

Epilepsy

Definitions

EPILEPSY- group of neurological disorders characterized by unprovoked epileptic seizures

- Chronic
- Many severities
- Psychosocial consequences

SEIZURE- clinical manifestation of disordered and hypersynchronized discharge in a network of cerebral neurons

Types

GENERALIZED- starts simultaneously in both hemispheres

| |
|----------------|
| Tonic = _____ |
| Clonic = _____ |

1. Typical absence- sudden loss and return of consciousness

| | |
|-------------|------------|
| | |
| < 10 sec | 20 sec |
| no movement | automatism |

2. Myoclonic- sudden brief jerks of a group of muscles

EX: bilateral arm jerks

3. Tonic-Clonic

1. Sudden onset
2. _____ phase – muscle groups stiffen
3. _____ phase – arms and legs jerk at the joints
4. Body relaxes
5. _____ phase- confused and drowsy

| |
|---|
| STATUS EPILEPTICUS- > ___ min or >___ seizures without recovery |
|---|

4. Atypical absence- similar to absence, but the patient is slightly responsive
5. Tonic- sudden increase in muscle tone
6. Atonic- sudden loss of muscle tone

FOCAL- starts in one part of the brain

1. Simple partial- remain in one area

- Motor:
- Sensory
- Autonomic
- Psychic

2. Complex partial- seizure spreads

- loose awareness

3. Secondary generalized- evolves to a tonic-clonic seizure

CAUSES

1. Idiopathic
 - No associated neurological damage
 - Suspected genetic component: specific syndromes polygenic
2. Symptomatic
 - associated with neurological deficit
 - Cortical malformation
 - Cerebral palsy
 - Metabolic conditions
 - Developmental disorder- autism
 - Trauma
 - Stroke
 - Tumors
 - Infection

NEUROPHYSIOLOGY

Disruption to the mechanism that creates a balance between excitation and inhibition

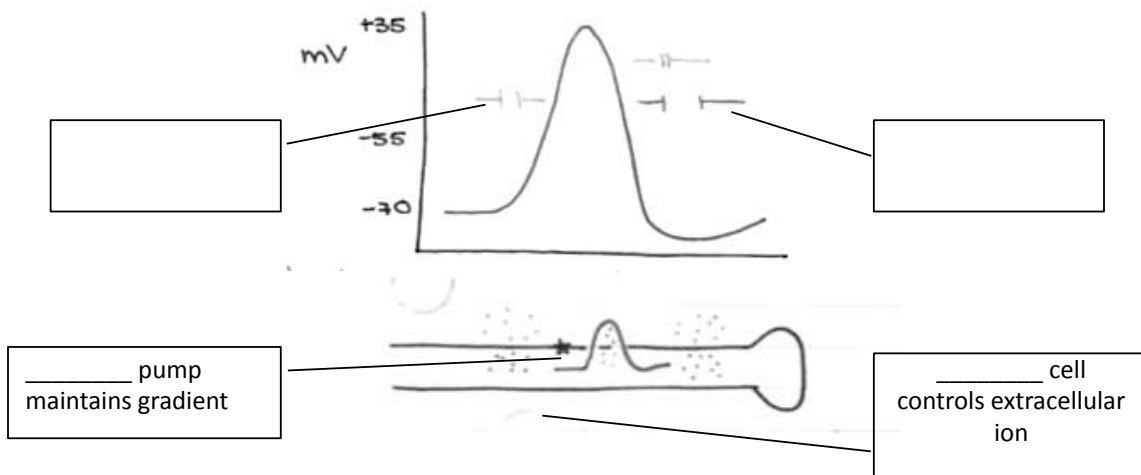
EPILEPTOGENESIS- molecular changes that make a group of neurons liable to a seizure

-
-
-

ICTOGENESIS- generation of a seizure

NEUROPHYSIOLOGY OF A SEIZURE- what happens to the neurons during a seizure

1. Initiation- _____ neuron fires
 - Result in _____ spikes
 - 2 types of dysfunction
 - _____ dysfunction = voltage gated ion channels and action potential



1. _____ channels open
2. _____ channels close
3. _____ channels open
4. _____ pump returns the ions to the original gradient
5. _____ cells mop up any excess ions

- _____ dysfunction = synaptic transmission



- Glutamate--- excitatory
 - Na = depolarize
- GABA--- inhibitory
 - Cl = hyperpolarize

NO DIRECT RELATIONSHIP BETWEEN GLUTAMATE AND SEIZURES

2. Synchronization- _____ _____ neurons fire

- Connected in 5 ways
 - Synapses
 - Glutaminergic synapses
 - Gap junctions
 - GABAminergic neurons- connect to many cells
 - Microdomain theory- electrical field around the neurons

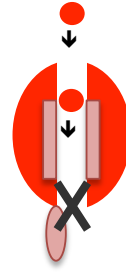
3. Termination

- Immediate
 - Inhibitory neurons
 - Refractory period of the voltage-gated ____ channels
 - Desensitization of glutamate receptors
- Delayed
 - _____ depletion
 - Acidification- build up of _____
 - _____ increase
 - Hyperpolarization from _____ channels

PHARMACHOLOGICAL TREATMENTS

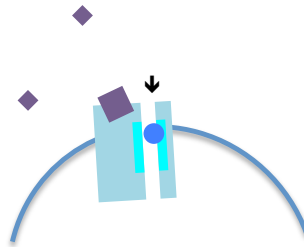
1. Na channel inactivation

- Blocks channels when:
 - Prolonged depolarizations
 - Repeatedly fires
- Does not bind to the resting channel
 - Minimizes side effects

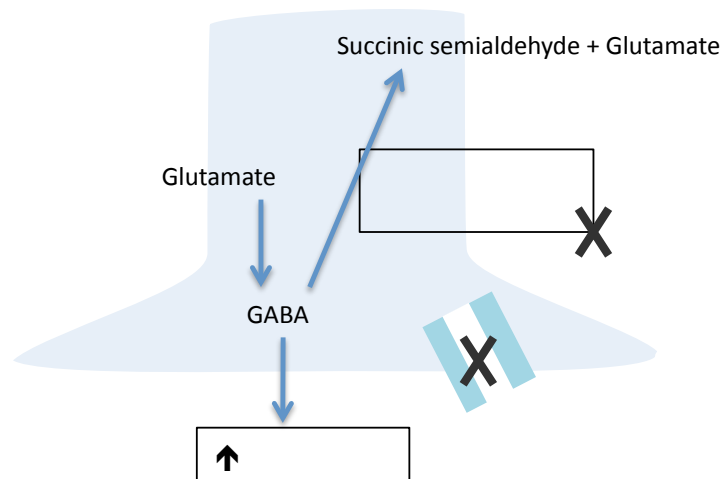


2. Increasing Cl at GABA receptors

- Hyperpolarize the cell
- Terminates the seizure



3. GABA increased in synaptic cleft



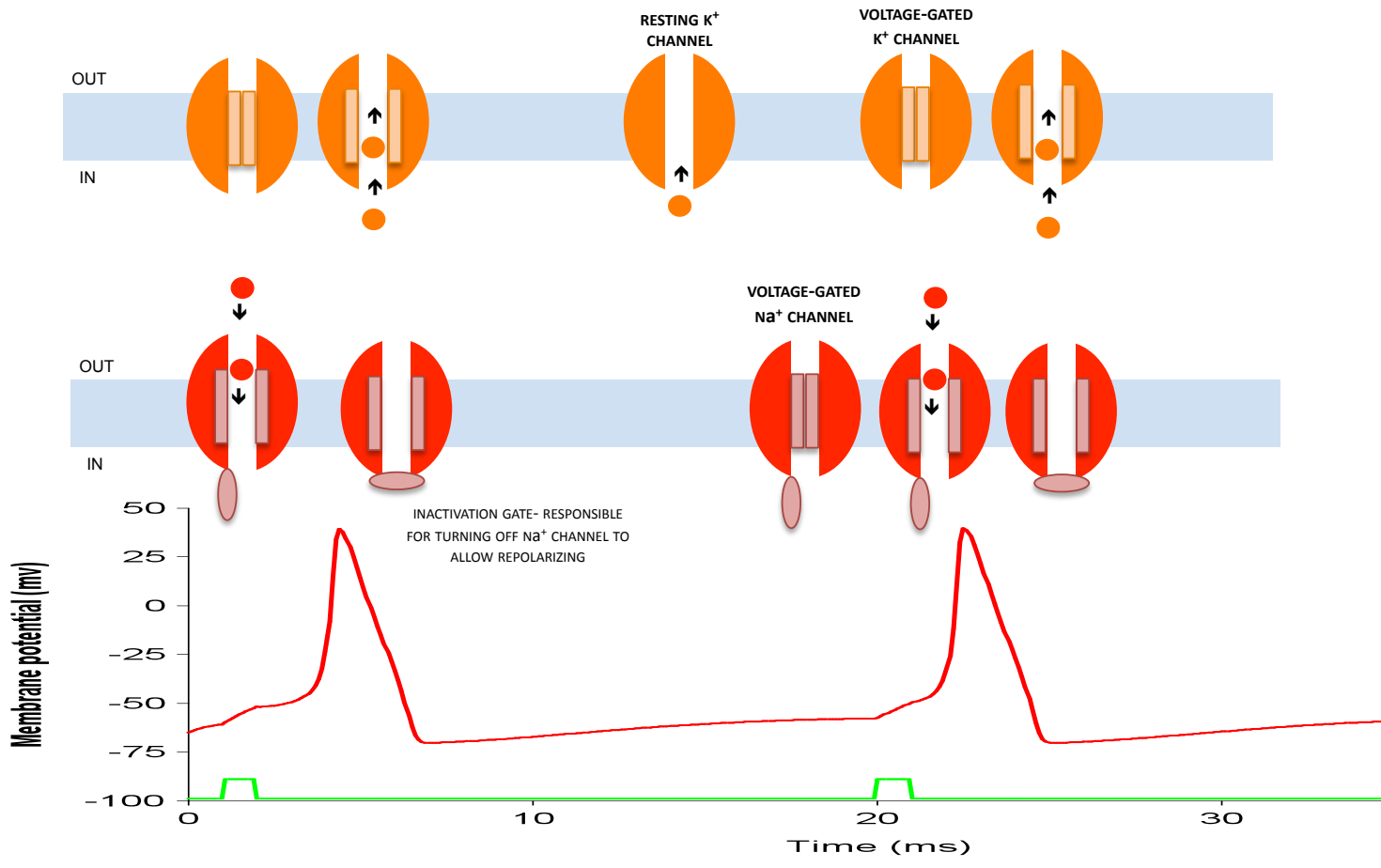
PSYCHOSOCIAL

- Medication side effects
- Driving
- Employment
- Anxiety
- Stigma
- Pregnancy
- Injuries
- Mortality
- Support groups
- Epilepsy Society
- Nurses



IT ISN'T JUST SEIZURES

| DRUG | SEIZURE TYPE | CONTRAINDICATED | MECHANISM (TARGET CHANNELS & RECEPTORS) | SIDE EFFECTS | INTERACTIONS |
|----------------|--|----------------------|---|---|---|
| Lamotrigine | Focal (1°) Generalized (1°) - T-C -myoclonus? -absence | --- | Na ⁺ channels (fast inactive.) -suppress burst activity -prevents spread | Few | Serum levels drop w/ COCP |
| Valproate | Generalized (1°) -myoclonus -absence -photosen. - T-C | | UNCERTAIN GABA? Inh. excit. trans.? CA ²⁺ ? K ⁺ ? | Teratogenic | |
| Carbamazepine | Focal(1°) Generalized (1°) -T-C | Myoclonus Absence | Na ⁺ channels (fast inactiv.) -suppress burst activity -prevents spread | Few | Many- b/c enzyme induction |
| Phenytoin | Generalized (2°) -T-C Focal (2°) | Myoclonus Absence | Na ⁺ channels (fast inactiv.) -suppress burst activity -prevents spread | Liver toxicity Psych Bones folic acid Teratogenic | •Many- b/c enzyme induction & inhibition •Variable absorption & metabol. (age related) • protein bound • non linear kinetics |
| Levetiracetam | Broad -Focal -myoclonus | ---- | UNCERTAIN Synaptic vesicle 2a? same as brivaracetam | Mood 10-20% | ---- |
| Topiramate | Broad -Focal -T-C | --- | Multiple [Cl ⁻ at GABA receptors | Sedation Psych. Wt. loss | |
| Clonazepam | Add on esp- myoclonus - absence | | | Tolerance Sedative | |
| Gabapentin | Weak add on- partial needs high dose | | UNCERTAIN GABA? CA ²⁺ ? NMDA? same as pregabalin | | |
| Ethosuximide | Absence | Non- absence | | GI Headache Psych. | |
| Benzodiazepine | Absence Myoclonus | | [Cl ⁻ at GABA receptors | | |
| Lacosamide | | | Na ⁺ channels (slow inactive.) -suppress burst activity -prevents spread | | |
| Retigabine | | | augment K ⁺ channel | Retina | |
| Perampanel | | | non-competitive AMPA antag. | | |
| Vigabatrin | | | GABA transaminase inhib. | Retina | |
| Tiagabine | | | GABA reuptake inhibit. | [Seizure length | |
| Phenobarbatol | | | [Cl ⁻ at GABA receptors | | |



BRAINSTEM: ANATOMY AND FUNCTION

RULE of 3s

3 main functions:

1. : connects SPINAL CORD, CEREBRUM and CEREBELLUM.
2. : III-XII supply the face, head, and viscera.
ALL EXCEPT SENSATION FROM NOSE (CNI) and EYE (CNII)
3. :
 - respiratory control-RR
 - cardiovascular system control-HR and BP
 - vomiting
 - pain sensitivity control
 - consciousness
 - sleep cycle
 - awarenessBRAINSTEM DEATH- NO CONSCIOUSNESS and NO BREATHING

3 parts:

- 1.
- 2.
- 3.

Location:

Posterior cranial fossa

Relations:

BELOW THALAMUS

ABOVE SPINAL CORD

ANTERIOR TO CEREBELLUM

TRAPASSED by the Ventricular SYSTEM

Blood supply:

Vertebral aa. Fusing to form **Basilar aa.(run anteriorly)**

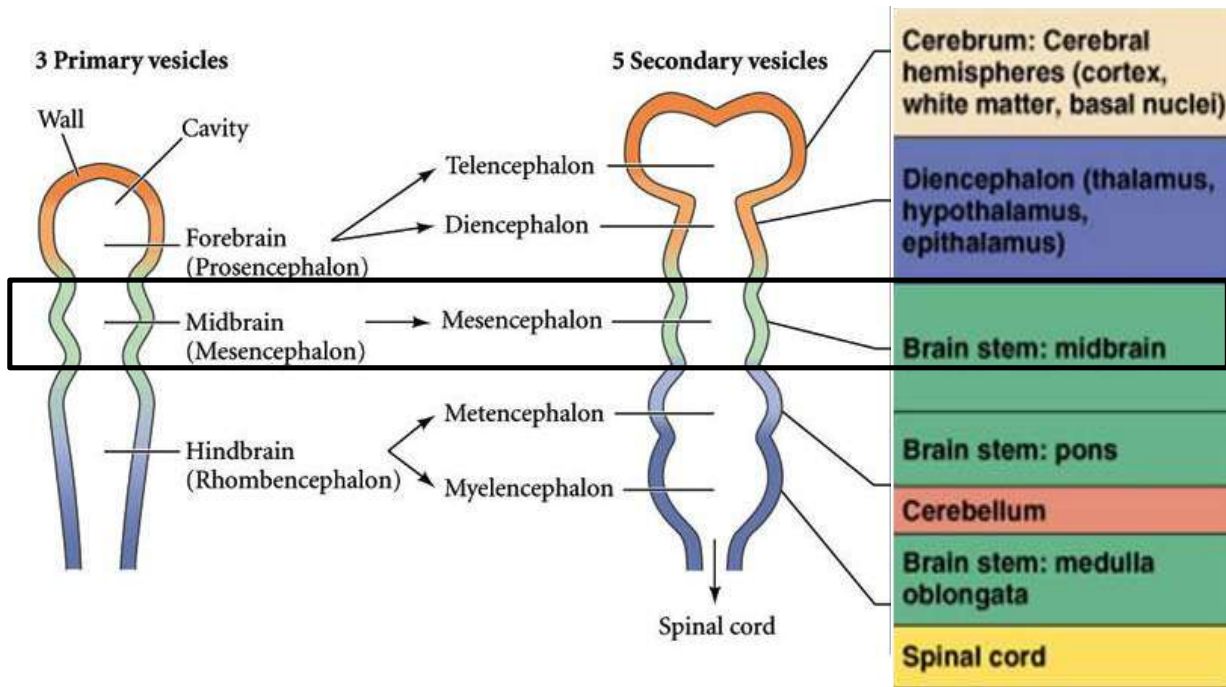
EMBRIOLOGY:

1st PRIMARY VESICLE: FOREBRAIN (TELENCEPHALON, DIENCEPHALON)

2nd PRIMARY VESICLE (MESENCEPHALON)- MIDBRAIN

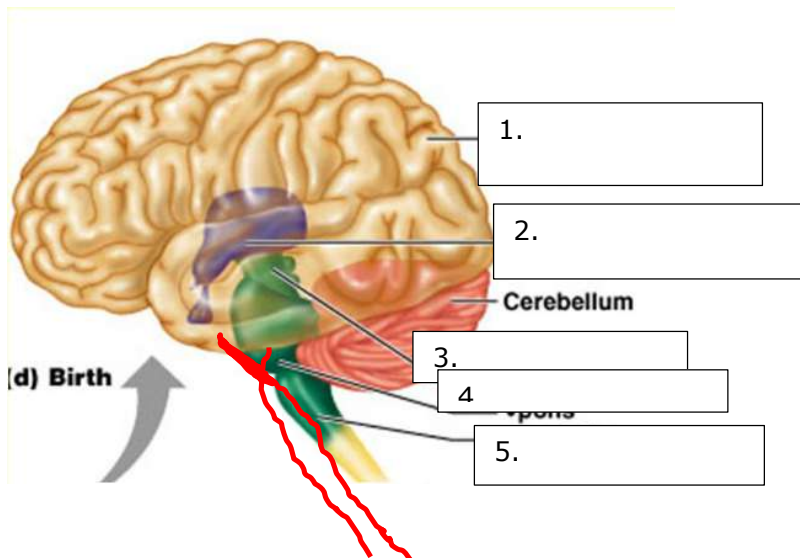
3rd PRIMARY VESICLE : HINDBRAIN

- METENCEPHALON (PONS and cerebellum)
- MYELENCEPHALON (MEDULLA OBLONGATA)

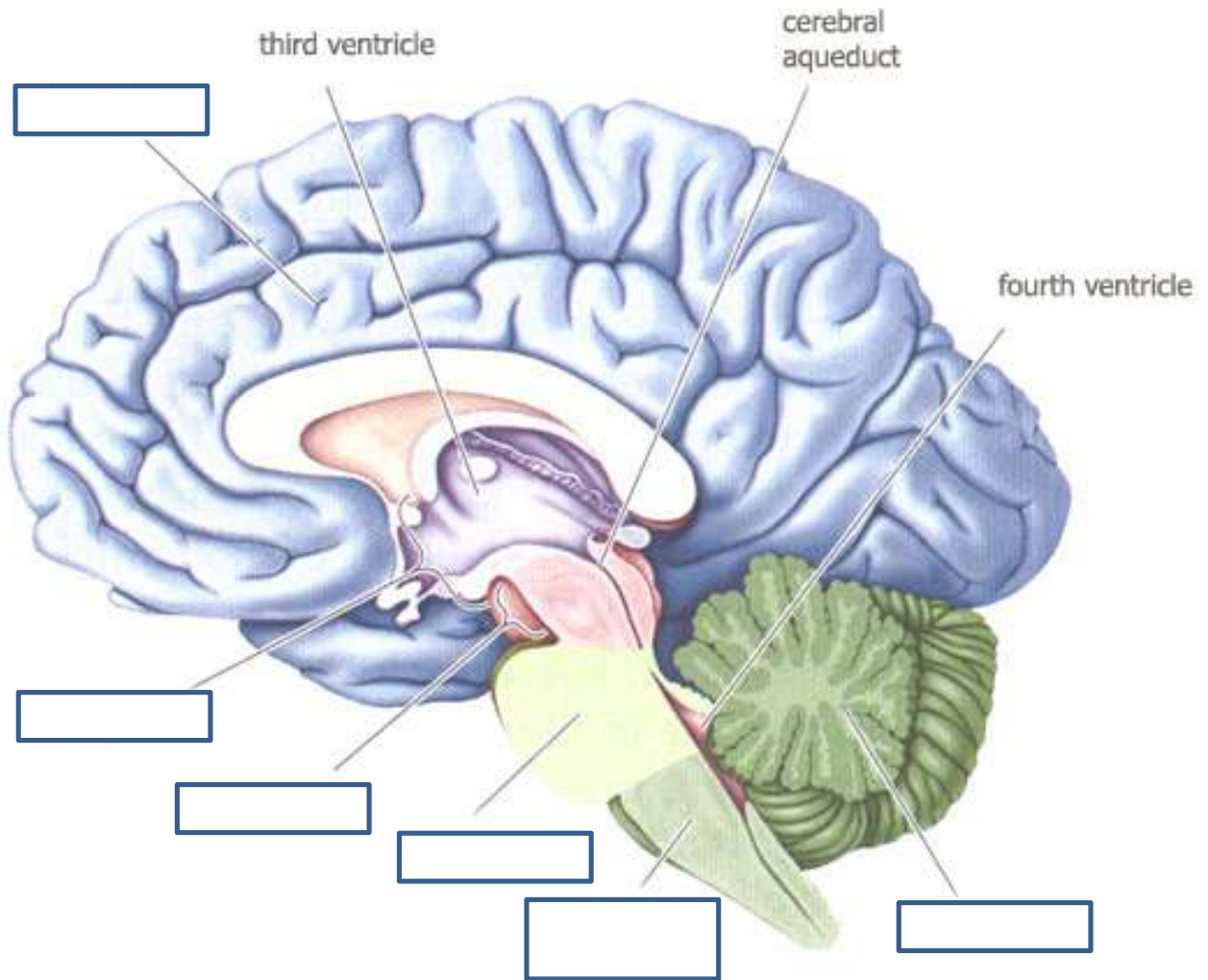


NB: development is above and below the

QUIZ:



VENTRICULAR SYSTEM AND BRAIN STRUCTURES

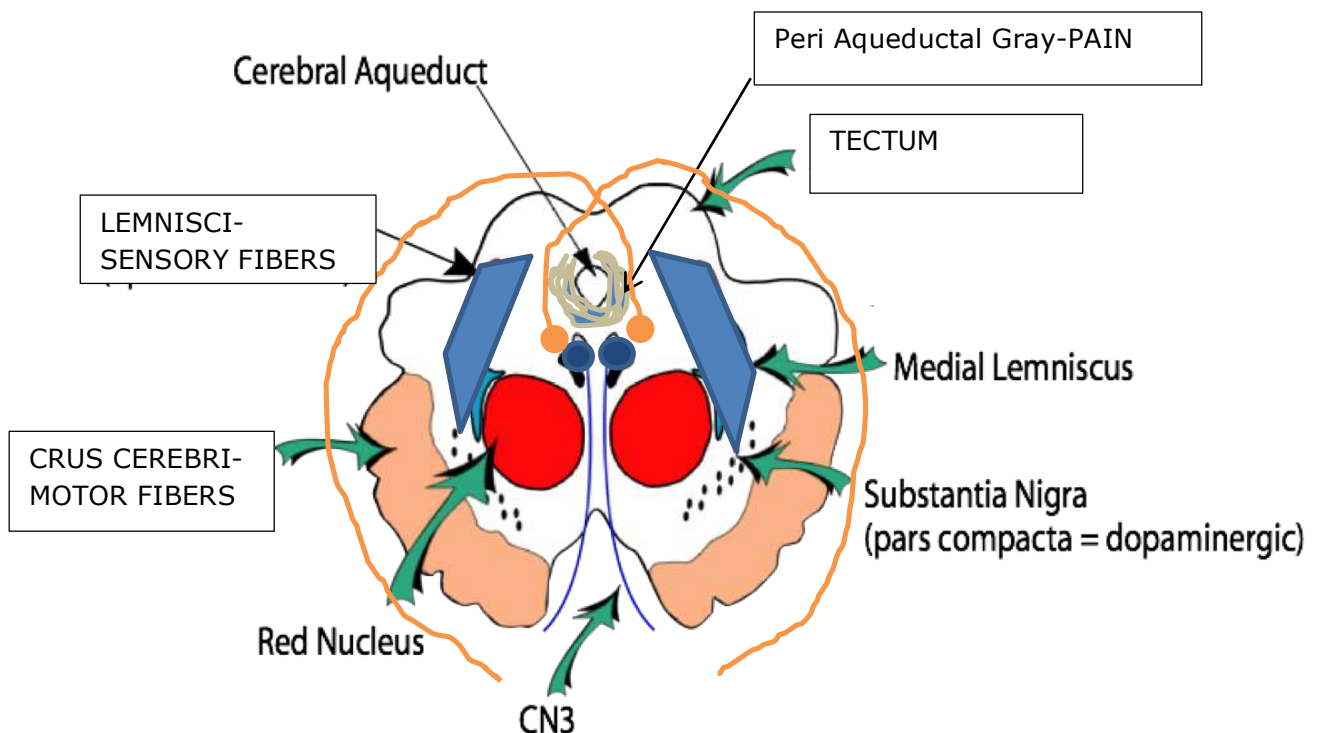


MID-BRAIN

MAIN FUNCTIONS:

1. Communicates to cerebral hemispheres
2. Basal ganglia (Substantia Nigra)
3. EYE MOVEMENTS (CN III, IV)
4. Involved in VISUAL and AUDITORY reflexes (SUP and INF COLLICULI)

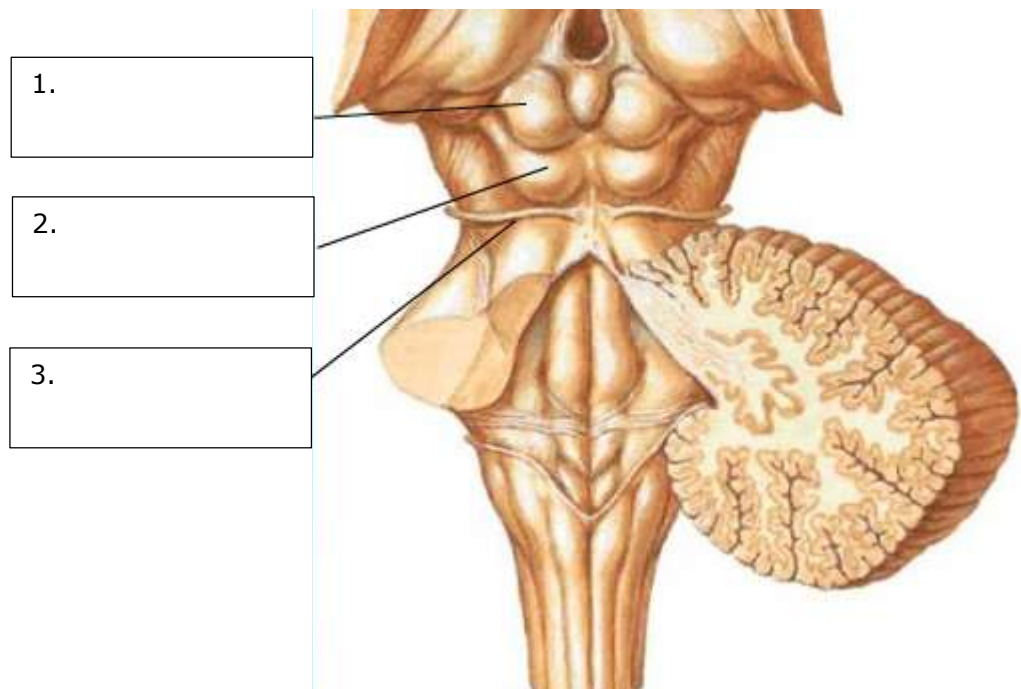
CROSS-SECTION of the MIDBRAIN:



3 areas:

1. **CEREBRAL PEDUNCLES (ANTERIORLY)-MOTOR**
 - **CRUS CEREBRI: MOTOR FIBERS** e.g. **CORTICOSPINAL** and **CORTICOBULBAR**
 - **SUBSTANTIA NIGRA**
2. **TEGMENTUM (MIDDLE)-**
 - **PAG-pain**
 - **LEMNISCI: ALL SENSORY INFO (DCML and SPINOTHALAMIC PATHWAY)**
 - **CN III and IV nuclei**
 - **RED NUCLEUS- RUBROSPINAL TRACT (MOTOR of little importance)**
 - **part of Reticular Activating System (RAS)-CONSCIOUSNESS, AWARENESS-more later**

POSTERIOR VIEW of the MIDBRAIN:



3. TECTUM “roof” (POSTERIORLY)

From superior to inferior:

- **2X SUPERIOR COLLICULI**
- **2X INFERIOR COLLICULI**
- **SUPERIOR CEREBELLAR PEDUNCLE-mainly cerebellar efferent**

The colliculi are INTEGRATION CENTRES

SUPERIOR COLLICULI:

VERTICAL EYE MOVEMENTS

with movement of the head to determine effective

INPUT: RETINA

OUTPUT: LATERAL GENICULATE nucleus of the Thalamus

INFERIOR COLLICULI:

Output: MEDIAL GENICULATE NUCLEUS of Thalamus, then AUDITORY CORTEX

MNEMONICS: EYE ARE ABOVE EARS

PONS: “bridge” between MIDBRAIN and MEDULLA OBLONGATA and CEREBELLUM

SAME LEVEL OF CEREBELLUM (both from METENCEPHALON)

2 parts:

BASILAR-ventral- Called like this because the A. RUNS on it

TEGMENTUM-posterior

NUCLEI IN PONS:

- **RESPIRATORY CENTRES (together with medulla)**
- **Movement and posture-MAIN OUTPUT TO THE CEREBELLUM (MIDDLE CEREBELLAR PEDUNCLE)**
- Sleep
- Swallowing
- bladder control
- RAS

CN V to VIII are in the PONS

NB: ONCE AGAIN MOTOR FIBERS TRAVEL more anteriorly than SENSORY fibers (like in the MIDBRAIN)

CNV is the biggest! (small root is motor component)

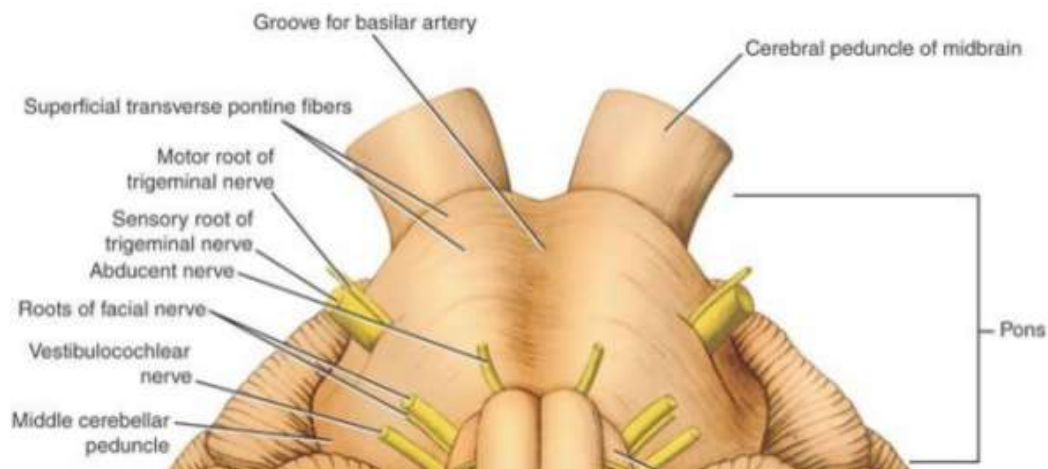
- Trigeminal sensory and motor nuclei CN (V)-FACE SENSATION and MASTICATION

CN VI to VIII lie just above the MEDULLA

- MEDIAL- **abducens nucleus (VI)**-EYE ABDUCTION
- MIDDLE- **facial nerve nucleus (VII)**-ANT 2/3 TONGUE SENSATION and FACIAL EXPRESSIONS etc
- LATERAL- **vestibular nuclei and cochlear nuclei (VIII)**-HEARING AND EQUILIBRIUM

NB: IF YOU NEED TO LABEL THE CNs go in order from SUPERIOR to INFERIOR, from MEDIAL to LATERAL

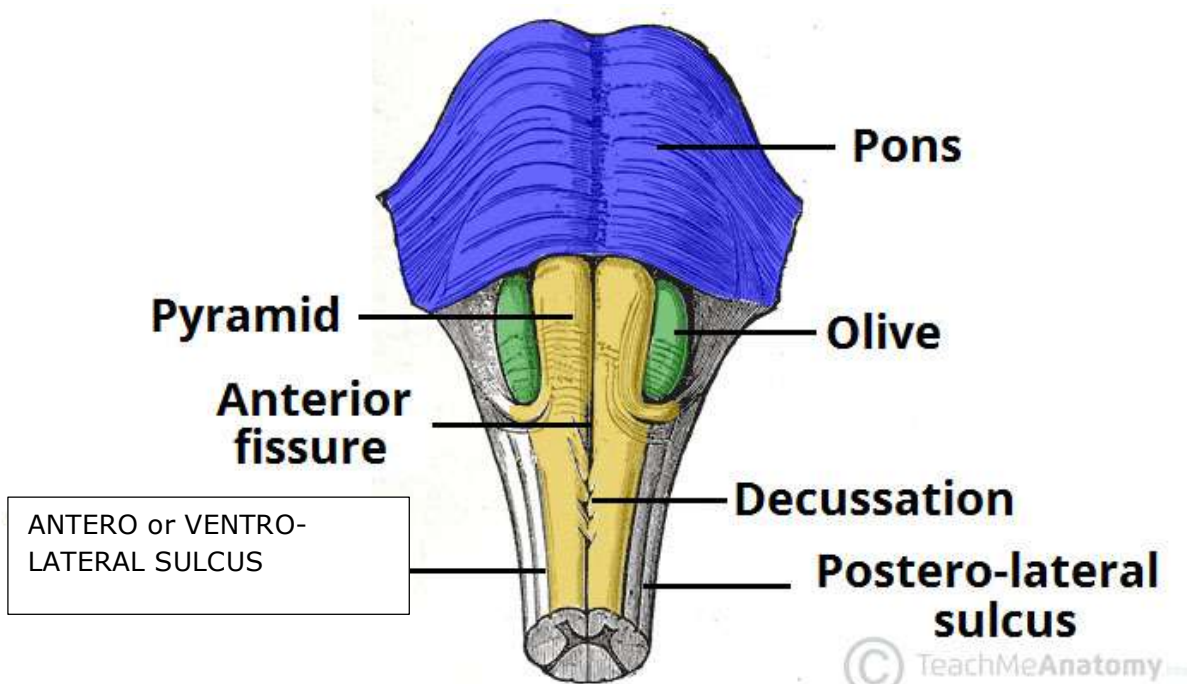
ANTERIOR VIEW of the PONS:



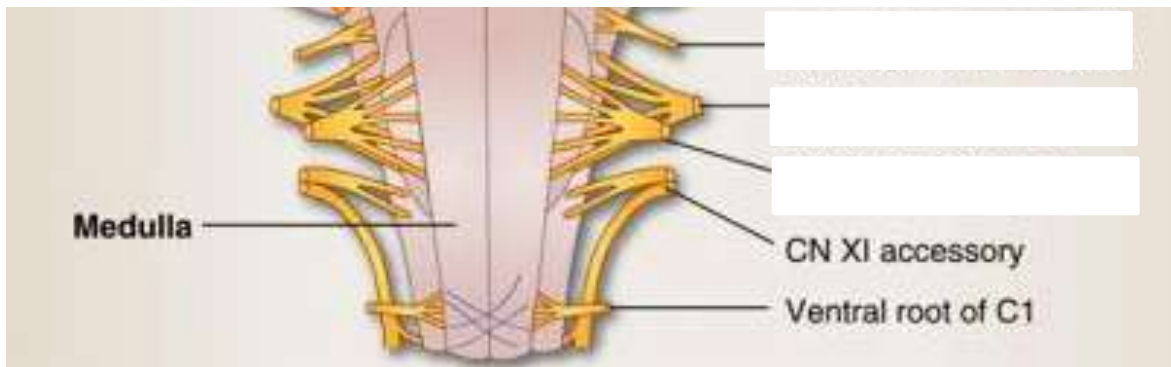
MEDULLA OBLONGATA:

- BOTTOM PART OF THE BRAIN STEM
- CONTAINS DECUSSATION OF THE -decussates at the
- Contains the centre controlling RESPIRATION (together with pons), CVS(HR and BP) and VOMITING etc
- CN IX,X and XII
- INFERIOR CEREBELLAR PEDUNCLE-OLIVARY BODY etc
- RAS

ANTERIOR VIEW of the MEDULLA:

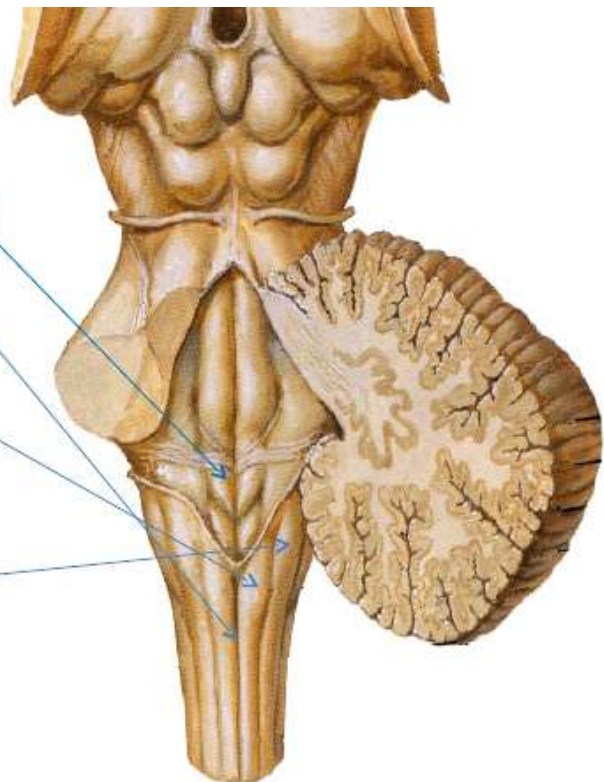


ANTEROLATERAL SULCUS: CNXII (exception to the rule)
 OLIVE: contain OLIVARY NUCLEI (CEREBELLAR AND AUDITORY)
 POSTEROLATERAL SULCUS: CNIX,X and XII
 NB: CN XI comes from below



POSTERIOR VIEW:

- **Superior half** : FLOOR OF THE 4TH VENTRICLE
- **Inferior half** : POSTERIOR MEDIAN SULCUS (PMS)
- **GRACILE TUBERCLE**
(Produced by underlying gracile nucleus)
- **CUNEATE TUBERCLE**
(Produced by underlying cuneate nucleus)

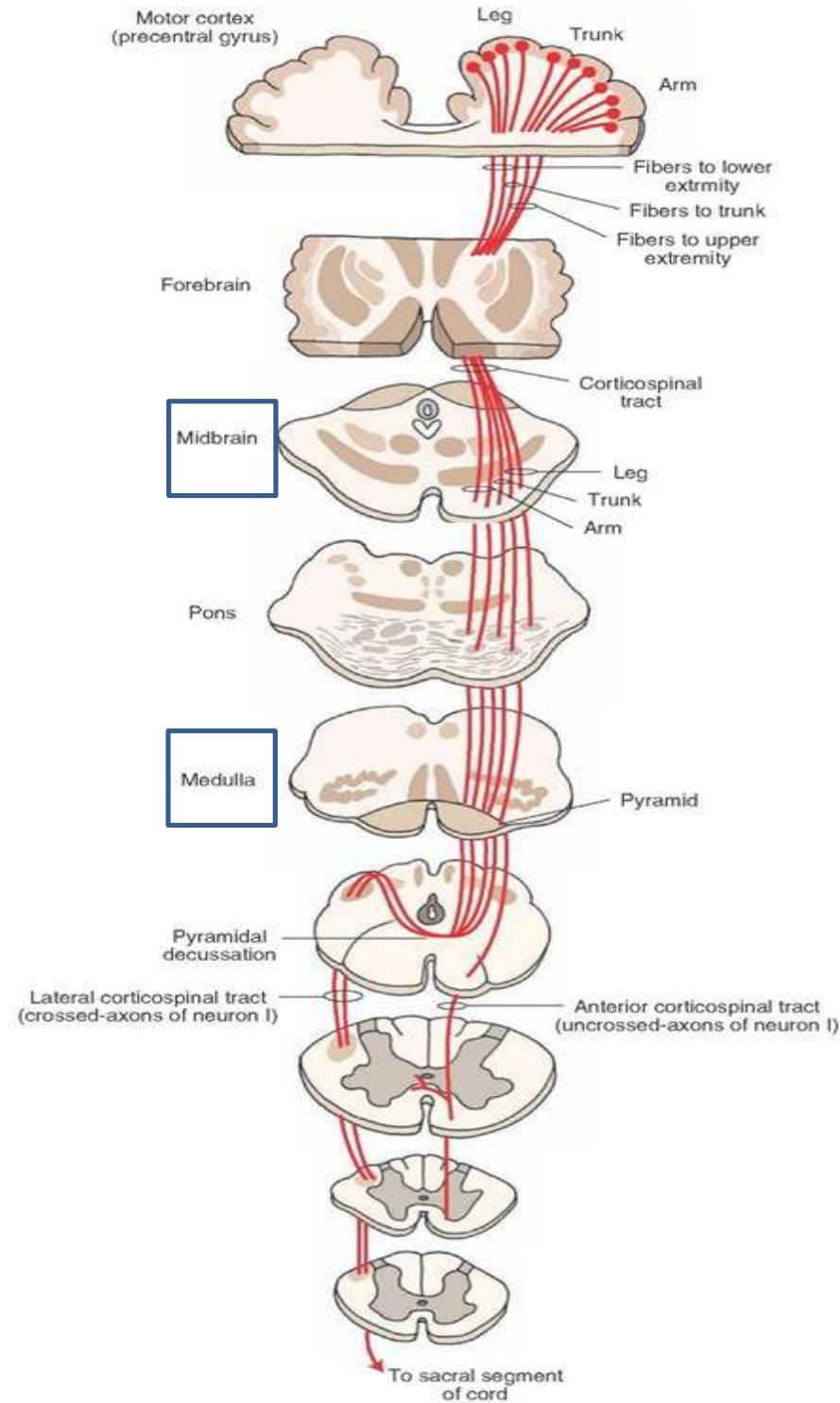


CORTICOSPINAL TRACT

NB: the decussating fibers (90%) move to the OPPOSITE SIDE and POSTERIORLY!-check its final position on the SPINAL CORD

Throughout their travel in the BRAINSTEM MOTOR FIBERS are

to SENSORY



FINAL RECAP:

ORIGIN OF BRAINSTEM:

MIDBRAIN?

PONS? MEDULLA?

Which one is at the level of the cerebellum?

CNs:

MIDBRAIN?

PONS?

MEDULLA?

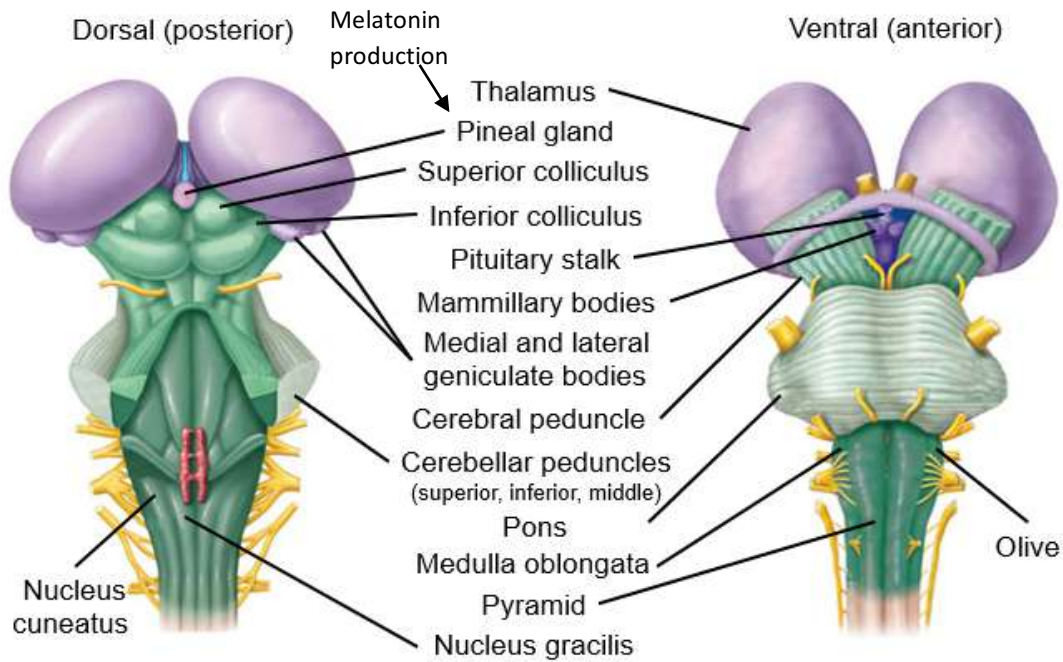
MAIN CONNECTIONS OF MIDBRAIN?

MAIN CONNECTION OF THE PONS?

MAIN CONNECTION OF THE MEDULLA?

Which sensory info pass through the brainstem?

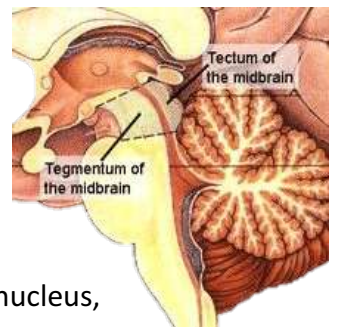
The Brain Stem



The brainstem is made up of:

- **Midbrain**

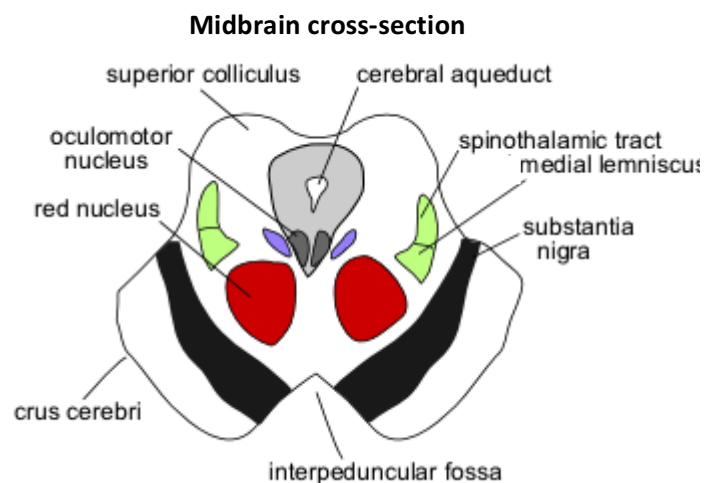
-
- Tegmentum (rostral end of the reticular formation, PAG, Red nucleus, Substantia Nigra, Ventral Tegmental Area)
-



- **Hindbrain (excluding the cerebellum)**

-
-

- **Reticular formation**



Functions:

1.

Takes sensory/motor information between the cerebellum/cerebral hemispheres and the rest of the body

2.

CN III-XII emerge from the brainstem

Contains many cranial nerve nuclei

3.

Contains nuclei which carry out “background” functions

- Cardiovascular system, respiratory system, pain sensitivity control (PAG), alertness/awareness (RAS), consciousness

Brainstem Tracts

- **Pyramidal Tracts**

- **Corticobulbar tract**
Made up of
- **Corticospinal Tract**

- **Extra-pyramidal systems**

Nuclei/tracts other than cranial nerves

Function =

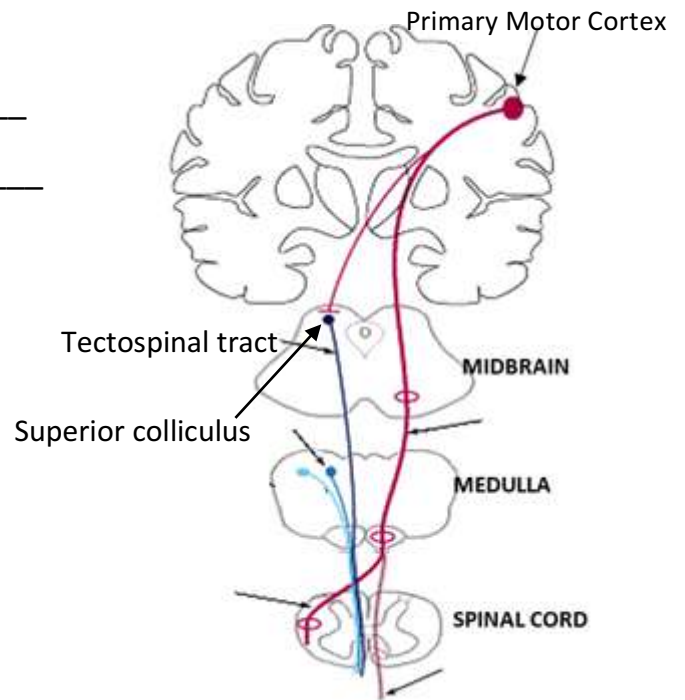
- **Tectospinal**
- **Vestibulospinal**
- **Reticulospinal**
- **Rubrospinal**

Tectospinal Tract

_____ → Decussates → _____

Receives input from the _____

Function = Head orientation to visual stimuli

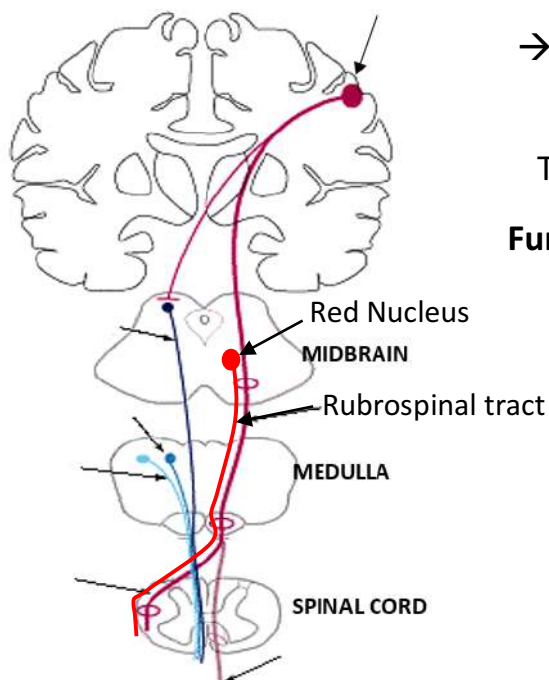


Rubrospinal Tract

_____ → Decussates
 → _____, parallel with the lateral corticospinal tract

Terminates in the _____

Function = Assists in voluntary control of the upper limb, compensates for deficits in the corticospinal tract



Vestibulospinal Tract

- **Medial:**

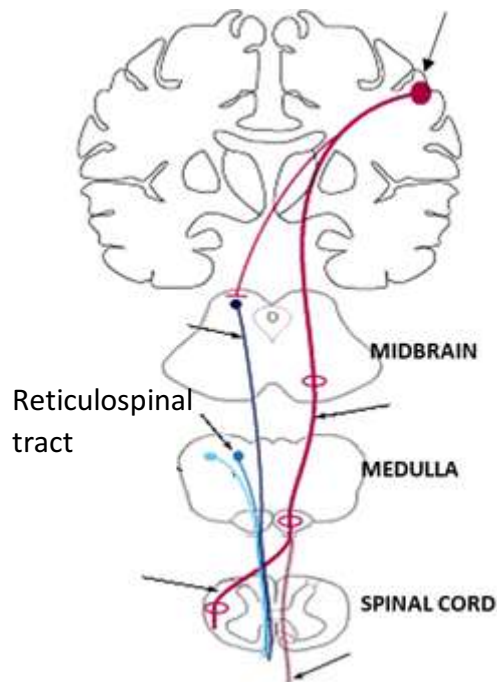
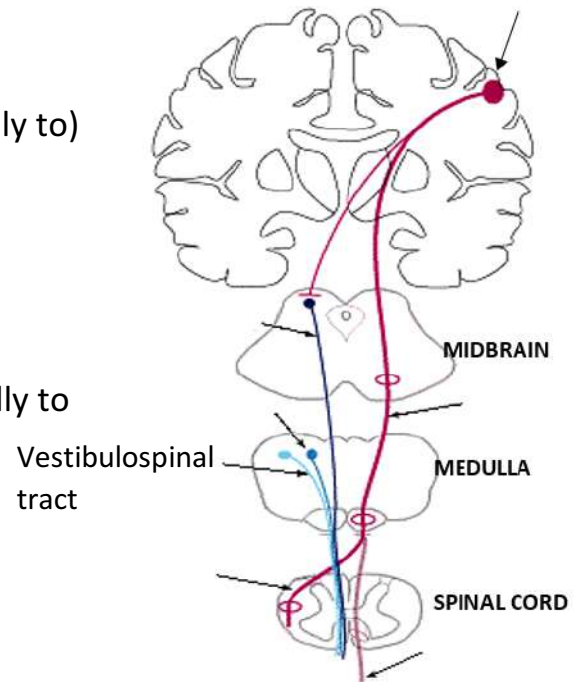
_____ → (bilaterally to)
ventral horns of the cervical spinal cord

Function =

- **Lateral:**

_____ → ipsilaterally to
interneurons in the spinal cord

Function = Extensor muscles in the legs –
upright balance and posture



Reticulospinal Tract

Function = Posture, facilitates and inhibits
voluntary movement

Medial Pontine

_____ → Spinal cord

Function = Extensor leg muscles

Lateral Medullary

_____ → Spinal cord

Function = Inhibits spinal nerves