Anatomy

Sheet

Lec No: 3

Subject: Embryology of CNS and Motor system

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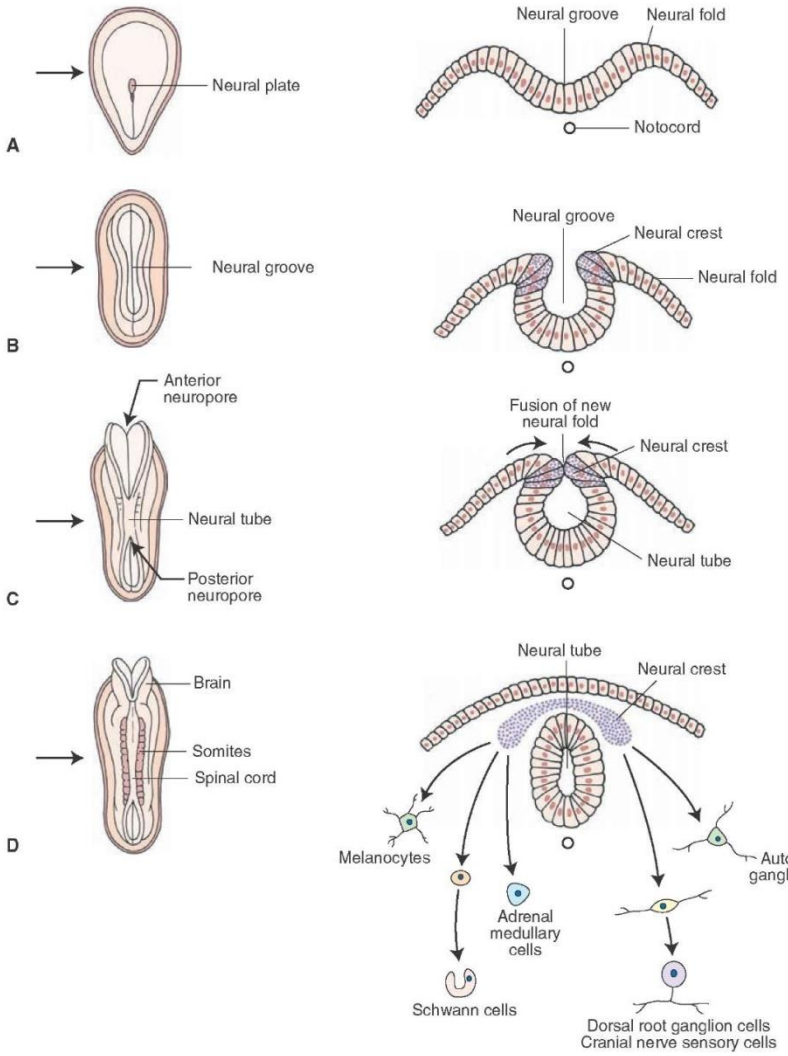
Embryology of central nervous system

✓ Brain and spinal cord are *ectodermal* in origin

◈ Formation of neural tube:

- At the beginning of **third** week, and under the **inductive** influence of the **notochord**, cells of dorsal ectoderm lying above the notochord start to divide and thicken in the midline forming a thick layer known as **neural plate**.



- At The lateral margins of neural plate, the neuronal epithelial cells beneath the margins increase in number and size and undergo changes in their shape and connections with surrounding cells. As a result of these changes the lateral margins of the plate become **elevated** to form the **neural folds** (two neural folds).

- In between the neural folds there is a depression known as **neural groove**. At about ٢٥th day, the neural folds start fusing to form the neural tube. The fusion begins at the ٤th somite (segment) and progresses rostrally and caudally. When fusion is completed **neural tube** is formed.

◈Notes:

- ✓ Neural tube remains opened for a short time at both ends (two ends of neural tube : **rostral neuropore** and **caudal neuropore**).
- ✓ The rostral neuropore closes at about the ٢٥th day and two days later the caudal neuropore closes.
- ✓ Rostral part of neural tube will form three vesicles :
  1. **Forebrain (prosencephalon)**
  2. **Midbrain (mesencephalon)**
  3. **Hindbrain (rhombencephalon)**
     - ➢ The three vesicles together will form the future **brain**.
- ✓ Caudal part of neural tube will form the **spinal cord**.
- ✓ Before the fusion of neural folds is completed, some cells at the margin of neural fold separate forming **neural crest** on each side (these cells don't incorporate into the neural tube).

◈ Derivatives of neural crest :

a) All ganglia (autonomic and sensory).
b) Adrenal medulla of adrenal gland (modified sympathetic ganglion).
c) Melanocytes in skin.
d) Parts of facial cartilages (although cartilage is mesodermal in origin, it is here derived from neural crest which is ectodermal in origin indicating the ability of some cells to transform from ectoderm into mesoderm).
e) Aorticopulmonary septum within embryo that divides truncus arteriosus into aorta and pulmonary trunk.

- ✓ The neural tube detaches itself from the ectoderm and sinks into the underlying mesoderm.

◈ Congenital **Defects of the central nervous system**

I. Anencephaly

- It means without brain
- A case in which the rostral neuropore fails to close.

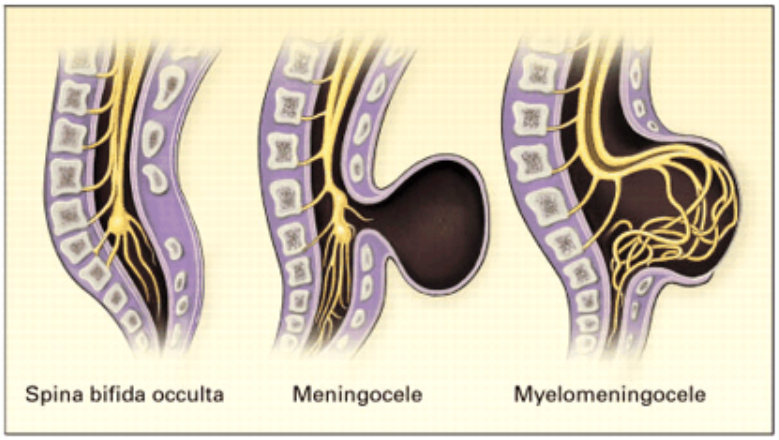
3.38

Figure 3.38. The lateral view of the same infant with anencephaly.

- At birth:
  - **a)** Vault of the skull is absent.
  - **b)** The Brain is largely absent and represented by a mass of degenerate tissue exposed to the surface.
  - **c)** Often accompanied with **<u>rachischisis</u>** in the cervical region and neck.
    - Rachischisis: a case of an <u>open spinal cord</u> due to neural tube defect. The neural tube is kept opened and doesn't close so the vertebral column is absent and spinal cord is opened.
- Quite common abnormality occurring in ١ for each ١٠٠٠ live birth.
- More in female than males (٤:١)
- Diagnosis: by **<u>ultrasound</u>** (sonar) in the first weeks of pregnancy (early diagnosis) → legal abortion. In the past they used a needle piercing the abdominal wall of the mother to take a sample from amniotic fluid around the embryo. **<u>High levels of alpha fetoprotein</u>** are found in case of anencephaly. (The diagnostic procedure is called *<u>Amniocentesis</u>*)
- If early abortion is missed and pregnancy is completed: **premature abortion** happens at ٧th month and newborn lives only for few hours.
- ***Defective swallowing reflex*** : the fetus *<u>lacks the control mechanism for swallowing.</u>* In the last weeks of pregnancy the embryo normally swallows the amniotic fluid and get rid of it as urine > no swallowing leads to increased amount of amniotic fluid around embryo a case known as **<u>hydramnios</u>**

II. Spina bifida

- ✓ The vertebra is normally composed of body anteriorly and pedicle and lamina (together vertebral/neural arch) posteriorly.
- ✓ In spina bifida the neural arch is incomplete الفقرة المشقوقة.
- ✓ **٣ cases are mainly related to spina bifida:**



١. **Spina pifida occulta**

- ➢ It is the simplest case in which spinal cord and meningies remain in place but neural arch is incomplete.
- ➢ The site of defect is often marked by a tuft خصلة of hair.
- ➢ Most cases of spina bifida are diagnosed accidently. The defect might goes unnoticed for many years. ex: a patient with symptoms of intervertebral disk disease would make an x-ray for his back and accidently finds that he has spina bifida (it causes no neurological symptoms).

٢. **Meningocele**

- ✓ more severe than spina bifida occulta.
- ✓ spina bifida in which neural arch is incomplete, spinal cord is in place but **dura matter is absent** in area of defect and the arachnoid layer bulges prominently beneath the skin كيس بارز في أسفل الظهر.
- ✓ It is **rarely** accompanied with symptoms of paralysis or incontinence (neurological symptoms are often **minor**).
- ✓ Menigocele is considered more or less **benign**.

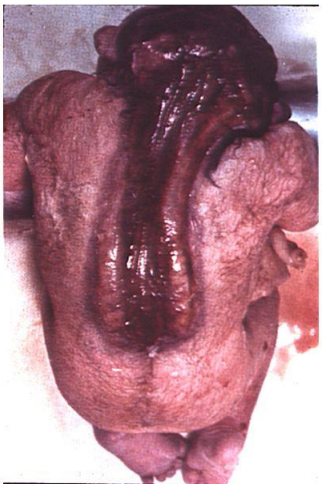
٣. **Meningomyelocele**

- ✓ The most severe defect.
- ✓ spina bifida accompanied with **absent dura matter** and **spinal cords which is displaced into protruding subarachnoid space** .
- ✓ It is usually accompanied with symptoms of **paralysis** or **weakness** in lower limbs if the defect is in the lower part of vertebral column.

III. Rachischisis

- ✓ It is even worst than the ٣ above
- ✓ Spina bifida is present with **spinal cord remaining in stage of neural plate** (**no folds and closure of neural tube**). the spinal cord is exposed or opened at surface which results in:
  a) Chronic infection
  b) Motor defects (weakness and paralysis) and sensory defects
  c) Disturbance of bladder function
  - Remember : in spinal cord lesions we always care about bladder function -> either urine retention or urine incontinence can happen.

Rachischisis: failure of neurulation; i.e., the neural tube does not close



Rachischisis: spinal cord
Cranioschisis: brain

Craniorachischisis: brain & cord

IV. As the spina pifida in vertebral column, similar defect can be related to the skull

- ✓ ٣ cases:
  ١) **Meningocele**
  It is associated with a **small** defect in the skull (the **skull is opened**) where **only meninges** protrude through the opening while brain is in its place. (frontal or occipital)
  ٢) **Meningoencephalocele**
  Part of the **brain** protrudes through a large opening in the skull.

٣) **Meningohydroencephalocele**
Part of the **brain** and **brain tissue containing part of the ventricular system** (contains the cerebrospinal fluid) protrude through the opening.

V. Microcephaly

- ✓ Usually after birth the circumference of skull of newborn is measured to know if his head is growing or not. In this case there is **no growth of both brain and skull (cranium)**.
- ✓ Since there is no development of brain, mental retardation occurs.
- ✓ **Causes :**
  - **a)** Early closure of sutures of skull (the joints of skull), no further development.
  - **b)** In most cases its etiology is **uncertain**. If we fail to know the exact etiology we say it is caused by a **combination of genetic and environmental factors.** (Environmental factors include radiation and drugs affecting the nervous system development).

◈ Myelination of brain and spinal cord

- ✓ A nerve fiber with no myelin is of zero value. This actually what a demyelinating disease does (multiple sclerosis is an example). If the disease is affecting optic nerve then vision is lost. If it is affecting motor pathways, weakness and paralysis occur.

i. Myelination of spinal cord

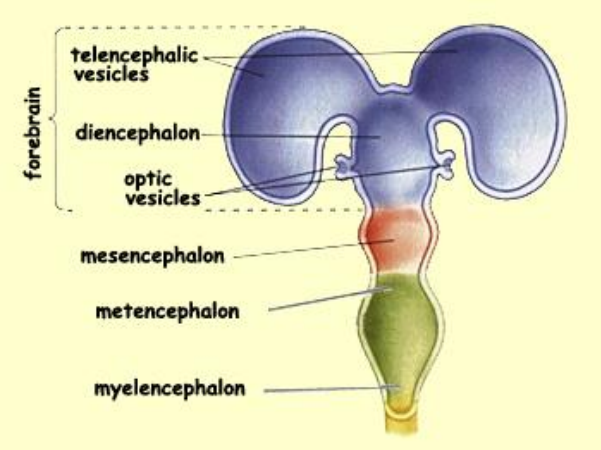
- The process of myelination begins within the cord about **third or forth** month. It starts within **cervical** region.
- **Sensory pathways are myelinated before motor**.
- Myelination of motor occurs **after birth**. At birth motor pathways are largely non-myelinated (which means they are not functioning) this explains why a newborn can't walk.
- **Ventral root is myelinated before dorsal root.**

ii. Myelination of the brain

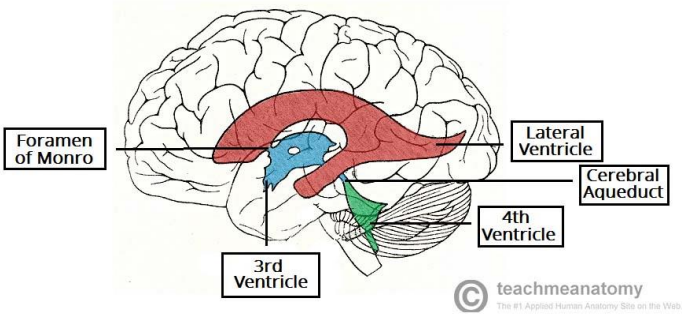
- Starts at **basal ganglia at ٦th month** of fetal life
- Most sensory and motor pathways at birth still largely unmyelinated.
- Sensory pathways are myelinated before motor.
- Most myelination of motor pathways (ex: corticospinal and corticobulbar pathways) starts at **<u>٦th month after birth and completed by the end of second year</u>** (this also explains why a newborn can't walk at birth).

◈Differentiation of cerebral vesicles and the ventricular system

- ✓ In early stages of development the upper rostral part of neural tube will form the brain. It initially develops into **٣ vesicles** : forebrain, midbrain and hindbrain.
- ✓ **Forebrain** or prosencephalon will develop into two parts: ***<u>telencephalon</u>*** and ***<u>diencephalon</u>***.
  - Telencephalon will give two **cerebral hemispheres**.
  - Diencephalon will give the **thalamus and hypothalamus**.
  - <u>Telencephalon develops faster</u> than diencephalon so it covers both sides of diencephalon → this explains why we can't see thalami(thalamus and hypothalamus) from outside because they are covered by cerebral hemispheres.



✓ **The ventricles of brain** : تجاويف



- The cavity of the telencephalon will form the ***lateral ventricle*** (٢ lateral ventricles one for each cerebral hemisphere)
- The cavity of the diencephalon (the space between the two thalami) will form the ***third ventricle*** (one third ventricle only).
- The communication between lateral ventricles and third ventricle is known as interventricular foramen of monro. This foramen might be congenitally obstructed or it might get narrowed or obstructed due to infection. This obstruction will prevent the passage of CSF produced in lateral ventricle to the third ventricle leading to an increase in the size of brain (a case that will be discussed later).
- The cavity of the mesencephalon remains as a narrow canal called the ***cerebral aqueduct.***
- The cavity of the rhombencephalon will form the ***fourth ventricle*** (a cavity bounded by the cerebellum, pons and medulla oblongata)

◈Production and circulation of CSF:

✓ CSF is produced by modified capillaries (a tuft of capillaries) known as **choroid plexus** found mainly in lateral ventricles. Choroid plexus is also found within third ventricle.

✓ **Circulation of CSF :**

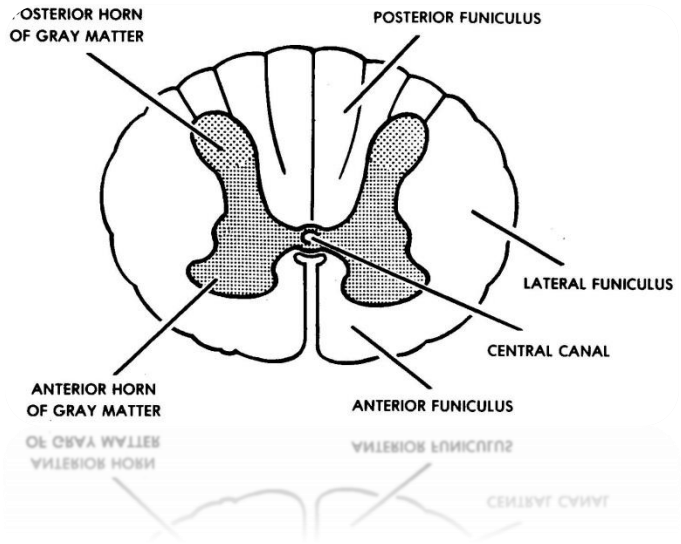
I. From lateral ventricle to third ventricle via interventricular foramen.
II. From third to fourth via cerebral aqueduct.
{In the roof of fourth ventricle there are ٣ openings**: Central foramen of magendie** and **two lateral foramina of luschka.}**
III. CSF leaves forth ventricle by these ٣ openings to subarachnoid space (a space between pia matter and arachnoid surrounding brain and spinal cord). Notice that CSF is found inside the brain in the ventricles and Outside the brain in subarachnoid space .
IV. CSF is then discharged to the blood (circulation) by venous sinuses inside the skull.

- ✓ Any obstruction of the flow of the CSF leads to enlargement of head and brain.
- ✓ Subarachnoid space contains blood vessels. Any rupture of a blood vessel there will lead to hemorrhage so the CSF is mixed with blood . This case is called ***subarachnoid hemorrhage*** . It is diagnosed by taking a sample of CSF around spinal cord by entering a needle between lumbar vertebrae ٣ and ٤. This process is called **lumbar puncture (LP).**

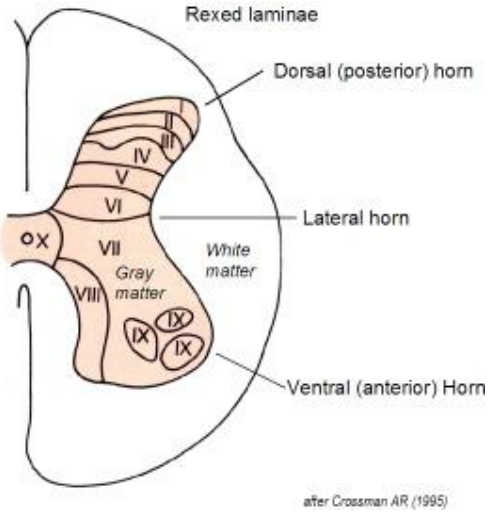
Spinal cord and motor pathways

Spinal cord is a bundle of nerve tissue that extends from the medulla oblongata in the brain stem to the lumbar region of the vertebral column.

The spinal cord has gray matter (cell bodies) and white matter (axons):
- white matter: dorsal (posterior) column, lateral column and anterior column
- gray matter:
a) dorsal horn: neurons in dorsal horn are mostly sensory or interneurons
b) ventral horn: neurons in the ventral horn are motor (Lower motor neurons, alpha and gamma)
c) Lateral horn (intermediolateral horn): only at the level of (T1-L2), sympathetic.



Over the past 50 years, the gray matter was classified into nuclei; group of cells with the same function, e.g. posterior marginal nucleus, substantiagelatinosa, nucleus proprius.



A scientist called Rexed, said: the neurons in the gray matter are arranged in columns rather than groups (nuclei), and every column has a group of cells with the same function along the spinal cord.
Cross section in the spinal cord shows the column in the form of layers (lamina), and he described 10 layers.
Lamina 1, 2, 3, 4, 5, 6 > present in the dorsal horn
Lamina 7 > in the middle between ventral and dorsal horns
lamina 8 > in the ventral horn
lamina 9 > the most important one > all neurons in lamina 9 are motor neurons
Lamina 10 > around central canal
Scientist Rexed , replaced the old terms and now we are using lamina instead of nuclei.
Note: the doctor read the table in page 7 in the hand out. Some clinical books still use the old terms.

Laminae I to IV are concerned with exteroceptive sensations, whereas laminae V and VI are concerned primarily with proprioceptive sensations, although they respond to cutaneous stimuli. Lamina VII acts as a relay between midbrain and cerebellum. Lamina VIII modulates motor activity, most probably via the gamma neuron. Lamina IX is the main motor area of the spinal cord. It contains large alpha and smaller gamma motor neurons. The axons of these neurons supply the extrafusal and intrafusal muscle fibers respectively.

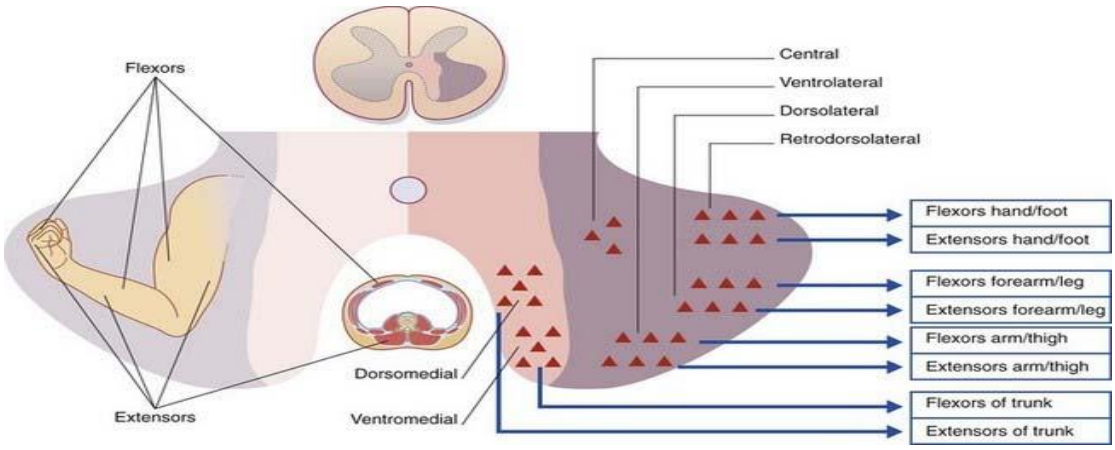
Table 5.1. Cellular Organization of Spinal Cord

Rexed terminology	Older terminology
Lamina I	Posteromarginal nucleus
II	Substantia gelatinosa
III, IV	Nucleus proprius
V	Neck of posterior horn
VI	Base of posterior horn
VII	Intermediate zone, intermediolateral horn
VIII	Commissural nucleus
IX	Ventral horn
X	Grisea centralis

When we talk about the motor system, lamina 9 concerns us, it contains motor neurons (LMN) .lamina 9 is arranged into subgroups; medial and lateral groups:
a) **Ventromedial**: supplies the extensors of the trunk (muscles of the back), this group is present all through cervical region, thoracic region, lumbar and sacral.

b**) Dorsomedial**: present only at the level of (T1 –L2), supply the intercostal muscles as well as the abdominal muscles.

c) **Ventrolateral**:
1) c5-c8 > to upper limb, supplies muscles of the arm.
2) L2-S2 > to lower limb, supplies muscles of the thigh.
d) **Dorsolateral**:
1) c6-c8 > supplies the muscles of the forearm.
2) L3-S3 > supplies the muscles of leg.
F) **Retrodorsolateral**: present in (C8-T1) mainly T1, supplies the intrinsic muscles of the hand used for writing, e.g. "lumbricals, interosseui ,…"

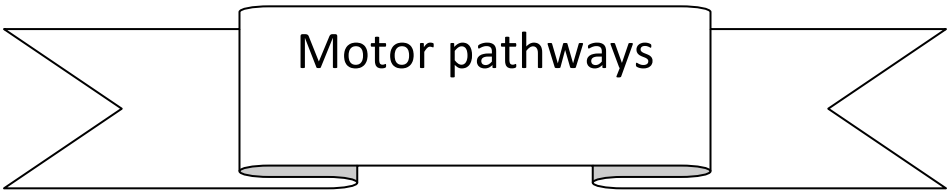


Lamina 9 in the ventral horn contains motor neurons (lower motor neurons) also a physiologist called ***Sherrington*** named the lower motor neurons as **"Final common path"** as these neurons receive impulses or orders from upper motor neurons in the cerebral cortex in the brain, when the order reach them, they send impulses to the muscle either to contract or to relax.

لذلك سميو بالطريق النهائي و المقصود الطريق النهائي لتنبيه العضلة

So LMNs = alpha and gamma neurons = final common pathway. The cell bodies of LMNs present in the ventral horn of the spinal cord and their axons form the ventral root of spinal nerve " Recall from last lec. the structure of the typical spinal nerve " .If the cell bodies destroyed the axon (nerve) dies > the muscle that is supplied by that nerve Atrophies , this is called **Lower motor neuron lesion**".

In **poliomyelitis**, the polio virus attacks the cell bodies of the nerves so the nerve dies and the muscle paralyses and after few weeks the muscle atrophies.



A tract or a pathway is a bundle of nerve fibers that have the same origin, same termination and carry same function.
Any motor pathway extend from the upper motor neurons to lower motor neurons
مكان صدور الاوامر > upper motor neurons
منفذ الامر > lower motor neurons

We have two motor pathways : pyramidal tract and extra pyramidal tract. Both originate from area 4, area 6 and area 3,1,2 .

Pyramidal pathways:
pyramidal pathway originate from both area 4 and area6 but mainly 4

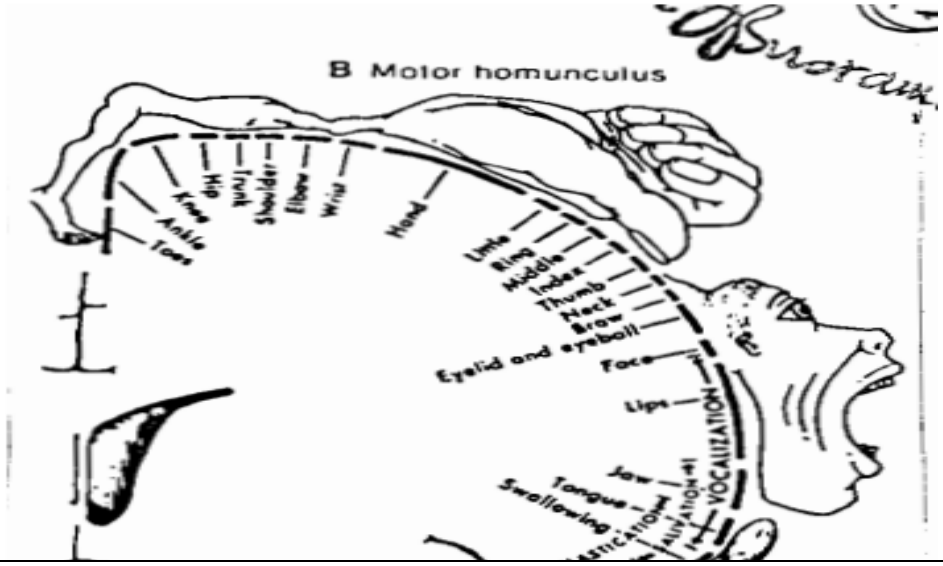
pyramidal pathways has two tracts: corticospinal and corticobubler.

Cortecospinal tract:
fibers of this tract descends from the cerebral cortex > pass through the corona radiata > then through the internal capsule > then they go down through the brainstem , passing through midbrain , Pons , medulla> terminates in the lower motor neurons of the spinal cord either directly by direct synapse on alpha and gamma neurons , or through an interneuron and mainly through interneurons.

Not mentioned by the doctor: In the lower part of the medulla 80-90% of descending fibers CROSS to the other side which means the fibers that come from the right goes to the left and vice versa which is called motor decussation or pyramidal decussation.

Corticobulber tract:
bulb means brainstem.
This tract does not reach the spinal cord it stays in the brainstem, the brain stem has lower motor neurons (alpha and gamma) of the **cranial** nerves that controls the facial muscles e.g. facial muscles → facial nerve
muscles of mastication→mandibular branch of trigeminal .

As the pyramidal tract originates mainly from area 4, let us discuss area 4:
Anatomical name: precentral gyrus, present in the frontal lobe,
Controls muscles of face and limbs (extremities)
the part in the area 4 that is responsible for hand movement is larger than other parts, i.e. number of cells that represent hand muscles are much more than the number of cells which represent the deltoid muscles for example, because when the muscles are responsible for skill movements we need more cells to control it.



شرح للكلام الي فوق :
المنطقة الرابعة في الدماغ حسب تصنيف **Brodmann** مسؤولة عن عضلات الوجه و عضلات الاطراف لكن مش موزعين عالمنطقة بالتساوي فمثلا الجزء المسؤول عن عضلات اليد اكبر من الجزء المسؤول عن عضلات الذراع و بكلمة اكبر نعني ان الخلايا المسؤولة عن حركة عضلات اليد اكثر عددا و تفسير ذلك يكون بان اليد مسؤولة عن حركات مهارتية و معقده اكثر من غيرها لذلك تحتاج خلايا اكثر لضمان حركة سلسة و صحيحة .

Extrapyramidal tract:

a group of descending tracts that arise in the brainstem under the influence of cerebral cortex , mainly area 6 .

1) **Reticulospinal tract:** originate from the reticular formation in the pons and medulla and ends in the spinal cord

2) **Rubrospinal tract:** Rubro means Red

so rubrospinal originate from the red nucleus in the midbrain and ends in the spinal cord.

Both Reticulospinal tract and Rubrospinal tracts receive

Orders from the cortex so to be more accurate we call these pathways

"corticoreticulospinal and corticorubrospinal"

3) Vestibulospinal tract: from the vestibular nuclei in the brainstem to the spinal cord

4) Tectospinal tract: from the superior calliculus of the midbrain to the spinal cord.

As the extra pyramidal tract mainly from area 6 , let us discuss area 6 :

area 6 divided into premotor area and supplementary . Fibers originate from this area go along with pyramidal and extrapyramidal and are responsible for axial and proximal (shoulder and hip) muscles.

Most of the nerve fibers in corticospinal tract DON'T synapse directly on alpha and gamma; they go to the interneuron and this interneuron link them to alpha and gamma.

*Why did they go to the interneuron??

Suppose I want to flex the elbow, this process needs stimulation of the biceps and inhibition of the triceps. I can't do flexion of the elbow if I stimulate both muscles. If you stimulate the biceps → flexion

But if the triceps interfere → extension, the result is an inaccurate flexion movement .

I need to stimulate the agonist and at the same time inhibit the antagonist, HOW?? By the interneurons

there's an excitatory interneuron, if I stimulate it, it will stimulate the alpha of the biceps. And also we have inhibitory interneuron, if I stimulate it, it will inhibit the antagonist.

So it’s one tract which is the corticospinal tract, at the same time it stimulates a muscle and inhibits another muscle. How? By the interneurons.
So again most of the corticospinal tract doesn’t synapse directly on alpha and gamma, it will use the interneurons. By these interneurons we can excite one muscle and inhibit its antagonist.

To do any movement I have to stimulate both alpha and gamma (the lower motor neurons) because from alpha and gamma arise the nerve that supplies the muscle.

Alpha and gamma both are stimulated through descending motor pathways, they also get stimulated through signals from the dorsal root from the muscle (reflexes).
A reflex happens when receptors on a muscle get stimulated they send signals through the dorsal root to the spinal cord in order to activate alpha and gamma neurons to respond to the first stimulus.

Signals that come from the muscles cause partial contraction in the muscle; this partial contraction is called tone "muscle tone".
The importance of muscle tone :

1) muscle tone in the lower limb help in returning blood to the heart " recall from the cardiovascular system"
2) building a better contraction or movement on a basal tone , where we can't build a movement on a zero tone.
3) Muscle tone plays an important role in posture (sitting, standing) and in fixing joints.

Alpha and gamma present in the spinal cord and arise from them spinal nerves.
Alpha and gamma present in the brain stem and arise from them cranial nerves.

Notes :
Notochord is at the middle of the embryonic disc.
Rostral neuropore also called anterior or superior
Caudal neuropore also called posterior or inferior