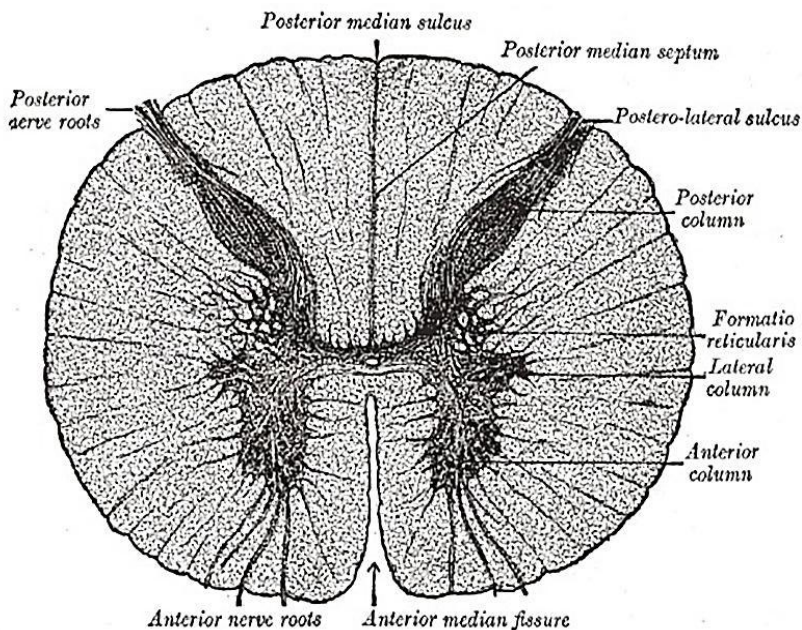
**Fig. 1.** A cross-section of the spinal cord

The gray matter of the spinal cord forms three pairs of horns (posterior, lateral and anterior horns). The posterior horn **(cornu posterior)** comprises small multipolar neurons that accept several sensory fibers from the posterior roots.

The lateral horn **(cornu laterale)** is in the area between C_8 and L_2, between anterior and posterior horns. There is the central intermediate substance, which continues medially into narrower gray commissure that connects left and right halves of the gray matter.

The anterior horn **(cornu anterior)** comprises large multipolar neural cells that live motor fibers for anterior roots (Fig. 2).
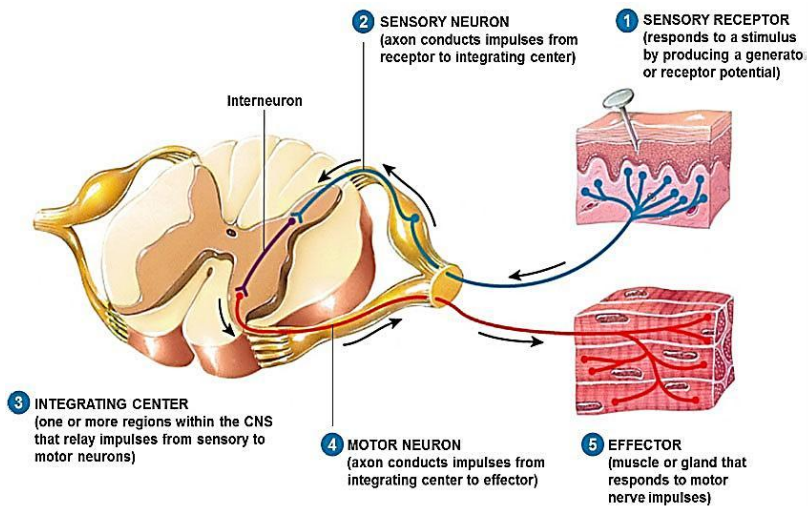
Fig. 2. A somatic reflex arc
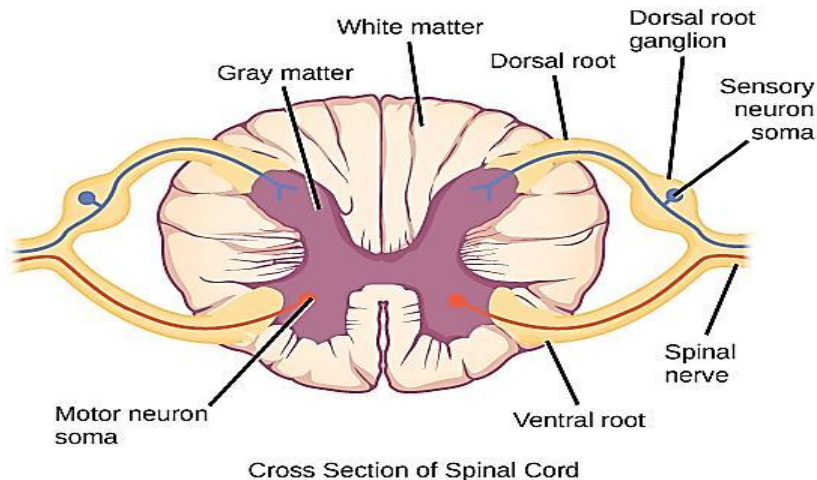
THE WHITE MATTER
(SUBSTATIA ALBA)

The white matter comprises the fasciculi of nerve fibers that form various **tracts (*tractus*).** It enfolds the white matter and divides into anterior, lateral and posterior funiculi. There are sulci and fissures among them.

− The **anterior median fissure (*fissura mediana anterior*)** is a deep one, it runs along the anterior surface from beginning down to a terminal portion of the spinal cord, it incompletely divides the spinal cord into left and right halves in front.

− The **posterior median sulcus (*sulcus medianus posterior*)** is not as deep as the previous one, it runs in the same way and physically separates left and right halves of the spinal cord arises.

− The **anterolateral sulcus (*sulcus anterolateralis*)** is marking the line of an exit of the anterior nerve roots.

− The **anteromedial sulcus (*sulcus anteriomedialis*)** is marking the line of an exit of the posterior nerve roots (Fig. 3).

Fig. 3. External structures of spinal cord

THE FUNICULI

The sulci that run along the white matter delimit several regions called the funiculi.

The funiculi are collections of neural fibers, which form the white matter of the spinal cord.

– **The anterior (ventral) funiculus** (*funiculus anterior*) is delimited by the anterior median fissure and anterolateral sulcus.

– **The lateral funiculus** (*funiculus lateralis)* is delimited by anterolateral sulcus and posterolateral sulcus.

– **The posterior funiculus** (*funiculus posterior)* is delimited by the posterolateral and posterior median sulci.

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THE ROOTS OF THE SPINAL NERVES

The roots of the spinal nerves are the white matter. They form two vertical rows. Each root consists of the *rootlets.* There are two types of the roots − the anterior and the posterior ones.

− The **anterior (motor) root (*ventral root*)** arises from the anterolateral sulcus and contains a set of axons of motor neurons located within the anterior columns. In humans, there are 31 pairs of anterior roots (Fig. 4).
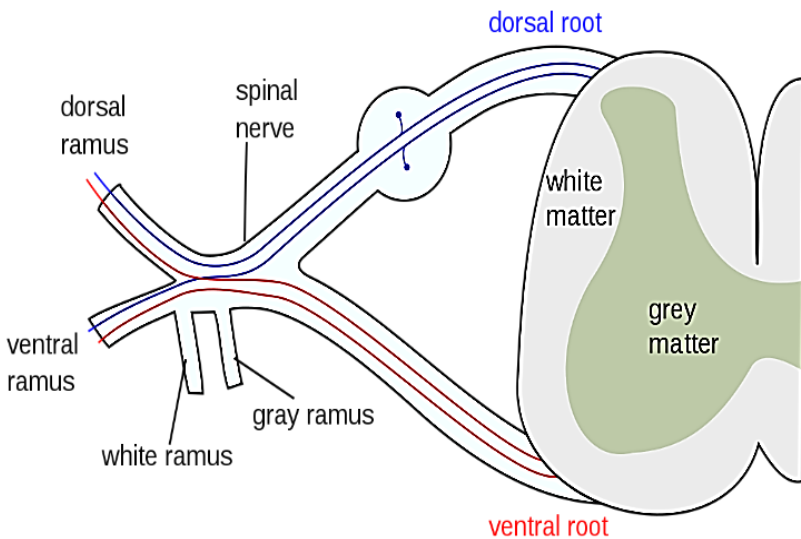

Fig. 4. A roots of spinal cord

− The **posterior (dorsal) root (*radix sensoria*)** is a set of central processes of sensory pseudounipolar neurons located within the spinal ganglia. In humans, there are 31 pairs of dorsal roots.

The spinal ganglion (ganglion spinale) includes inside pseudounipolar body cells belonged to the posterior root and situated inside the intervertebral foramen.

REFLEX ARC

Reflex arc it is a nerve pathway involved in a reflex action, including at its simplest a sensory nerve and a motor nerve with a synapse between (Fig. 5). Reflex arc is responsible for passages of nervous impulses from preceptors to CNS and for transportation of electric impulses to target organs (muscles).
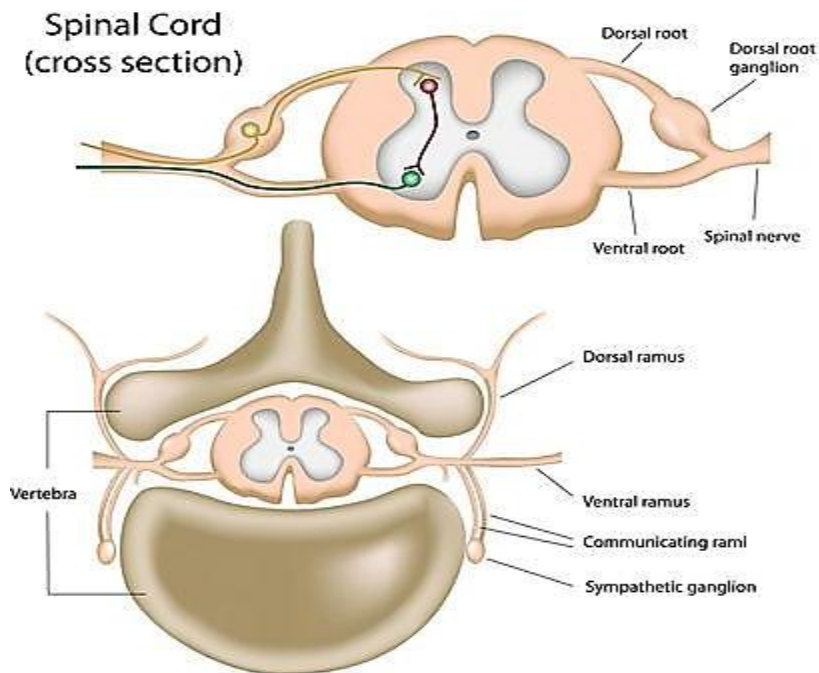

Fig. 5. Topography of spinal cord in vertebral canal

The **first-order neurons** present in spinal ganglia (they are pseudounipolar body cells). The peripheral processes run to receptors of the muscles, ligaments, and joints. The central processes direct to the posterior horn of the spinal cord.

The **second-order neurons** are small multipolar cells. The axons of the second-order neurons go to the anterior corn of the spinal cord (are interneuron) and interrupt here.

There are large multipolar neurons in the anterior horn of the spinal cord. These are the **third-order neurons.** The axons of the third-order neurons run from anterolateral sulcus to target organ (Fig. 6).
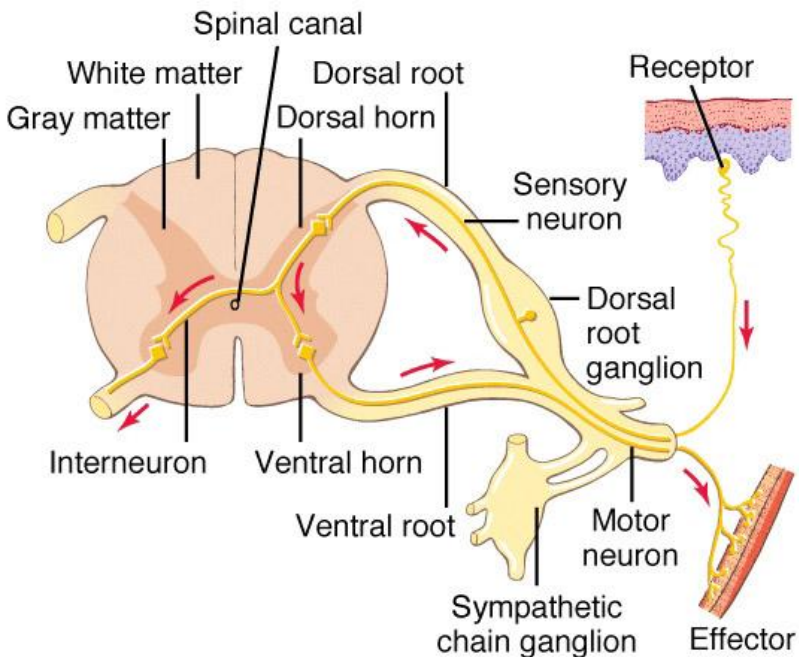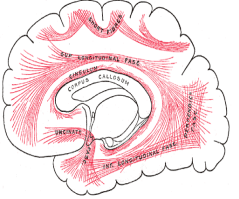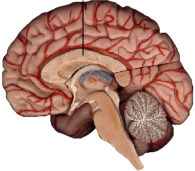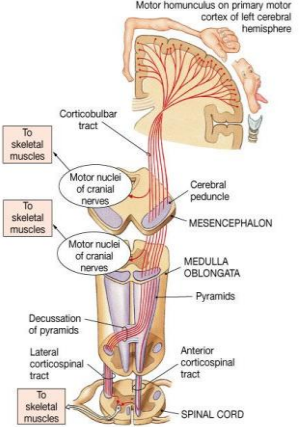

Fig. 6. The somatic and autonomic reflex arc

THE NEURAL PATHWAYS

Introduction. The neural pathways are bundles of the white matter of the brain or the spinal cord that connected similar centers in CNS.

CLASSIFICATION
OF NEURAL PATHWAYS

1. ASSOCIATIVE	2. COMMISSURAL	3. PROJECTIVE
– the tracts connecting functional areas of one hemisphere of the brain.	– the tracts connecting functional areas in two hemispheres of the brain.	– the tracts uniting the similar enters in the brain and the spinal cord.
a. Fasciculus longitudinalis inferior. b. Superior longitudinal fasciculus. c. Uncinate fasciculus d. short fibers.	**a. Corpus callosum.** **b. Fornix.** **c. Anterior cerebral commissure.**	**a. The afferent pathways** – to cerebellum (the anterior spinocerebellar tract (Gower's tract), the posterior spinocerebellar tract (Flechsig's tract)), – to cerebral cortex (the spino-bulbo-thalamo-cortical tract). **b. The efferent pathways: corticospinal tract, reticulospinal tract, tectospinal tract, rubrospinal tract, vestibulospinal tract** – the pyramidal system; – the extrapyramidal system; – the extrapyramidal pathways.

| 1. ASSOCIATIVE	2. COMMISSURAL	3. PROJECTIVE

The neural pathways are the spatial interrupted association lines. They are formed by the neurons, which give off the bundles of fibers that transmit the impulses from the periphery to CNS and in opposite direction: from the brain and the spinal cord down to the effectors.

ASCENDING (AFFERENT) PATHWAYS

I. THE PROPRIOCEPTIVE PATHWAYS
TO THE CEREBELLUM

1. ANTERIOR OR VENTRAL SPINOCEREBELLAR TRACT
(GOWER'S TRACT)

The *first-order neurons* reside in spinal ganglion (it is a common rule for spinal tracts). There are pseudounipolar (sensory) neurons here. The peripheral process runs to a receptor's area of the muscles, ligament, and joints. The next is the central process that forms the posterior root of the spinal cord and enters the posterior horn of the spinal cord. Here they synapse with cells of proper nuclei of the posterior horn of the spinal cord (*second-order neurons*)**.** The axons of the second-order neurons form **decussation** and reach lateral funiculus (the ventral side) of the spinal cord. There is the anterior spinocerebellar tract of the spinal cord here. The axon ascends to *medulla oblongata* and runs to superior medullary velum. Upon entering the velum, the fibers decussate again and go to **superior cerebellar peduncles.** The fibers terminate in the cortex of *vermis* (Fig. 7).
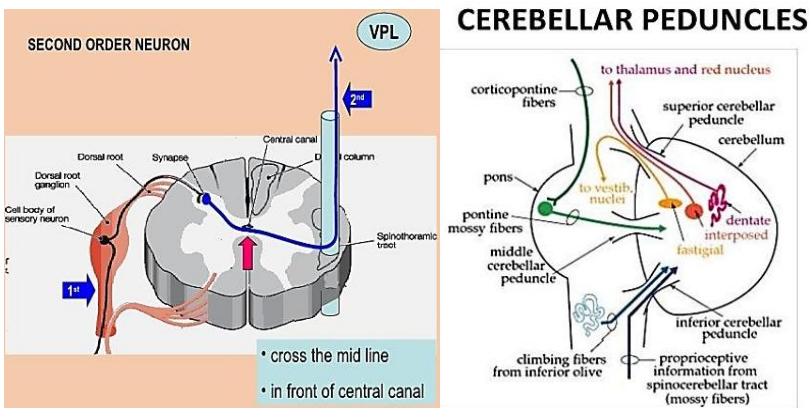
Fig. 7. Formation of Spinocerebellar tract

2. POSTERIOR OR DORSAL SPINOCEREBELLAR TRACT
(FLECHSIG'S TRACT)

The *first-order neurons* reside in spinal ganglion (it is a common rule for spinal tracts). There are pseudounipolar (sensory) neurons here. The peripheral process runs to a receptor's area of the muscles, ligament, and joints. The next is the central process that forms the posterior root of the spinal cord and enters the posterior horn of the spinal cord via the dorsolateral sulcus. In the spinal cord, they synapse with the cells of the *thoracic nucleus,* which are the second-order neurons. The axons of the *second-order neurons* **do not decussate** and proceed to lateral funiculus of the spinal cord on the same side where they from the posterior spinocerebellar tract. The latter reaches the medulla oblongata and enters the cerebellum via the **inferior cerebellar peduncles.** These fibers also terminate with the cortex of the **vermis** (Fig. 8).
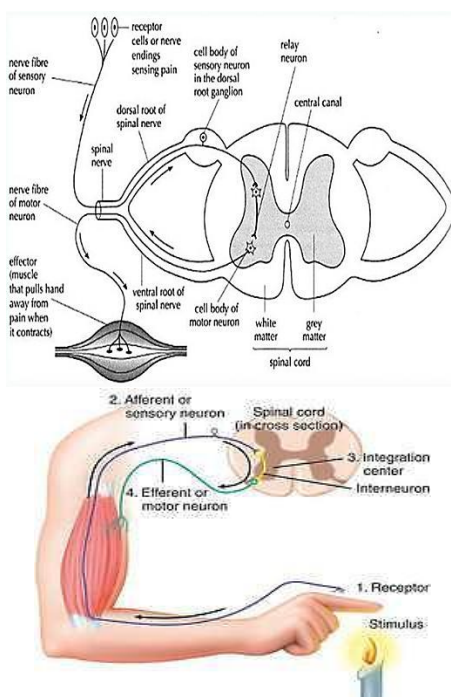

Fig. 8. Formation of electric impulses

THE PROPRIOCEPTIVE PATHWAYS
TO THE CEREBRAL CORTEX

3. SPINO-BULBO-THALAMO-CORTICAL
TRACT

The *first-order neurons* reside in spinal ganglion (it is a common rule for spinal tracts). There are pseudounipolar (sensory) neurons here. The peripheral process runs to receptor's area of the muscles, ligament, and joints. The central processes (identical to axons in the multipolar cells) form the posterior roots of the spinal cord or the sensory roots of the cranial nerves and enter to the spinal cord or the brainstem. In the spinal cord, the fibers run directly to the posterior funiculi to form the *cuneate and the gracile fasciculi.* The *gracile* (*GOLL's*) *fasciculus* carries the impulses from the lower portion of the body. *The cuneate* (*BURDACH's*) *fasciculus* carries the impulses from the upper part of the body and upper limbs and the neck. It begins from Th4 and upper. The cuneate and gracile fasciculi reach the medulla oblongata to synapse with the neurons of the *gracile and cuneate nuclei* (*the second-order neurons*)**.** The second-order neurons of the chain reside within the previously mentioned nuclei. They give off the *external arcuate fibers and the internal arcuate fibers.* The internal arcuate fibers decussate, form *the medial lemniscus,* and run through the posterior area of the medulla oblongata, the tegmentum of the pons, the tegmentum of cerebral.

The peduncles and eventually reach the ventrolateral nucleus of the dorsal thalamus. The *third-order neurons* of the chain reside within the ventrolateral nuclei of the thalamus (on each side). Their axons ascend and pass through the posterior limb of the internal capsule, joint the *corona radiate* and terminate within the cortex of the postcentral gyrus. As the result of fibers decussation, the right half of the body is associated with the left postcentral gyrus and vice versa (Fig. 9, 10).
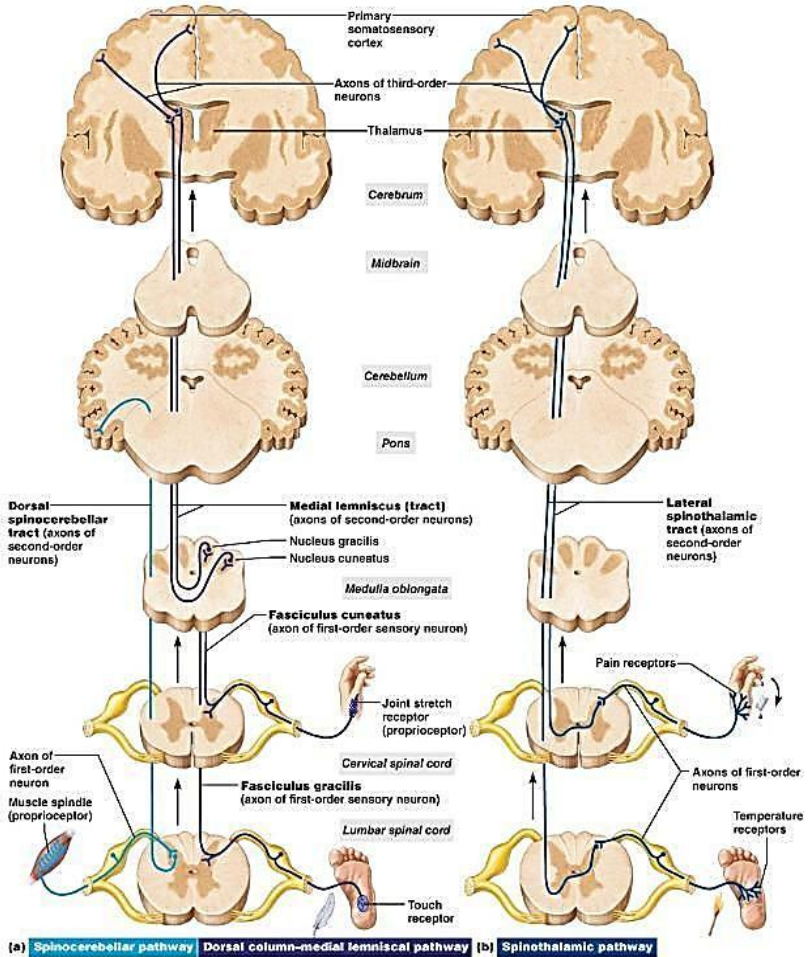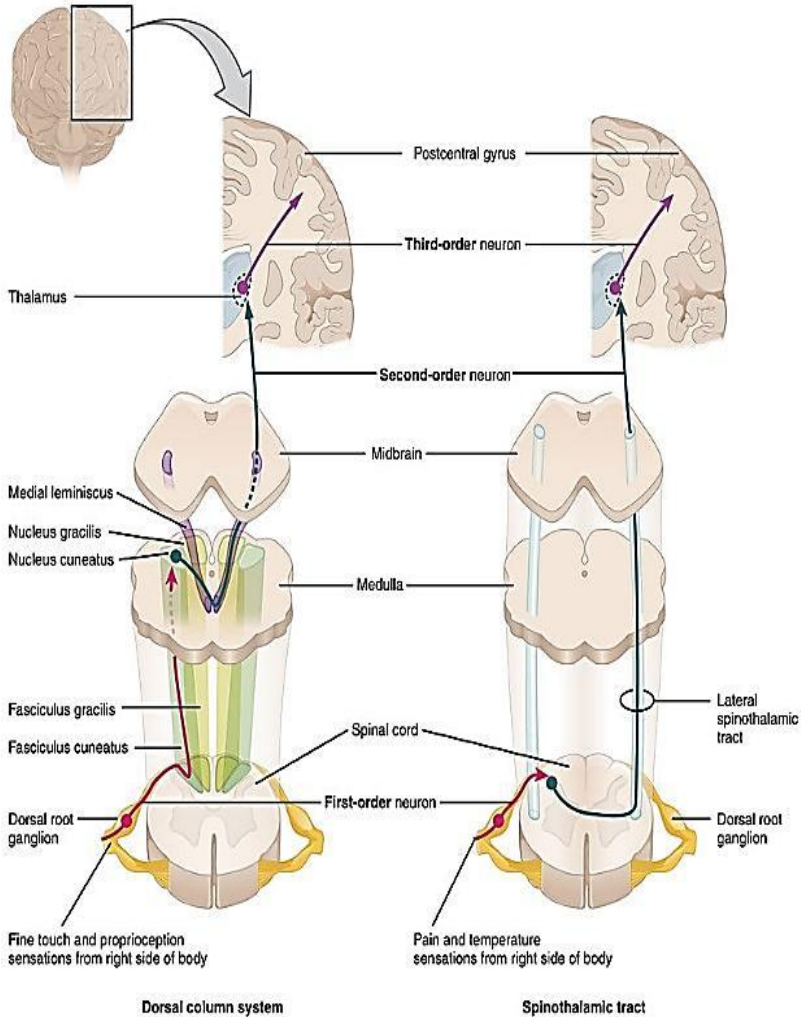
Fig. 9. A spino-bulbo-thalamo-cortical tract

Fig. 10. A spino-thalanic tract

THE EXTEROCEPTIVE PATHWAYS

The exteroceptive pathways transmit the impulses from the skin of the trunk (skin sensitivity), the retina (visual sensitivity), and the internal ear (auditory sensitivity) and from tongue papilla (taste sensitivity).

4. THE PATHWAYS FOR PAIN AND TEMPERATURE SENSATION LATERAL SPINOTHALAMIC TRACT

The *first-order neurons* reside in spinal ganglions. The peripheral processes of these sensory pseudounipolar cells run to the skin receptors. The central processes run from the posterior roots and enter the spinal cord via the dorsolateral sulcus. The *second-order neurons* reside in the **nucleus proprius of posterior grey column.** The axons decussate and enter lateral funiculus to form the *lateral spinothalamic tract*. The tract runs medially from the anterior spinocerebellar tract, it also transverses the medulla oblongata, the tegmentum of pons, the tegmentum of cerebral peduncle and reaches the ventrolateral nucleus of thalamus. The *axons of the third-order neurons* join the thalamocortical bundles that pass through the posterior limb of internal capsula, join the **corona radiate** and terminate in the postcentral gyrus (Fig. 11, 12).
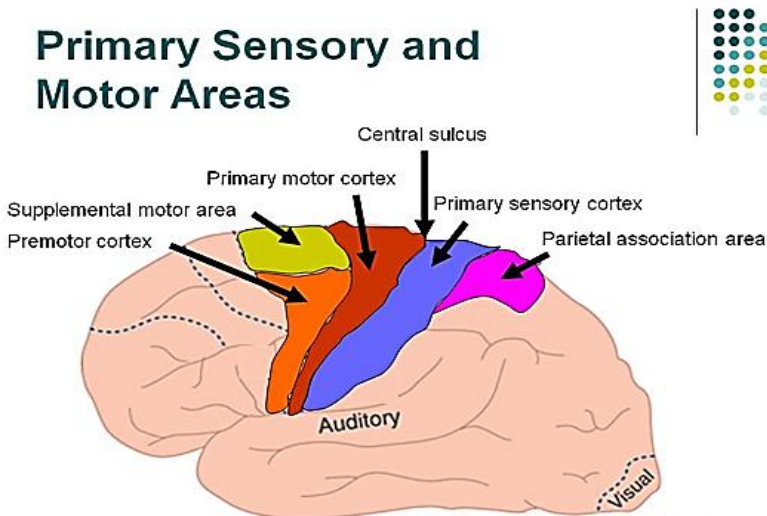
Fig. 11. A cortical center of general sincerity
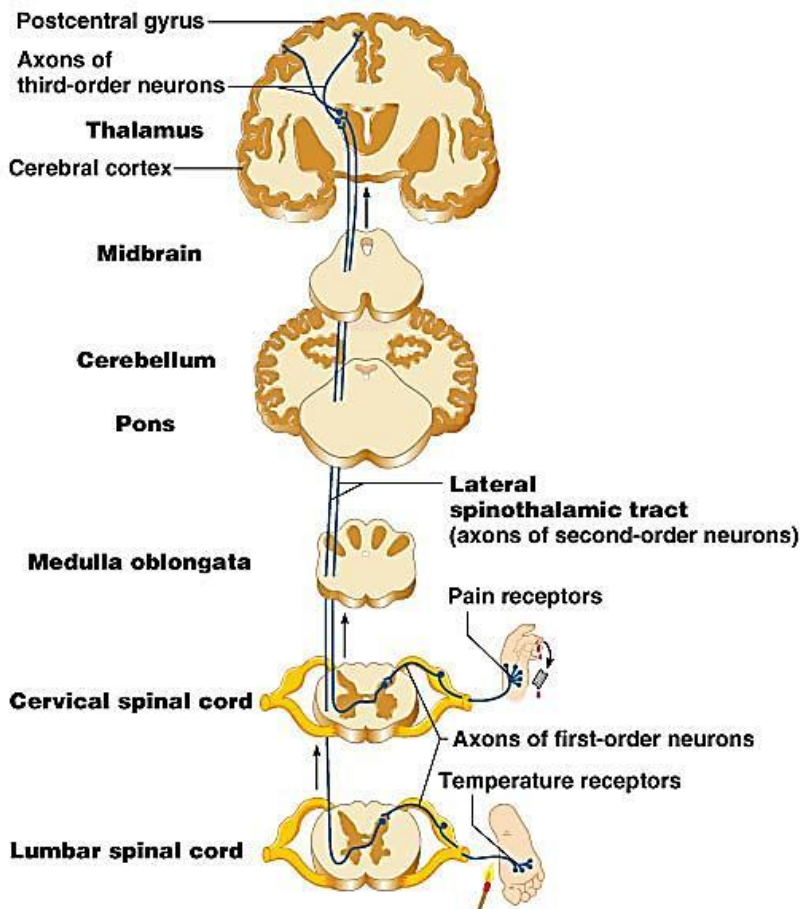
Fig. 12. A lateral spinothalamic tract

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THE ANTERIOR SPINOTHALAMIC TRACT
(FOR TACTILE SENSORY)

The *first-order neurons* reside in spinal ganglions. The central processes of the cells enter the spinal cord in two different ways. Some fibers let the posterior funiculus run directly to posterior grey column that contains the *second-order neurons*. The second-order neurons occupy the dorsal periphery of the gelatinous substance. The axons decussate and enter anterior funiculus to form the **anterior spinothalamic tract.** The tract ascends and joins the medial lemniscus. The third-order neurons reside within the ventrolateral nucleus of thalamus. Their axons join the thalamocortical fibers and finish in postcentral gyrus.

II. DESCENDING PATHWAYS

The motor pathways have two systems of descending fibers as follows:

1) Pyramidal system (it conducts voluntary motor impulses from the cerebral cortex).

2) Extrapyramidal system (it deals with the basal nuclei).

3) Extrapyramidal pathways.

THE PYRAMIDAL SYSTEM

The pyramidal fibers conduct the impulses for well-coordinated targeted voluntary movements. The system is the **pyramidal fasciculus** (fasciculus pyramidalis) and subdivides into the *corticonuclear fibers* and the *corticospinal fibers.*

The **first-order neurons** are the giant pyramidal cells (also known as pyramidal cells of Betz) situated in the precentral gyrus and in the paracentral lobule (the motor area). The axons of cells form the pyramidal fasciculus that passes through the genu and the anterior portion of internal capsule and descends to the brainstem and the spinal cord. Some fibers have already decussated in the brainstem and terminated on the motor nuclei of cranial nerves that reside within the midbrain (the 3rd and 4th), with pons (from 5th to 8th pairs) and with medulla oblongata (from 9th to 12th pairs). This portion of the pyramidal fasciculus constitutes the *corticonuclear fibers*.

The motor cells of the previously mentioned nuclei of the cranial nerves are the second-order neurons of the chain. Their axons leave the brainstem as cranial nerves and reach target areas (Fig. 13).

The larger portion of the fibers descends to pyramids of medulla oblongata as the *corticospinal fibers.* On reaching the spinal cord, about 80 % of fibers decussate (*decussation of pyramids*) and enter lateral funiculus to form the lateral *corticospinal tract.* The rest of fibers proceed to anterior funiculus directly and form anterior corticospinal tract.
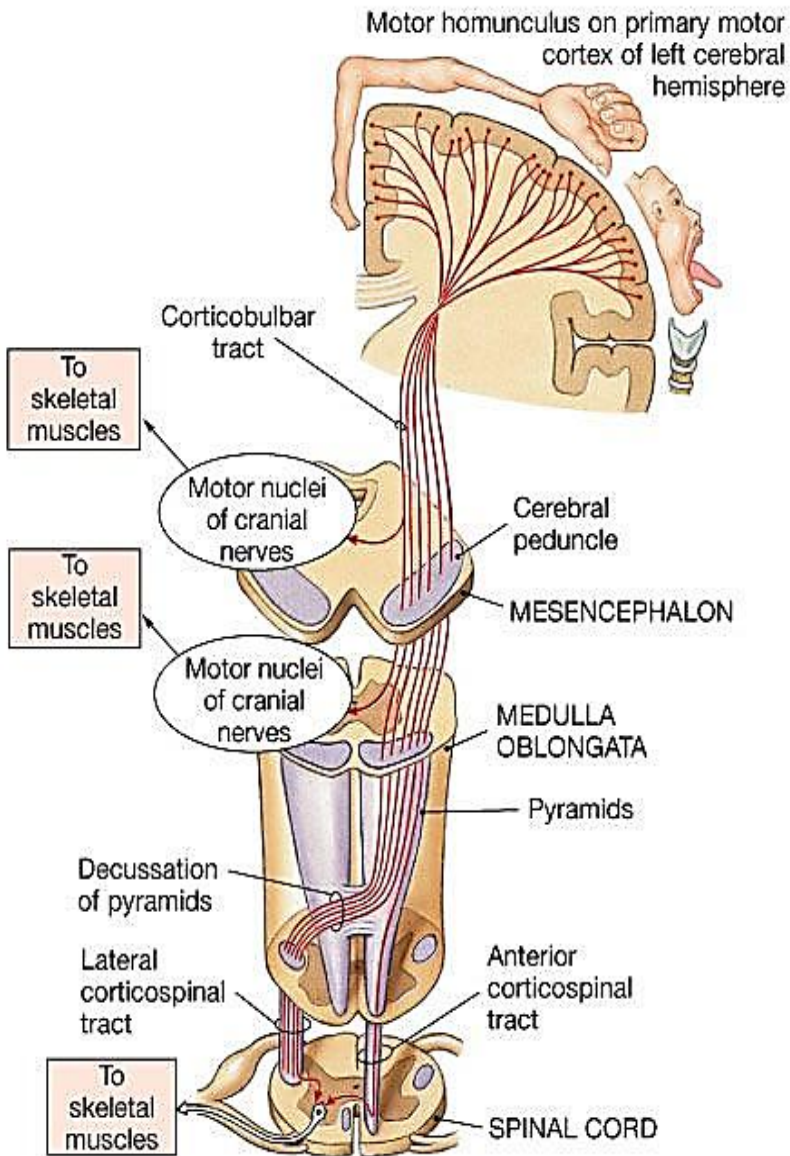
Fig. 13. Descending pathways

THE EXTRAPYRAMIDAL SYSTEM

The extrapyramidal system ensures adequate muscle tonus and tuning of locomotor apparatus. It automatically sets the muscles to background alert mode necessary for fast highly differentiated movements specified by the pyramidal system. The extrapyramidal system acts in concert with the pyramidal system, both systems constitute a single whole.

The nuclei of the extrapyramidal system as follows:

– **Corpus striatum** (caudate and lentiform nuclei) form striopalidary system.

– **The subthalamic nucleus** (nucleus of Luys) situated in the ventral thalamus.

– **The red nucleus** situated in the midbrain (Fig. 14).

– **The substance nigra** situated in the tegmentum of cerebral peduncles.

The extrapyramidal nuclei feature vast associations among each other, cerebral cortex and cerebellum. The nuclei of the *tectal plate* are **vestibular nuclei, inferior olive nuclei, and nuclei of the reticular formation.**
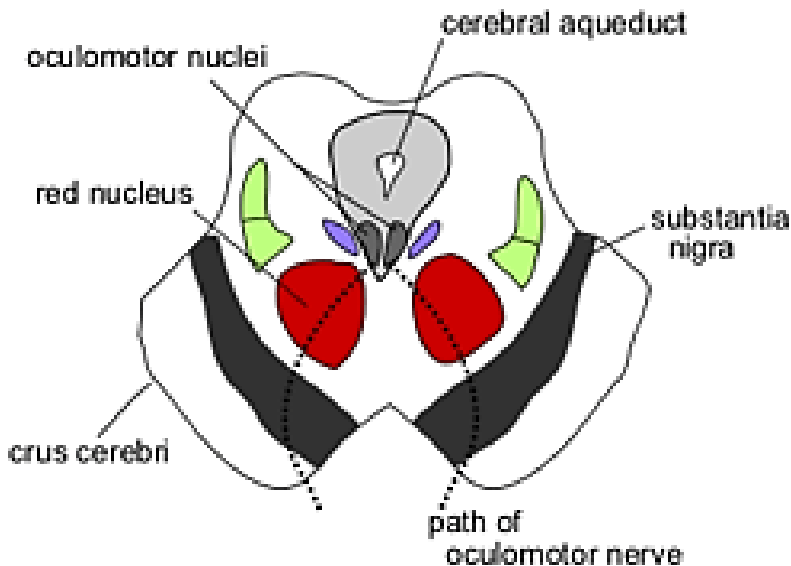
Fig. 14. A cross of midbrain with red nuclei

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THE EXTRAPYRAMIDAL PATHWAYS

The extrapyramidal pathways conduct the impulses from the subcortical nuclei to the motor nuclei of cranial nerves and the motor nuclei of anterior grey columns of the spinal cord. They comprise the fibers as follows:

− *The rubrospinal tract* **(tractus rubrospinalis)** arises from the red nuclei. The fibers of the tract decussate and proceed to the lateral funiculus of the spinal cord. The tract is important because it conducts the impulses from the corpus striatum and the cerebellum (Fig. 15).
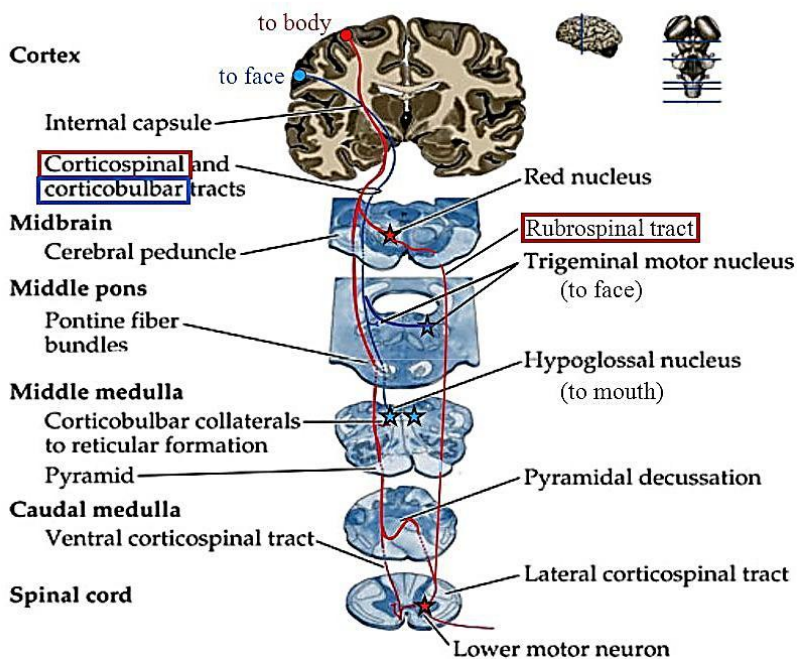
Fig. 15.

− **The tectospinal tract (tractus tectospinalis)** arises from tectum of the midbrain (the nuclei of colliculi).

− **The vestibulospinal tract (tractus vestibulospinalis)** arises from vestibular nuclei.

− **The olivospinal tract (tractus olivospinalis)** arises from inferior olivary nuclei.

– **The reticulospinal tract (tractus reticulospinalis)** arises from the reticular formation of the brainstem. The corpus striatum lacks direct associations with the spinal cord, therefore, its impulses relay on the subcortical nuclei and the nuclei of the reticular formation. Thus, the reticulospinal tract appears to be an important extrapyramidal pathway (Fig. 16).

DESCENDING TRACTS

ASCENDING TRACTS

F.Grasilis (Conscious proprioception)

F. Cuneate (Conscious proprioception)

Lateral corticospinal (Voluntary motor activity)

Rubrospinal (Control of movement)

Dorsal spino-cerebellar (Unconscious proprioception)

Lateral spinothalamic(Pain and thermal sensations)

Ventral spino-cerebellar (Unconscious proprioception)

Olivospinal tract

Vestibulo-spinal (maintain upright posture and balance, Head position)

Spino-Olivary tract)

Tectospinal tract

Anterior cortico-spinal (Control of skilled movement)

Anterior spinothalamic(Touch & Pressure)

Fig. 16. A tracts in funiculi

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THE EXTRAPYRAMIDAL SYSTEM

The extrapyramidal system is responsible for muscle tonus and tuning of the motor apparatus. It automatically sets the muscles to an initial alert mode necessary for fast highly differentiated movements specified by the pyramidal system. The extrapyramidal system acts in concert with the pyramidal system: both systems constitute a single whole (Fig. 17).
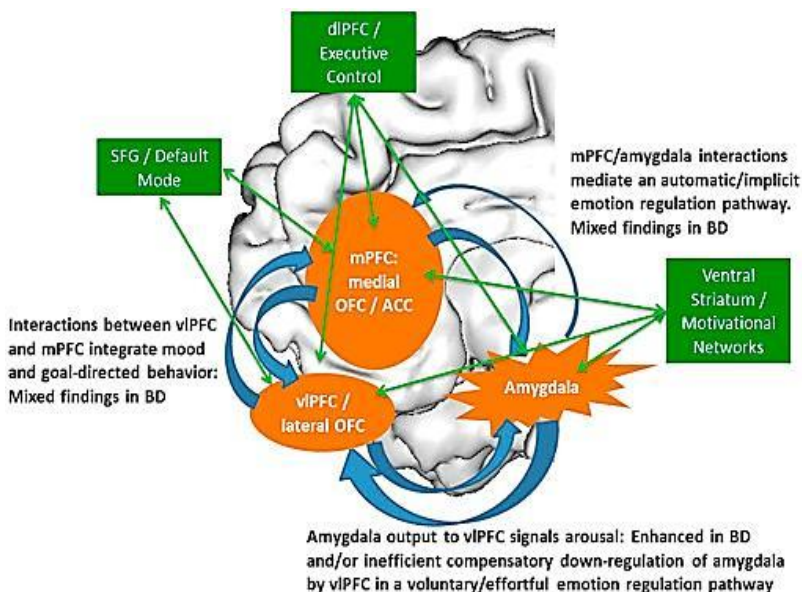

Fig. 17. A extrapyramidal system

THE NUCLEI
OF THE EXTRAPYRAMIDAL SYSTEM

The extrapyramidal system comprises the nuclei as follows:

− **The corpus striatum** – it consists of the caudate and the lentiform nuclei (striopalidary system). They are nuclei of the superior extrapyramidal centers.

− **The subthalamic nucleus (n. Luys)** situated within the ventral thalamus.

− **The red nucleus (n. ruber)** situated within the tegmentum of the midbrain.

− **The substantia nigra** is a black crescent-shaped plate that delimits the tegmentum and the base of cerebral peduncle.

The extrapyramidal nuclei feature associations among each other, the cerebral cortex and cerebellum. The latter provides movements coordination. Thus, it is included into the system as well as the nuclei of the tectal plate, the vestibular nuclei, the inferior olive, and the reticular formation.

Clinical application. Disorders of extrapyramidal system (diseases)
Disorders of basal ganglia function

There is no definitive list of structures that are included in the extrapyramidal system, but all lists would include the basal ganglia (caudate, putamen, and globus pallidus), and the subthalamic nucleus. The substantia nigra is an associated structure with important basal ganglia interconnections. The cerebellum and, perhaps also, the red nucleus play an important role in some abnormalities associated with basal ganglia disorders. Important interconnections of the basal ganglia are the nigrostriatal pathway, and the ansa and fasciculus lenticularis, and the fasciculus thalamicus, which interconnect the globus pallidus and the ventral lateral and ventral anterior (VL-VA) nuclei of the thalamus, and the VL-VA thalamocortical fibers, the subthalamopallidal pathway, striatopallidal fibers, and cerebellothalamic interconnections.

The normal functions of the human basal ganglia have largely been deduced from study of functional problems associated with destructive or irritative lesions. To a large degree, the deficits are in motor function and therefore, the extrapyramidal system and basal ganglia have been associated

with movement disorders. For the most part, these clinical understandings have been supported and expanded by basic science investigations, although it is becoming increasingly evident that these brain regions are involved in a greater array of functions than was heretofore obvious. Although far from complete, this understanding has permitted development of some effective therapies for movement disorders.

In lower vertebrates the basal ganglia are a major motor control system. With progressive evolution of the brain in higher vertebrates, culminating in humans, the pyramidal system and the neocerebellar cortices have assumed a greater level of importance in motor control. However, as is true in many brain functions, the «more primitive» portions of the brain have not been discarded, but rather remain in control of some of the more primitive functions of the nervous system.

Some deficits observed with basal ganglia disease reflect loss of the preceding functions. However, other manifestations fit less easily into a scheme of lost normal function. One can only conclude that they reflect how the remaining normal brain functions when components of the basal ganglia are missing.

There are two major disorder complexes associated with disease of the basal ganglia and related structures: **the parkinsonian syndrome and the choreas.** Athetosis and the dystonias, also basal ganglia disorders, are much less common, with the exception of spasmodic torticollis and dystonias produced by certain neuroleptic drugs.

Parkinsonian Symptoms

«Parkinsonism» is a relatively common complex of neurologic symptoms that can be seen with many types of extrapyramidal disease. This constellation of symptoms appears as the end product of many degenerative disorders of the brain, although some produce the symptoms much earlier in the course than others. For example, most patients with a generalized dementing condition of the brain will eventually develop symptoms of parkinsonism. However, this occurs quite late in the course of the disease for most of these conditions. Cerebrovascular disease can also target the extrapyramidal system (especially when diffuse), leading to parkinsonian symptoms. On the other hand, symptoms occur relatively early in conditions that selectively target the basal ganglia and related structures. Examples include progressive supranuclear palsy, cortico-basal ganglionic degeneration, striatonigral degeneration, multi-system atrophy and diffuse Lewy body disease.

In the case of idiopathic Parkinson's disease, the constellation has been related specifically to deficient function of the nigrostriatal dopaminergic systems. In this case, the major underlying pathologic abnormality is either a degeneration of neurons of the substantia nigra pars compacta (which are the source of the dopamine in the striate nuclei), or a drug-induced suppression of dopamine effectiveness. The latter is a common cause of the parkinsonian syndrome because of the widespread use of certain neuroleptic (tranquilizing) drugs (phenothiazines, butyrophenones, and reserpine) and it can be easily reversed by discontinuation of the drug.

A rare cause of acute and irreversible parkinsonism is poisoning with the «designer drug» MPTP, a derivative of the narcotic analgesic meperidine. The free radical breakdown product of MPTP, MPP+ appears to be the toxic molecule, which destroys the pigmented dopaminergic cells in the substantia nigra. A major experimental model has arisen from this tragic discovery (monkeys and other mammals also develop the parkinsonian syndrome when exposed to this toxin). The toxicity can be blocked by antioxidant therapy (Vitamin E, etc.) and a monoamine inhibitor, deprenyl. This has led to speculation concerning the etiology of parkinsonism and to clinical trials of both entities to determine a possible prophylactic effect in idiopathic parkinsonism.

Ameliorative but not curative medical therapy is now available for Parkinson's patients, mainly in the form of dopamine repletion or deep brain stimulation.

Clinical features

Parkinsonism is characterized by varying degrees of: (1) rigidity, (2) bradykinesia, (3) tremor, and (4) postural defects. Dementia, usually appearing late and less severe than the other abnormalities, is also relatively common (approximately 20 %) and considered secondary to degeneration of cerebral cortical neurons that can be involved in a more diffuse degenerative process (as in diffuse Lewy body disease). Parkinsonism may also be part of a more prominent dementing process such as Alzheimer's Disease, presumably because the degenerative process also affects the basal ganglia.

Rigidity is plastic in nature and present in all ranges of passive manipulation and active movement. This appears to be due to overactivity in descending motor pathways from the brain stem. The gamma motor system probably is not involved because cutting the dorsal roots does not modify the rigidity. The rigidity has a superimposed cogwheel halting character if tremor is part of the syndrome.

Bradykinesia is actually not a slowness of movement so much as an inability to initiate or carry out movements despite the presence of adequate strength. An illustration of this presumed dyspraxia is seen in the parkinsonian patient who, frozen with bradykinesia, leaps from their wheelchair and runs with full coordination from a burning house and then safe, settles back to an inability to initiate volitional locomotion. The capability for catastrophe motivated, well-learned, and relatively automatic behavior is present, but volitional behavior is defective. Once movement is initiated, it can often be continued with reasonable speed. Bradykinesia and rigidity are additive in hindering movement and are usually present together. Bradykinesia is, however, not dependent on or necessarily proportional to rigidity, and vice versa. There is a small population of patients who have pure bradykinesia without other characteristic parkinsonian deficits. They have been described as having a pure «ignition» syndrome.

Also included by many under bradykinesia is the characteristic depression, or loss, of associated movements, such as arm swinging while walking, and emotional expression – e.g., an immobile face when the patient is happy or sad despite the ability to grimace voluntarily. Facial muscle rigidity can also partly or completely account for the «masked facies».

The tremor of parkinsonism is a rhythmic (four to eight per second) oscillation of opposing muscle groups, which is particularly prominent in the distal portions of the extremities. The upper extremities are affected earlier than the lower extremities. The neck and cranial muscles may also be involved.

Early in parkinsonism the tremor may begin in one extremity, so may rigidity and bradykinesia. In the absence of tremor, the presentation of parkinsonism may be erroneously diagnosed as hemiparesis. The absence of true weakness, the character of rigidity (full range instead of clasp knife) and the decrease in associated movements help to differentiate the two. Generalization to both sides of the body ultimately occurs in most patients with parkinsonism. The tremor has been erroneously considered a tremor at rest, but actually it is a tremor of postural or resting muscle tension. When the patient is completely at rest and relaxed (which is nearly impossible for most patients with Parkinson's disease), the tremor disappears. It is most characteristic that a parkinsonian tremor may be seen with the hands folded in the lap or when walking with the hands hanging by the sides.

The postural (e.g., arm held in position demanding muscle tone) or resting muscle tension tremor of parkinsonism is to be differentiated from the tremor of cerebellar damage, which is not present until the patient directs their limbs into purposeful activity (i.e., intention tremor). The tremor of Parkinson's disease is suppressed by the initiation of voluntary movement. As the disease progresses, however, many patients may begin to develop a coexisting intention tremor, which supports a hypothesis that involvement of the cerebellar system is important in the pathogenesis of parkinsonian tremor. All forms of tremor, and indeed most adventitious movement abnormalities, are increased by anxiety or any other stress that increases muscle tension; they are reduced to varying degrees by relaxation or sedation.

Postural deficits are less well studied and understood. However, it is characteristic for a person with parkinsonism to have difficulty adjusting to postural change. This can be demonstrated by seating the patient on the edge of a tilt table. When the table is tilted, the normal response is to lean uphill, thus preserving one's balance. The parkinsonian patient tilts with the table without adjusting and topples over. If the patient is given a good shove backward, instead of normally catching their balance s/he tends to fall back like a tree. In some patients this retropulsion can be initiated by simply having the patient attempt to look up or back up. Patients with moderately advanced parkinsonism frequently have a flexed (stooped) posture, which may well be a compensation for the postural imbalance that causes retropulsion. Falling is a common problem for parkinsonian patients because of the combination of their rigid/bradykinetic shuffling gait and the postural adjustment deficit. They are unable to make the appropriate kinetic-postural adjustment necessary to prevent them from falling. A bizarre but typically parkinsonian fall occurs when the patient is unable to initiate stepping movement with their feet although she has already initiated forward movement of the trunk. To avoid falling on their face, she usually drops to the knees.

Parkinson Disease

Parkinson disease (PD) is the single most common (and most treatable) condition that produces parkinsonism. Most cases are sporadic, although there are some clearly defined families with autosomal dominant inheritance patterns. Most of these families have inherited defective genes for one of several intracellular proteins. The ultimate pathology in PD is the presence of Lewy bodies (ubiquitin-containing granules) in the cytoplasm

of neurons in the degenerating substantia nigra pars compacta (the region of dopaminergic neurons projecting to the substantia nigra). Because there are some small clusters of Parkinson's disease and because of cases of poisoning with MPTP (a byproduct of amateur attempts at synthesis of meperidine), there are some suspicions of environmental factors in the genesis of the disease. It appears that compounds that generate free radicals when oxidatively metabolized have a particular predilection for damaging the substantia nigra (due to the high oxidative functions of these neurons).

Although PD can occur at any age, it is rare before the 30s, and increases in frequency with advancing age. This can be explained by gradual, age-related loss of neurons in the substantia nigra.

Most often, the symptoms begin asymmetrically. There is a variable constellation of tremor, bradykinesia, rigidity, difficulty initiating movements and delayed postural corrections. The condition can present with tremor or with rigidity. Rarely, it can primarily present with balance issues in the absence of other symptoms. These cases are particularly difficult to diagnose.

The fundamental pathology in pure cases of PD is a deficiency of dopamine in the striatum of the basal ganglia (the caudate and putamen). Dopamine has the effect of stimulating the direct circuit through the basal ganglia, while inhibiting the indirect pathway. Ultimately, since the direct pathway is facilitatory to movement and the indirect pathway is inhibitory, the net effect of dopamine is to increase the excitability of the motor areas of the cerebral cortex and increase movement (see this discussion of functional anatomy if you desire further elucidation). Therefore, when the tonic activity of dopamine is lost, the motor and premotor cortex are less excitable and the patient is less mobile, with slower responses and less spontaneous movement.

As our understanding has progressed, it has become apparent that some patients have a pure dopamine deficiency. These patients have near-complete resolution of their symptoms when dopamine is replaced. However, there are also patients with additional degeneration of the extrapyramidal system. These patients usually have incomplete resolution of symptoms, with improvement based on how much additional damage has been done.

Treatment of PD is often initiated with the combination of levodopa (a dopamine precursor that crosses the blood-brain barrier) and carbidopa (an inhibitor of dopa decarboxylase that does not cross the BBB). This latter

medication prevents conversion of levodopa to dopamine outside the brain, thereby minimizing dopaminergic side effects and assuring as much delivery of dopamine as possible to the brain. The entry of dopamine to the brain can be diminished by competition with other amino acids, and some patients have their response to levodopa blocked by a protein meal.

Levodopa is easily converted to dopamine in the brain and results in an increased concentration and storage of dopamine in dopaminergic neurons. Although the levodopa is typically quite short-lived in the peripheral circulation, the fact that it boosts dopamine storage in the brain can result in improvement of symptoms lasting many hours. However, as the condition progresses, the capacity to store dopamine declines and the duration of action becomes shorter (sometimes only persisting for the hour or two of high blood levels). This progressive decline in dopamine storage results in «wearing off» of the drug that can occur at progressively shorter intervals and, eventually, severely fluctuating symptoms. These fluctuation can result in «on-off» periods that can occur quite abruptly. The patient can even freeze in place unpredictably.

After long-term administration of levodopa, over-responsiveness to dopamine may develop. Striatal neurons appear to become particularly sensitive to dopamine after years of exposure to levodopa (and, to a lesser extent, other Parkinson's treatments) due to proliferation of dopamine receptors. This can result in the «peak-dose dyskinesia» that is seen as choreoathetosis (see below).

Other complications of Parkinson's treatment include nausea (due to stimulation of peripheral dopamine receptors), hypotension (which can also occur due to PD, itself) and hallucinations/nightmares. These latter are typically visual in nature.

Other treatments for PD include anticholinergic medications (these have limited effect and many side-effects), direct dopamine agonists (drugs that stimulate the dopamine receptors directly) and medications that slow the breakdown of dopamine (either by blocking centrally-acting monoamine oxidase or catechol-O-methyl transferase). Other methods of delivery of levodopa are being explored and, if medications are producing excessively variable responses, neurosurgical procedures (mostly either destruction of the medial globus pallidus or stimulator implantation into the subthalamic nucleus) are often used. Symptoms are invariably progressive, although there has been great interest (and slight evidence) for neuroprotective approaches to prevent this progression. Eventually, most patients develop

less response to medication, coupled with increased side-effects. This probably occurs due to degeneration extending to other neuronal cell populations as well as proliferation of dopamine receptors on remaining neurons.

Parkinson's plus

There are some conditions characterized by symptoms of Parkinson's disease plus areas of degeneration. Multiple system atrophy (MSA) commonly has additional pyramidal signs (spasticity and upgoing toes), autonomic dysfunction (bladder and blood pressure control) and cerebellar findings along with symptoms of Parkinson's disease. This is associated with a very specific pathology, the presence of glial cytoplasmic inclusions, in many brain regions (accounting for diffuse symptoms). There are 3 main variants of this condition, all with similar neuronal pathology, each of which has its greatest effect in different brain regions. When the extrapyramidal system is mostly affected, this is termed «striatonigral degeneration». When the cerebellar systems are mostly affected, the diagnosis is «olivopontocerebellar atrophy». And when the autonomic preganglionic neurons are targeted, the condition has been called Shy-Drager syndrome. This latter condition produces profound orthostasis and bladder dysfunction as early symptoms. With progression of any of these variants, elements of the other conditions may come out. None of these conditions are as responsive to treatment as is Parkinson's disease (and side-effects to medications are typically greater).

«Parkinsonism»

As we described previously, any condition that results in sufficient degeneration of the extrapyramidal system can result in «parkinsonism». However, there are several specific causes of parkinsonism that deserve a little more discussion. These are all characterized by some appearance of the above-described symptoms of parkinsonism, especially rigidity and bradykinesia.

Progressive supranuclear palsy (PSP) is a condition of degeneration, with prominent accumulation of neurons containing tau proteins in many areas including the rostral midbrain. Symptoms usually start in the 50s or 60s. Most of these patients have early gait difficulty and there is often a significant dysarthria early in the course. Voluntary vertical gaze is also affected very early in the course. The patient has trouble looking up and down although the eyes can be moved much further by oculocephalic tests. Many patients eventually develop retrocollis (a dystonic extension of the

neck) and they often develop severe swallowing troubles (that can lead to pneumonia). Emotional lability, personality change and cognitive problems usually occur a little later. This condition progresses more rapidly than does Parkinson's disease and death is due to pneumonia or the effects of debility. There is little response to Parkinson's medications.

Cortical basal ganglionic degeneration (CBD) is a rare, degenerative condition that results in degeneration of both the fronto-parietal region of the cerebral cortex and various structures of the extrapyramidal system. There may be large, ballooned neurons and other neurons containing neurofibrillary tangles. This condition usually begins in the 50s and 60s and presents with asymmetrical motor difficulties that can include prominent apraxia of a limb («I just can't make it do what I want to»). Sometimes this is so severe that it has been termed «alien hand». Dystonia of one limb is a common symptom. Patients usually don't have significant memory loss but may have «executive» function problems (i.e., distractible, trouble planning movements, deficient judgment, etc). Patients may also have trouble with graphesthesia despite intact sensations. There is no effective treatment other than palliation.

Diffuse Lewy body disease (DLBD) is a condition where neurons in the cerebral cortex and extrapyramidal system are undergoing degeneration with prominent ubiquitin-containing inclusions (Lewy bodies). This condition is most remarkable for vivid and severe hallucinations early in the condition, along with confusion, a progressive dementia and parkinsonian features. These patients are very sensitive to the older antipsychotic medications which are often administered in an attempt to quell the hallucinations, that are often accompanied by paranoid delusions. Some of the newer antipsychotics are significantly better in this regard (such as quetiapine and clozapine). Some of the anticholinergic treatments (as used for **Alzheimer's disease**) may be helpful, but only for a short period.

Chorea

Chorea is the term for a type of involuntary movement disorder characterized by irregular and fleeting movements of the limbs and/or axial musculature also including the muscles of the face, jaw and tongue. The intensity of movement varies from very minimal buccolingual chorea characteristic of long-term neuroleptic toxicity to the wild and exhausting limb-flailing chorea called hemiballism.

Degenerative and destructive processes in the striatum or striatal inhibition (due to certain classes of drugs) are the major pathologic

substrates of chorea. Superficially it appears paradoxical that the most common causes of choreiform movement disorders are the same neuroleptic drugs (phenothiazines, butyrophenones, and reserpine) that are the most common causes of parkinsonian disability. Unfortunately the choreiform abnormalities are not so easily reversible and may be permanent in some cases.

The model for choreiform disorders is Huntington's chorea. This condition is a rare, inherited (autosomal dominant), degenerative process involving the striatum, particularly the small-cell population (the large-cell neurons are relatively spared), and also the cerebral cortex, giving rise to a combination of progressive limb and axial chorea and dementia. Sometimes, early in the disease, a parkinsonian syndrome with rigidity and bradykinesia precedes the chorea, presumably because of involvement of the dopamine system of the striatum. This changes to chorea with progression. When this unfortunate process is recognized in a family, genetic counseling becomes paramount as an exercise in prevention.

Sydenham's or rheumatic chorea is a mild, self-limited limb and axial disorder associated with rheumatic fever in children. The decreasing incidence of rheumatic fever may soon make Sydenham's chorea an historical curiosity. It is occasionally exacerbated or uncovered in adult women who are pregnant (chorea gravidarum) or taking birth control pills. Because it is reversible and not progressive or fatal, very little is known of the pathophysiology. However, it is presumed that the substrate is striatal dysfunction, because the same drugs that to some degree ameliorate Huntington's chorea are also effective against Sydenham's chorea.

A variety of metabolic conditions are associated with choreiform movements. Among these are hyperthyroidism, lupus erythematosus (presumably the vasculitis affects the arteries supplying the striatum), atropine poisoning, anticonvulsant toxicity (e.g., phenytoin, carbamazepine, and phenobarbital), and L-dopa therapy for parkinsonism. Relief coincides with clearing of the metabolic derangement.

Hemiballism

Hemiballism is a violent, flailing chorea of the limbs opposite a lesion in the subthalamic nucleus or, rarely, the striatum. With few exceptions the pathogenesis is infarction, less often hemorrhage, and rarely tumor. Fortunately, in most cases the disease is self-limited because the process (e.g., ischemia) resolves or because the lesion enlarges to involve either the cerebral peduncle or the internal capsule, causing weakness from

involvement of the pyramidal system; the chorea, which is expressed through an intact pyramidal system, disappears.

Athetosis

Athetosis is a rare movement disorder characterized by involuntary, slow, twisting, writhing movements of the trunk and limbs. It frequently has associated erratic choreiform components. Striatal injury, particularly prominent in the putamen, has been considered the pathophysiologic substrate; however, widespread brain damage is usually present and confounds any clear analysis. The most common causes are perinatal hyperbilirubinemia, which involves the brain (kernicterus) and prematurity (which can result in damage to developing forebrain, often with periventricular hemorrhage). These leave the infant with cortical and prominent basal ganglia damage, with subsequent choreoathetosis and, usually, mental retardation.

Dystonias

With one exception, the dystonias are uncommon disorders. They are characterized by torsion spasms of the limbs, trunk, and neck. They may be progressive or static and are related to past encephalitis in a few cases but are usually idiopathic. In a few individuals who were well studied post mortem, either no pathology or various combinations of basal ganglia lesions were seen. Spasmodic torticollis is the most common idiopathic form and is characterized by intermittent excessive and involuntary contractions of the sternomastoid muscle on one side (rarely bilateral giving retrocollis). Interestingly, the head can be guided back to a neutral position with very gentle pressure on the side of the face. The head drifts back to its distorted position when the pressure is released. Therapy with anticholinergic medications has had a minimal positive effect on dystonic disorders. Recently, intramuscular injections of weak solutions of botulinum toxin, a powerful neuromuscular transmission blocking agent, have been shown to be useful in relieving dystonia for periods up to four to six months.

The one frequently seen dystonia is related to an overdose of neuroleptic drugs and is always reversible when the drug is withdrawn or counteracted by anticholinergic drugs. Involuntary and occasionally severe tonic contraction of axial muscles is most common, ranging from jaw clenching similar to the trismus (lockjaw) of tetanus to severe opisthotonic posturing (back and neck in sustained extension) similar to that seen in decerebration. Recognition of this easily reversible cause of these otherwise ominous signs

is obviously important. A good history can usually clarify the situation, and reversal of the dysfunction with anticholinergic medication confirms the diagnosis.

Tics

Tics are fleeting, purposeless actions that may be simple (appearing as a muscle twitch) or complex (which may involve more repetitive behavior. While these are not voluntary, they can usually be suppressed for a period to time through force of will (often increasing for a time afterwards). They should be distinguished from fasciculations and from myokymia (such as that often occurs in eye muscles with fatigue). These disorders come in many varieties.

Tics are common and usually transient in children (often brought on by stress, which worsens all tic disorders). However, some children have multiple motor tics and repetitive vocal tics (throat clearing, snorting, sniffing, etc) that represent Tourette syndrome. At its most severe, the vocal tics may include words, including expletives (coprolalia). Symptoms usually begin between 5 and 18 years and fluctuate with time. Symptoms may resolve or persist into adulthood. The tics are often accompanied by symptoms of obsessive-compulsive disorder and children also often have symptoms of ADHD (psychostimulants used to treat ADHD usually worsen tics).

The majority of cases have some evidence of genetic factors, though the specific gene (or, more likely, genes) are not known. There are also environmental factors including, potentially, autoimmunity and psychosocial factors, that may play a role in expression and severity.

Treatment is not necessary in all cases. However, tics can be suppressed by neuroleptic medications (anti-psychotic; dopamine blocking drugs). These have many potential side-effects. The alpha-2 blocking drug clonidine may suppress symptoms as well, however this is a powerful anti-hypertensive agent.

It should be kept in mind that Tourette's does not affect longevity and is entirely compatible with normal cognitive function, health and lifespan.

Tardive dyskinesia

Tardive dyskinesia is the term given to the iatrogenic axial chorea seen most often in women exposed to long-term neuroleptic use. The neuroleptic drugs (phenothiazines and butyrophenones), among many other effects, block both dopamine and, to a lesser degree, acetylcholine systems and usually cause parkinsonian side effects; dystonia is caused by acute

overdose. On withdrawing the drugs or decreasing the dose, these difficulties usually clear. In its mildest form, constant mouthing with protrusion of the lips, mandible and tongue is seen, not unlike the movements of some very elderly persons and individuals who continually adjust loose upper dental plates. In more advanced stages the trunk muscles are involved and there is a characteristic irregular, incessant pelvic thrusting, which can cause the patient to become a recluse. Unfortunately, after chronic use, axial and, occasionally, limb choreiform movements are uncovered in some cases and persist. Treating these patients with the same dopamine-blocking neuroleptics is usually successful in improving symptoms for a while, presumably on the basis of production of parkinsonian side effects. Unfortunately, the choreiform-causing changes continue to occur and finally break through the parkinsonian effects so that the dose of the drug must continually be increased. Withdrawing the drug leaves a worse choreiform problem.

The mechanism of tardive dyskinesia appears to be due to a compensatory increase in the number of dopamine receptor sites following long-term administration of neuroleptic drugs, producing hypersensitivity. When the drugs are withdrawn, uncovering blocked dopamine receptor sites or increasing dopamine levels toward normal, the total number of active sites may become so great that there is an excessive dopaminergic response (chorea) to normal levels of dopamine elaboration in the striatum.

Some of the newer «atypical neuroleptic» drugs are less likely to do this but most still can result in dyskinesia. Antioxidant prophylaxis and therapy has recently shown some promise in preventing and, to a lesser degree, reversing tardive dyskinesia. However, this may not be as effective as was first suspected. Nonetheless, it might be prudent to include antioxidants concomitantly with chronic neuroleptic therapy.

Neurotrauma is on the increase, given our sensex prosperity sans civic sense and driving discipline. The merchants of speed- the vehicle makers- owe a debt to all those whose neurotrauma they promote. The current phylogenic thought holds the human headn-neck as but the 5th limb that sticks out of the trunk. Speed, sports, and violence are aplenty around to take toll of this vulnerable part of human anatomy encasing the brain that is no more dense than congealed CSF. Neurotraumatology is now a discipline by itself, boasting of minute basic research and even clinical trials. There is some trouble with the term neurotrauma. Earlier medical lexicons synonymized it with trauma to a nerve. Now neurotrauma also connotes

trauma to the neuraxis. Taking advantage of this dichotomy, it is useful to classify neurotrauma using innovative terms pregnant with meaning. The above tentative attempt prevents the error of terminologically putting grave brain injuries with minor nerve injuries on par with each other. The neologisms aren't complicated and are self-evidently helpful in telling what is injured and what to expect out of reparative efforts. Neurotrauma, involving the neurons biologically classified as perennial/ postmitotic/ indivisible cells, can spawn no restorative neuronal multiplication. A neurone is a post-mitotic cell- once lost, lost for ever, for it cannot multiply. Our main aim should be to minimize the axial displacement of the central nervous system axis to offer the best chance of healing. Our other ally would be the enormous compensatory mechanism that the brain particularly has. The entire nervous system, from the ependymal lining to the tips of toes and fingers is a heap of snowflakes, a gigantic non-fibrillar (non-collageneous) cytoma, suspended in an isodense medium called CSF, and perpetually commutative with it. Next to blood, the nervous system is the most unstitchable tissue of the animal body. The stitchability of nervotrauma in its periphery is not of the neural tissue itself, but of the Schwann cell system that ensheathes the nerve to provide to the repairer a semblance of vector-healing. The ancillaries of the nervous system are, like the tyre of a car, repairable. The neural tissue, like the air within, is NOT. Whatever the fill-in-the-gap, healing is by multiplicability of the neurogliocytes (reactive gliosis) which belong to the expanding/mitotic cell population.

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