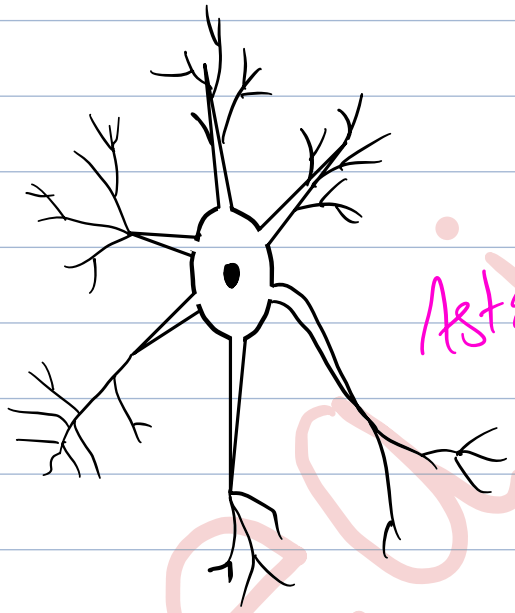
Functions of Glial Cells:

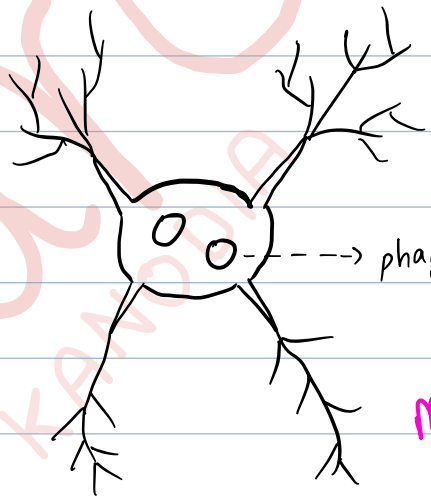
→ form mechanical matrix for neurons
→ metabolic & nutrive role for neurons
→ regulate blood flow through brain
→ source/sink of ions
→ insulate axons & synapses
→ phagocytose neural debris



Astrocyte

Astrocyte:

- form mechanical matrix for neurons
- metabolic & nutrive role for neurons
- electrically insulate synapses



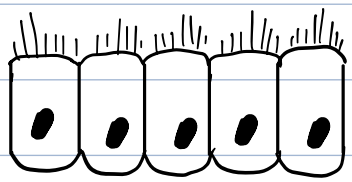
Microglia

Oligodendrocyte:

- myelinate neurons of CNS

Schwann cell:

- myeliate peripheral nerves



Ependymal

Microglia:

- smallest cells
- scavenger cells in brain
- phagocytic

Ependymal cells:

- produces CSF in ventricals of brain & central canal of spinal cord

Mechanism:

Presynaptic mechanism

Arrival of action potential at presynaptic axon terminal

↓

Depolarization of presynaptic membrane

↓

opening of voltage-gated Ca^{2+} channels

↓

Ca^{2+} enters active zone

↓

Docking & priming of vesicles

↓

Increased Ca-mediated exocytosis of Nt vesicles

↓

Nt diffuses passively across synaptic cleft to postsynaptic membrane

→ Nt binds with receptors in post-synaptic membrane

Postsynaptic mechanism

confirmational change

↑

opens ion channel which help in generating second messenger

↑

change in ionic permeability

↑

depolarization / hyperpolarization

↑

(excitatory / inhibitory) synaptic potential

Excitatory Postsynaptic Potential (EPSP)

→ If potential change is towards depolarization

→ EPSP produced at one synaptic knob is small, EPSP at many synaptic knobs summate.

→ During EPSP, excitability of postsynaptic neuron increases to other stimuli.

→ neurotransmitters ⇒ acetylcholine, nor-adrenaline

Ionic Basis: caused by opening of Na^+ or Ca^{++} ion channels (influx) & closure of K^+ ion channels.

(Slow EPSP - due to decreased K^+ conductance).

Inhibitory Postsynaptic Potential (IPSP)

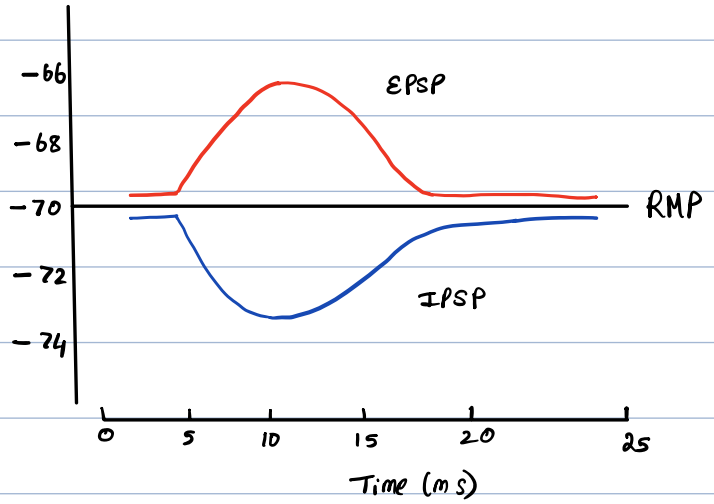
→ If potential change is towards hyperpolarization

→ during IPSP, excitability of postsynaptic neuron decreases to other stimuli

→ local response & can be summated

→ neurotransmitters ⇒ GABA, glycine

Ionic Basis: due to opening of Cl^- channels (influx), opening of K^+ channels (efflux), closure of Na^+, Ca^{++} channels (Slow IPSP - due to increased K^+ conductance)



Properties of Synapses:

Law of Forward Conduction: Impulse travel in one direction only in chemical synapses

Synaptic Delay: time required for the impulse to be transmitted through the synapse (≈ 0.5 ms)

↳ time spent in entry of Ca^{++} into presynaptic knob, release of Nt, action of Nt on postsynaptic membrane.

Law of Convergence & Divergence:

Convergence: many-to-one projection
Divergence: one-to-many projection
} physiological basis for summation & facilitation at synapses.

Postsynaptic Potentials: EPSP or IPSP.

Synaptic Inhibitions: prevents the explosive situation (of widespread activation of many neurons) & prevents unnecessary spread of impulse.

Direct / Presynaptic Inhibition:

→ occurs through formation of IPSP at postsynaptic neuron.

Ex: inhibition of anterior horn cells (AHC) by descending inhibitory fibers in spinal cord

→ involves the release of inhibitory Nts.

Indirect / Postsynaptic Inhibition:

→ passage of impulse is inhibited by another earlier impulse originating from a separate neuron

→ due to decreased release of Nt or due to refractory period of neuron.

Mechanism of Presynaptic Inhibition: 3 mechanisms :-

(i) Activation of presynaptic receptors facilitate Cl^- conductance ∴ decrease Ca^{++} influx ⇒ decreased Nt release

(ii) " " " " opens voltage-gated K^+ channels ⇒ K^+ efflux ⇒ decreased Ca^{++} influx.

(iii) Direct inhibition of Nt release

GABA: 2 receptors → $GABA_A$ ⇒ increasing Cl^- conductance
→ $GABA_B$ ⇒ increase K^+ conductance.

Feedback Inhibition

Ex: Renshaw cell Inhibition

→ negative feedback inhibition in which collateral from spinal motor neuron ends on an inhibitory interneuron called Renshaw cell, which in turn inhibits discharge of the same motor neuron

→ a collateral from Renshaw cell also inhibits neighbouring motor neuron, called lateral inhibition.

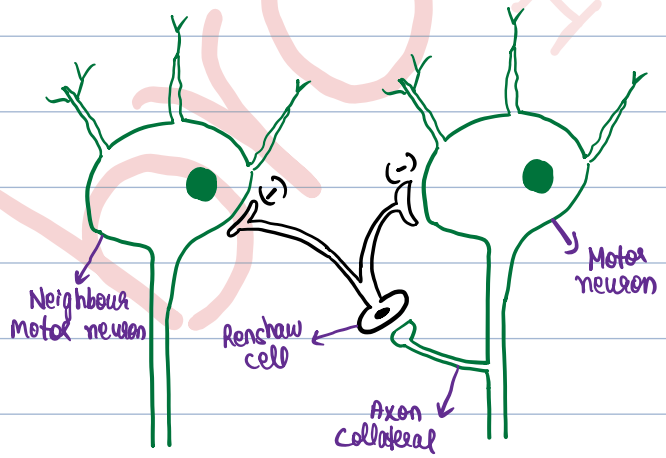
Feed forward Inhibition

Ex: Inhibition of Purkinje cell output by parallel fibers from granule cells in cerebellum.

→ Nt secreted by Purkinje cells is GABA

Mossy fibers stimulate Granule cell which through its parallel fibres activates Purkinje cells.

∴ stimulation of mossy fiber - parallel fiber pathway activates inhibitory output of Purkinje cells



Synaptic Facilitation: process by which transmission through a synapse is increased

→ due to increase in Nt release ⇒ presynaptic facilitation

→ prolongation of action potential ⇒ voltage gated Ca^{++} channel remain open for a longer duration ⇒ greater Ca^{++} influx → increased Nt release

Serotonin = 5-hydroxy tryptamine (5-HT)

↳ causes synaptic facilitation by increasing intraneuronal cAMP levels → induce phosphorylation of one group of K^+ channels that closes K^+ channels (no efflux of K^+)

→ repolarization is slowed ⇒ action potential is prolonged.

Summation: synaptic potentials are graded

Temporal Spatial

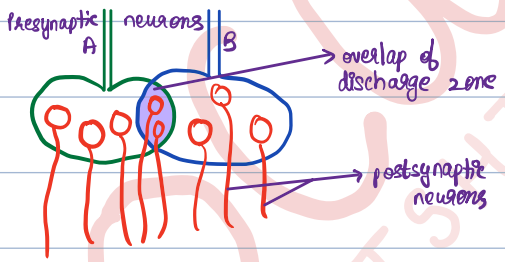
Temporal Summation: same input stimulates the postsynaptic neuron repetitively in such a way that 2nd synaptic potential arrives before postsynaptic cell recovers from first synaptic potential (action potentials arrive in rapid succession.)

Spatial Summation: 2 or more separate inputs arrive simultaneously

↳ if all inputs have the same sign (+/−), posynaptic response evoked is larger.

Occlusion:

A = 5
B = 5
A + B ≠ 10
A + B = 8



- when A fires ⇒ 5 postsynaptic neurons discharge
- " B " ⇒ 5 " " "
- when A & B are fired ⇒ 8 postsynaptic neurons are discharged instead of 10
  ↳ This is called occlusion

Habituation: gradual decrease of Nt release in response to repeated transmission of impulses.

Sensitization: when a transmission is accompanied by a painful or unpleasant sensation

↳ response increases more by presynaptic facilitation (due to increased Ca^{++} influx)

Potentiation: enhanced synaptic transmission for a prolonged duration

Ex: Post-tetanic potentiation ⇒ due to increased Ca^{++} in presynaptic knob ⇒ increased Nt release

→ Long-term potentiation occurs due to increased Ca^{++} in postsynaptic neuron due to opening of NMDA (N-methyl-D-aspartate) channels

GABA: (inhibitory)

↳ in brain

→ formed by decarboxylation of glutamate by enzyme glutamate decarboxylase

→ taken up by nerve terminal by vesicular GABA transporter (VGAT)

→ metabolized to succinate by transamination

Receptors:

- $GABA_A$: ionotropic ⇒ hyperpolarize by promoting Cl^- influx
- $GABA_B$: metabotropic ⇒ produce fast IPSP
- $GABA_C$: ionotropic → hyperpolarize by promoting Cl^- influx

Sensory Receptors:

Receptors: transducers that convert various forms of energy in the environment into action potentials in sensory neurons
↳ endings of afferent nerve fibres

→ usually associated with non-neural cells that surround it; Receptors + non-neural structure = Sense organ

→ specific for a particular stimulus

→ Adequate stimulus: form of energy to which the receptor is most sensitive
(ex: adequate stimulus for rods & cones in retina is light)

Classification -

Based on Function

Exteroceptors - present in skin & subcutaneous tissue

Interoceptors - detect changes in internal environment [Ex: baroreceptors, chemoreceptors]

Proprioceptors - provide information about position of body in space at any given time
they are mechanoreceptors present in muscles, tendon, joints

Teleceptors - receptors that receive stimuli or sensation present far away from the body
(ex: auditory receptors)

Based on Adequate stimulus:

Mechanoreceptors - respond to application of mechanical stimulus

→ 3 categories - (i) Expanded endings: Merkel's disc, Ruffini's endings
(ii) Encapsulated endings: Pacinian corpuscles, Meissner's corpuscles, Krause's end-bulbs
(iii) Naked nerve endings: for elicitation of cutaneous sensations.

Thermoreceptors - sensitive to changes in temperature

→ Two types — warmth receptor
— cold receptor

Nociceptors - respond to painful stimuli (stimuli that are harmful to the organism)

→ Two types - (i) Aδ mechanical nociceptors - fast pain (ex: sharp pain due to pricking)
(ii) C-polymodal nociceptors - thermal & chemical stimuli

Chemoreceptors - respond to chemical stimuli

Ex: taste receptors, olfactory receptors

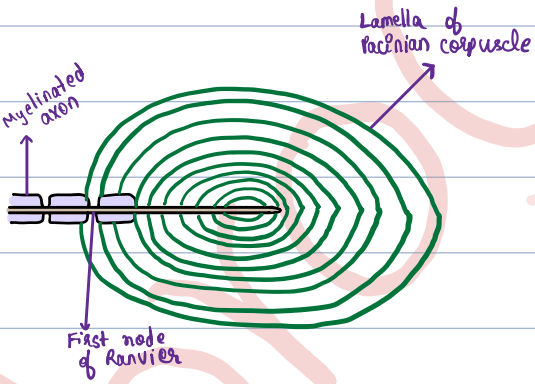
Photoreceptors - stimulus is light (photons)

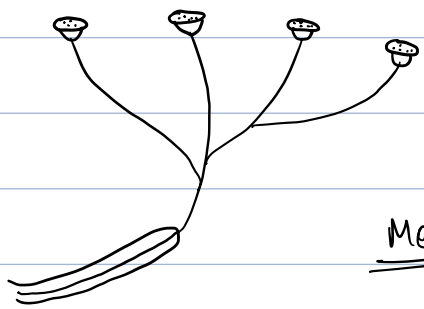
Ex: rods & cones of retina

Based on Location
- Superficial – in skin
- Deep – in muscles, bones, tendons, etc
- Visceral – in viscera

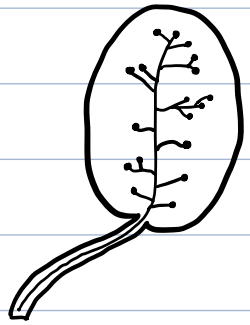
Pacinian corpuscle (largest mechanoreceptor)	rapidly adapting	vibration, touch & pressure
Meissner's Corpuscle	rapidly-adapting	vibration, touch
Merkel's Disc	slowly adapting	touch-pressure
Ruffini Endings (most superficial)	slowly adapting	crude touch
Krause's End-Bulb (smallest)	rapidly adapting	touch, pressure

Large myelinated Aα & Aβ fibres ⇒ mechanoreceptors
Small myelinated Aδ fibres ⇒ nociceptors (fast pain), cold receptors
Small unmyelinated C fibres ⇒ slow pain, temperature.

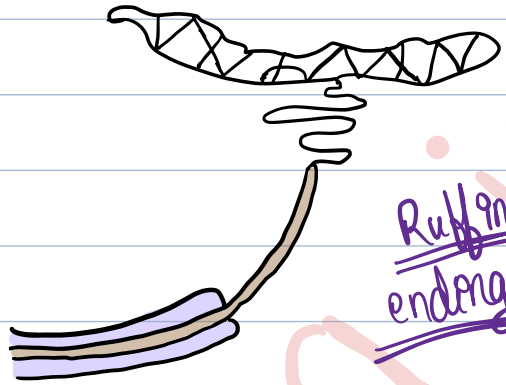




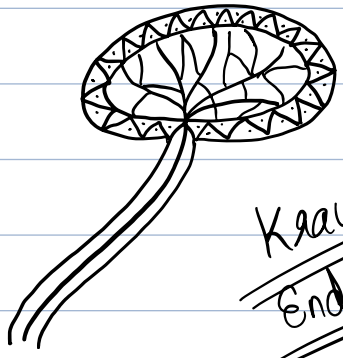
Merkel's disc



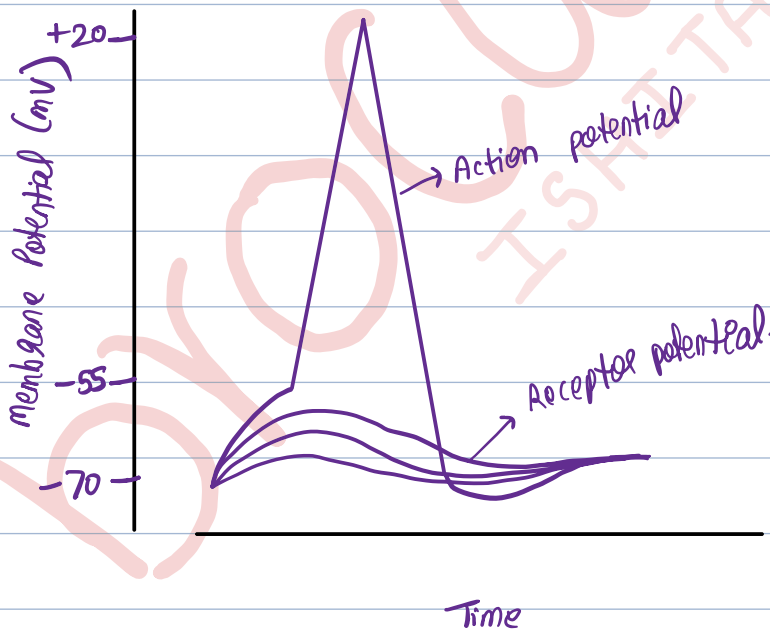
Meissner's corpuscle



Ruffini ending



Krause's End-Bulb



Properties of Receptors:

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Specificity: specific to a particular type of stimulus

Adequate Stimulus: form of energy to which receptor is most sensitive

Adaptation: when stimulus of constant strength is applied continuously to a receptor, frequency of action potential decreases (called desensitization)

- **Phasic Receptors**: rapidly adapting (touch, pressure)
- **Tonic Receptors**: slowly adapting (baroreceptors in carotid sinus & aortic arch, pain receptors)

Acuity: precision of stimulus localization

↳ depends on no. of receptors present in receptive field area

Intensity: receptors discharge depending on strength of stimulus

- when stimulus strength is less, receptors present close to the site of stimulus & receptors with low threshold discharge
- when stimulus strength is more, neurons fire at more rate & receptors that are present away from site of stimulus also discharge ⇒ Receptor Recruitment.

Weber-Fechner Law: magnitude of sensation felt is proportional to log of intensity of stimulus.

Law of Projection: irrespective of site of application of stimulus in sensory pathway along its course to cortex, sensation evoked is felt at the receptors.

This forms the basis of phantom limb (patient complains that he feels pain/itch in the amputated limb).

Muller's Doctrine of Specific Nerve Energy: sensation evoked depends on the precise area of brain activated by stimulus (pathways are specific & discrete)

Sensory Unit: single sensory axon & all its peripheral branches

Receptive Field: area from which a stimulus produces a response in that unit.

Receptor Recruitment

Dorsal Column Pathways:

First order neurons

Gracile fasciculus ⇒ medially placed

↳ lower extremity & lower part of trunk

Cuneate fasciculus ⇒ laterally placed

↳ upper extremity & upper part of trunk.

Dorsal Column nuclei ⇒ nucleus gracilis & nucleus cuneatus

Somatotopic organization of Dorsal Column Nuclei

↳ face placed laterally

→ trunk & hind-limb medially.

Dorsal Column Pathways:

- → Fine touch
- → Vibration
- → Proprioception
- → Tactile localization
- → Tactile Discrimination
- → Stereognosis

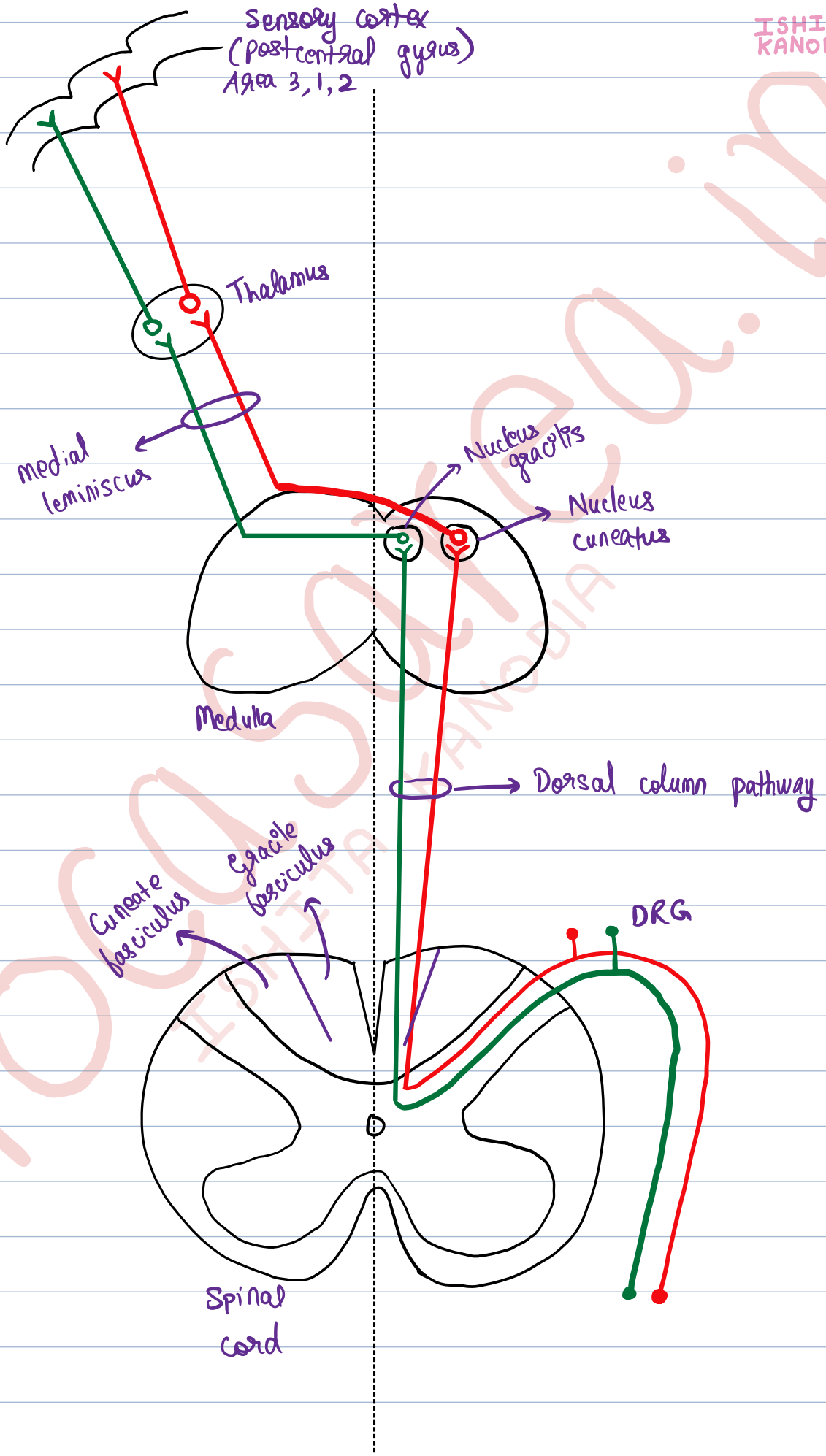
Anterior spinothalamic tract → crude touch

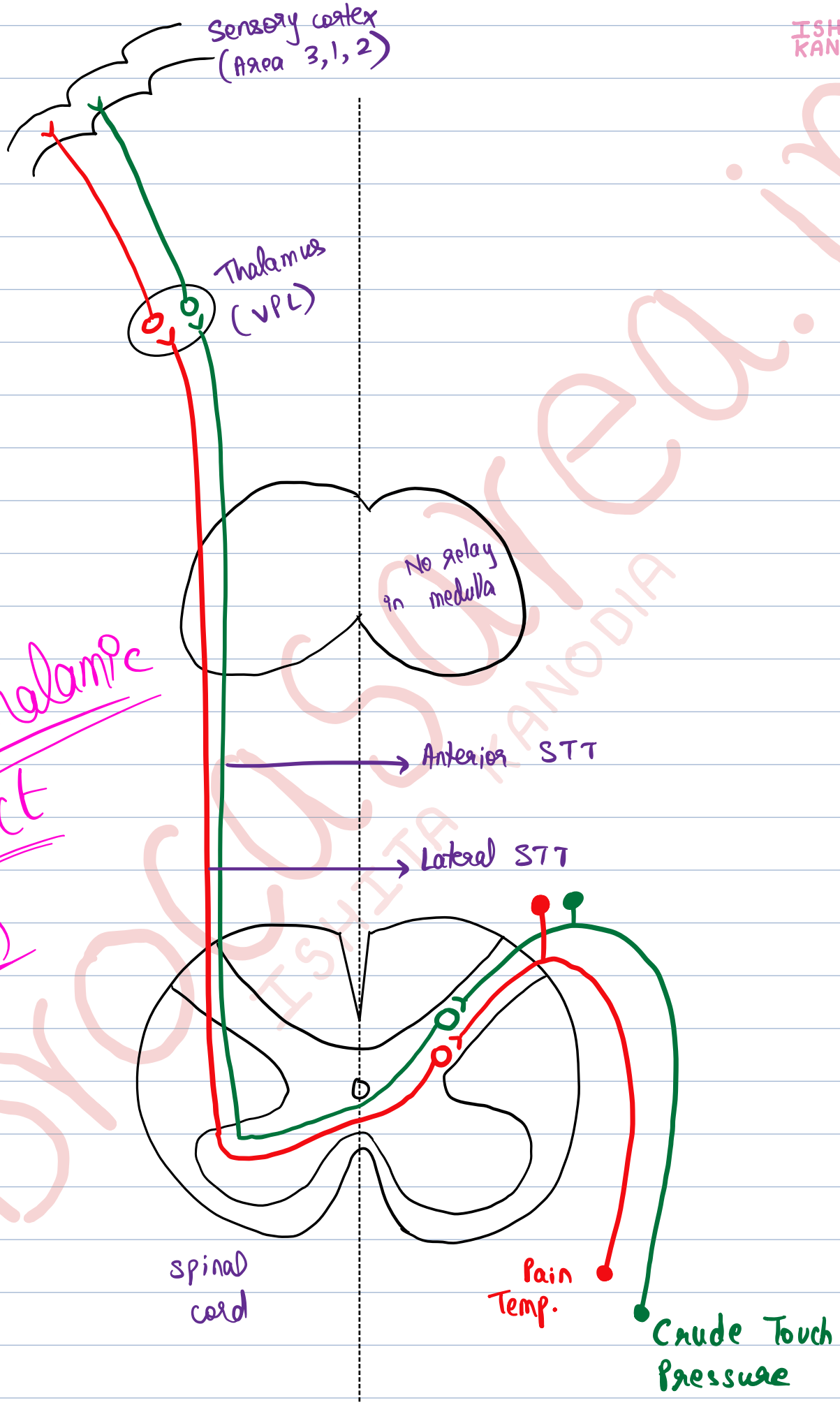
Lateral spinothalamic tract → pain, temperature

other ascending pathways:

- → spinocerebellar (dorsal & ventral)
- → spinoreticulothalamic
- → spinocervical thalamic

Dorsal Column Pathway





Spinothalamic Tract (STT)

Dissociated Anesthesia:

→ sensation of pain & temp. is lost

→ touch sensation is preserved

Causes – Syringomyelia
– Syringobulbia

→ spinal cord grey matter surrounding central canal is damaged.

Pain Pathway:

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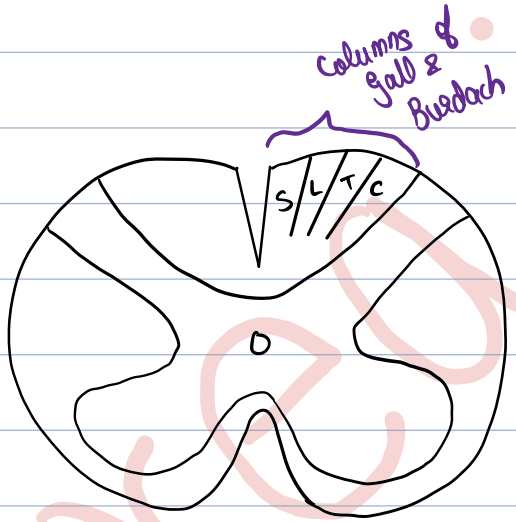
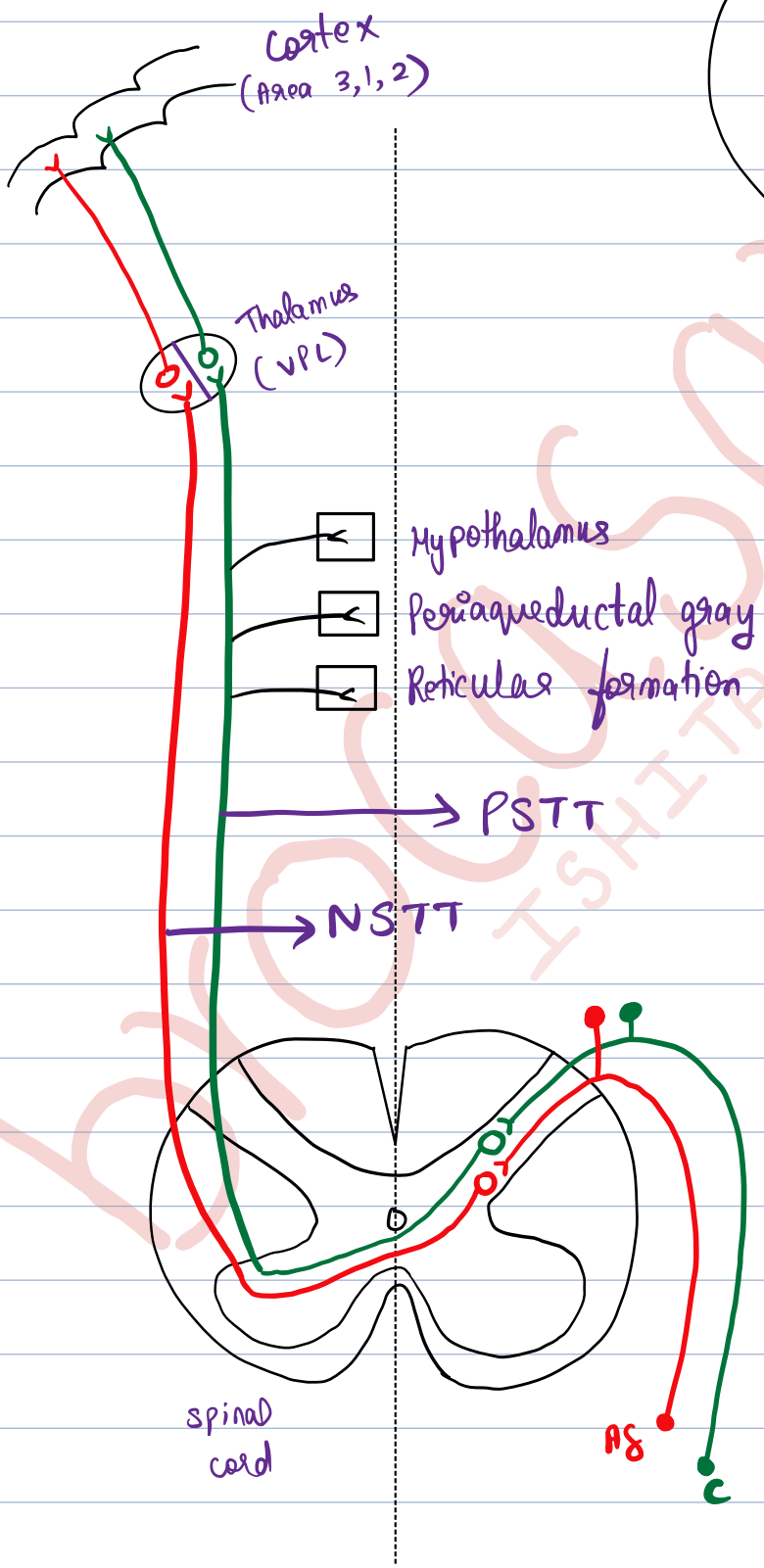
Paleospinothalamic (PSTP): slow pain

↳ mostly C fibers

Neospinothalamic (NSTP): fast pain

↳ mostly Aδ fibers





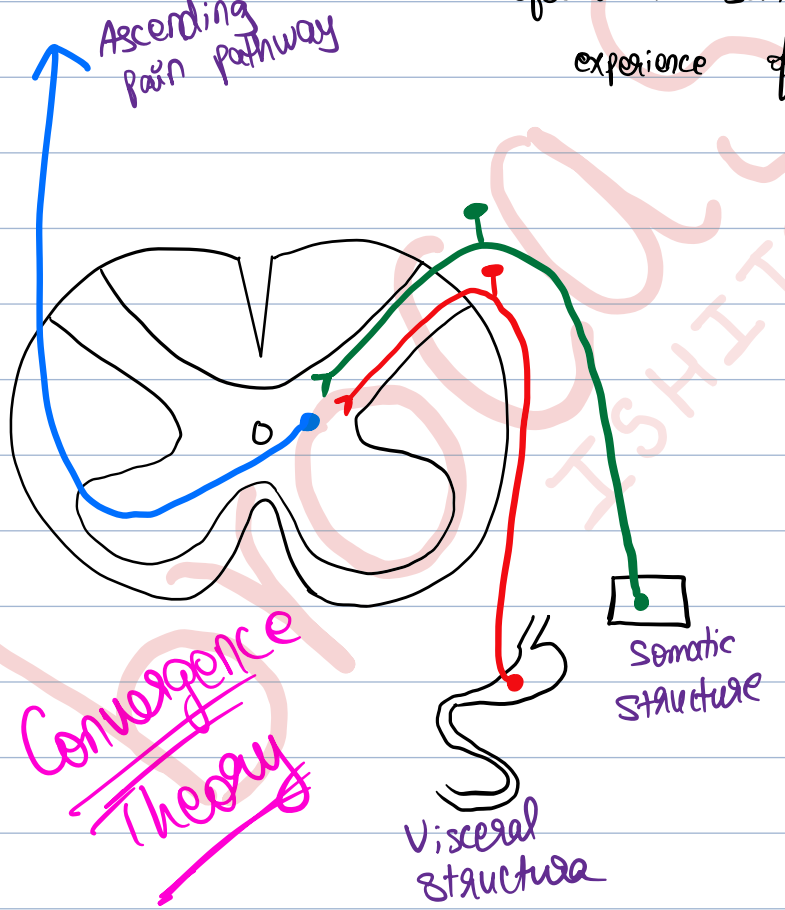
Referred Pain:

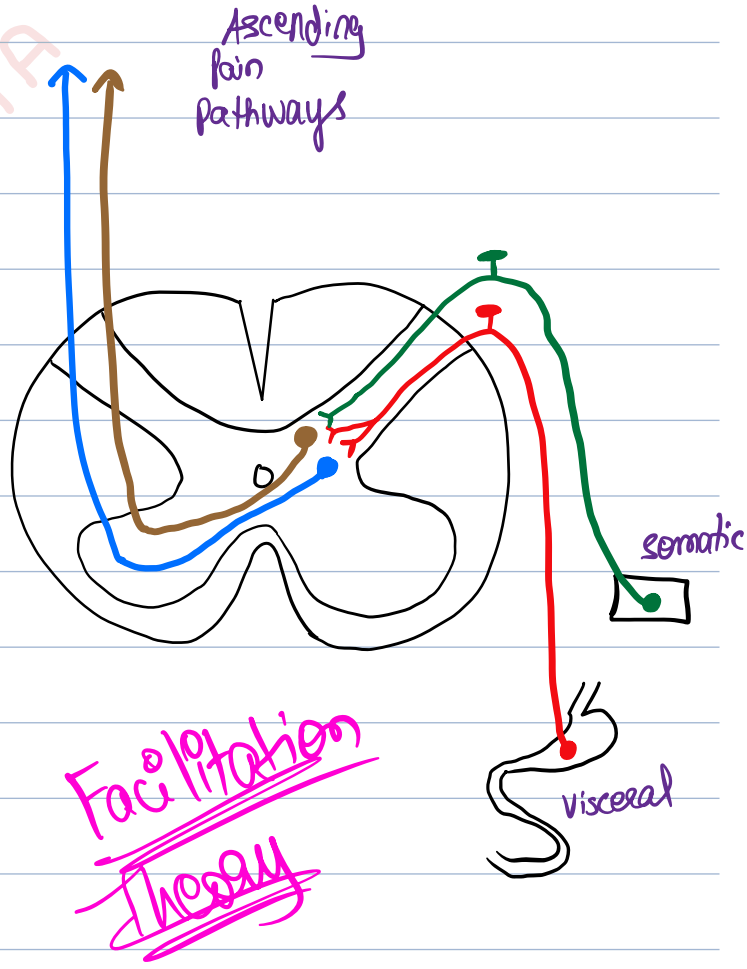
→ visceral pain may be referred to somatic structures located away from viscera (areas of skin innervated by same embryonic spinal segment)

Ex: Pain of Acute MI is referred to inner aspect of left arm
Pain in acute cholecystitis is referred to tip of right shoulder.

Theories: – Dermatomal: visceral pain is referred to a structure that develops from same embryonic segment (dermatome)

– Convergence
– Facilitation
– Experience: pain instead of being felt at its usual site, may be referred to some other area in which patient had an experience of pain earlier





Endogenous Neural Analgesia System

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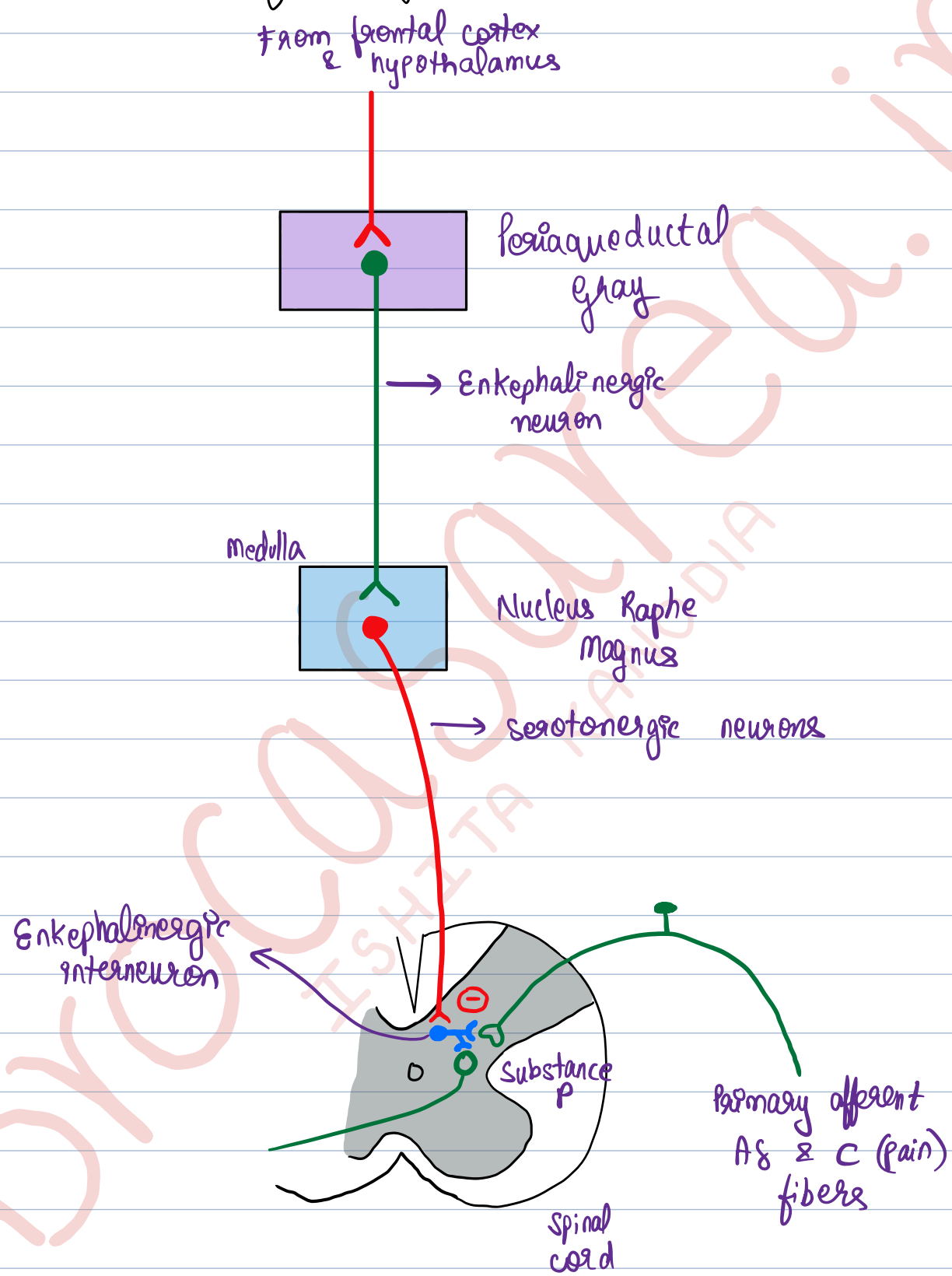
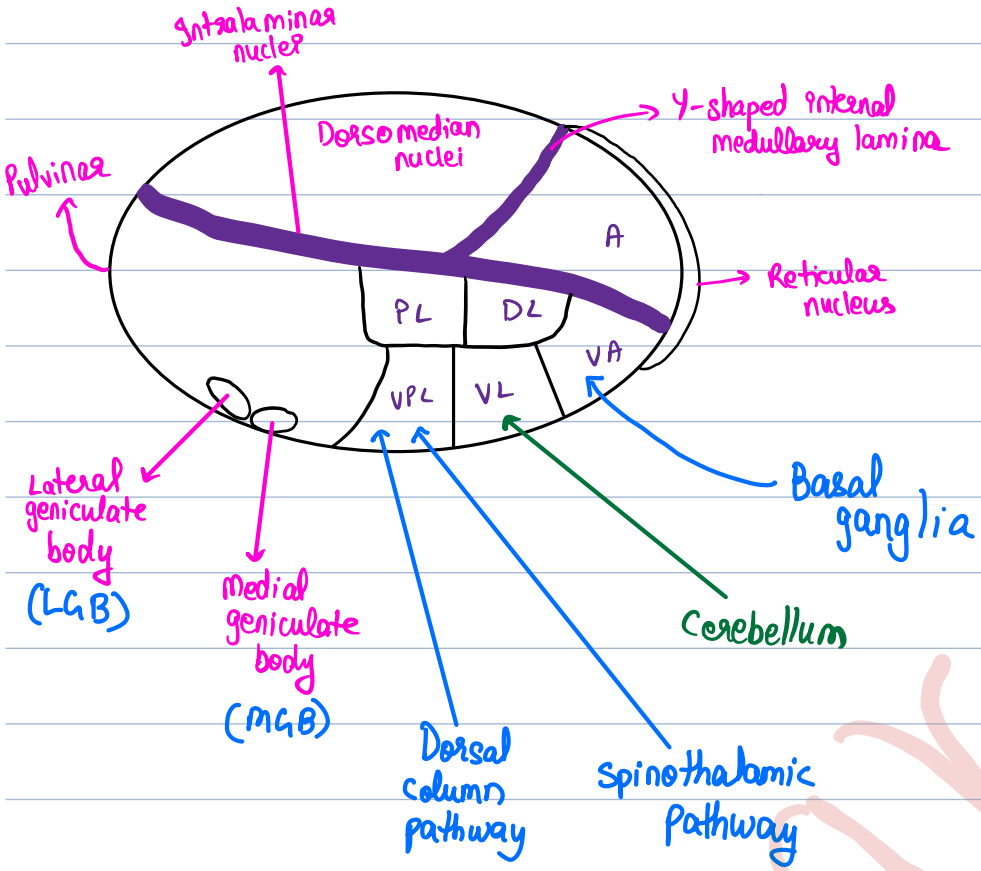




A = anterior
VA = ventral anterior
VL = ventral lateral
VPL = ventral posterolateral
DL = lateral dorsal
PL = Lateral posterior

Thalamic Nuclei

Specific Relay Nuclei

→ ascending afferent inputs synapse here

- VBC (ventrobasal complex)
- LGB
- MGB
- Anterior nucleus

Association nuclei

→ receive inputs from sensory cortex & limbic system

- Pulvinar nucleus
- Dorsal nucleus
- PL nucleus

Non-specific nuclei

→ inputs from reticular formation & paleospinothalamic tract

- Intralaminar
- centromedian
- reticular nucleus

Motor nuclei

→ input from cerebellum & basal ganglia

- Lateral
- VA
- VL

Functions of Thalamus:

Relay station for all somatic sensations – major relay station for sensory inputs
↳ centre for sensory integration

Relay of special sensations: all special sensations (except olfaction)
↳ LGB – visual afferents
MGB – auditory afferents
VPL – taste afferents

Subcortical perception of pain, temperature, pressure

Motor function:
→ influences postural movements
→ influences planning & programming of movements

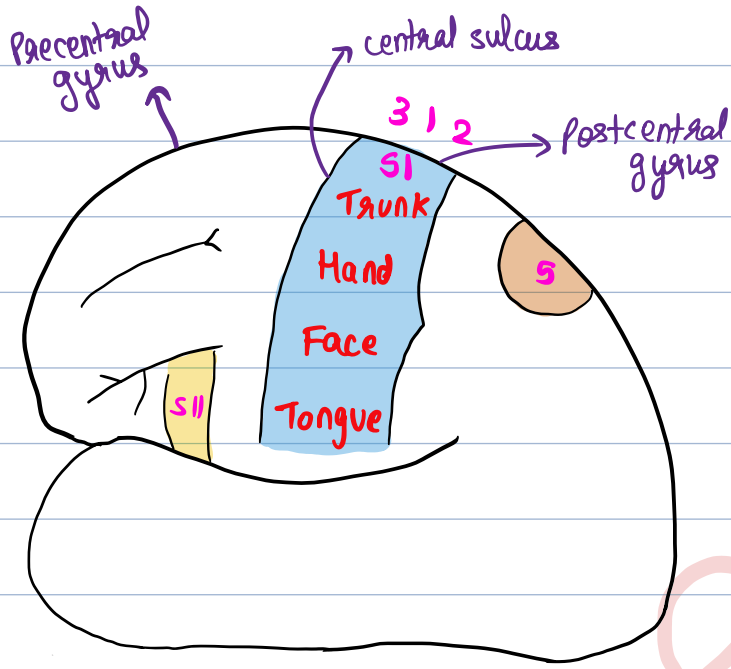
Memory & Emotion
→ anterior thalamus is a constituent of Papez circuit which receives input from mamillary body of limbic system

Role in sleep:
→ Thalamocortical loop is important in generating pattern of brain activity in sleep-wake cycle.

Sensory Motor Coordination
→ Coordination between sensory & motor functions

→ Concerned with language & speech.

Thalamic Syndrome: Lesion of VPL due to thrombosis of posterolateral branch of posterior cerebral artery
→ severe impairment of discriminative touch & pressure sensation on contralateral side.
→ decreased muscle tone & ataxia
→ emotion may be affected
[Vascular lesions usually spare medial thalamus including VPM ∴ sensations in face & head often remain intact].



Brown - Sequard Syndrome:

→ occurs in hemisection of spinal cord

→ Cause - injury to spinal cord
- tumors

on the side of lesion - fine touch
- proprioception
- tactile discrimination

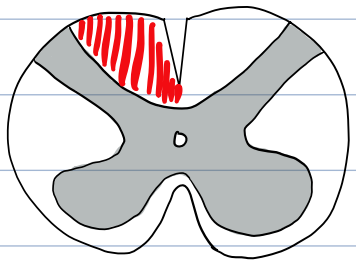
on opposite side - pain
- thermal sensations

} Sensory deficit

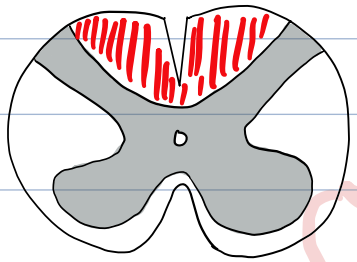
Motor Deficit:

→ There is damage to corticospinal tract on side of hemisection

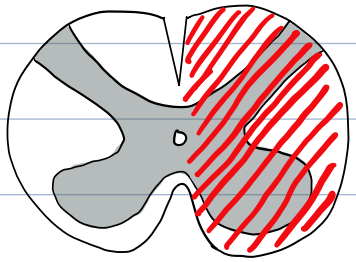
∴ paresis (muscle weakness) & spasticity on same side of body.



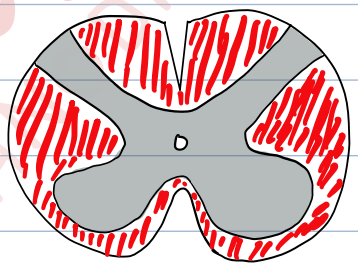
Tabetic Syndrome



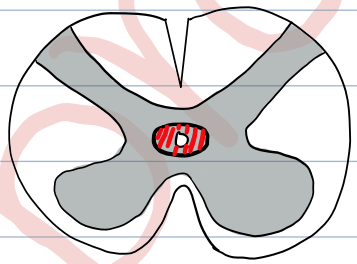
Posterior column syndrome



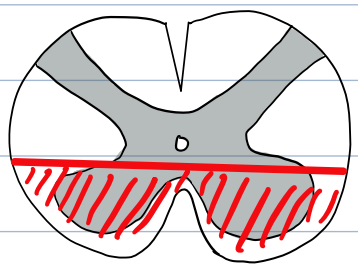
Hemisection
(Brown sequard syndrome)



Complete transection

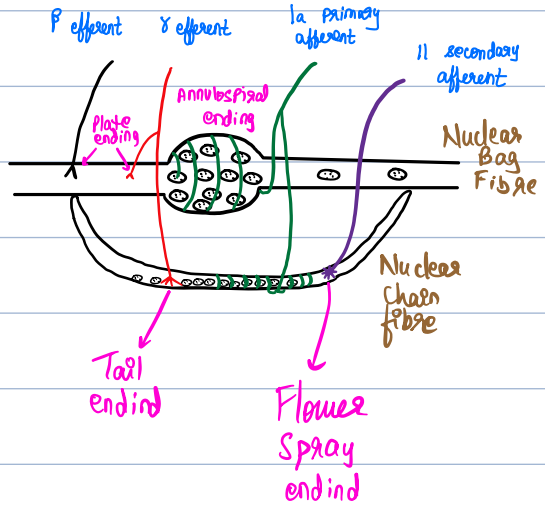


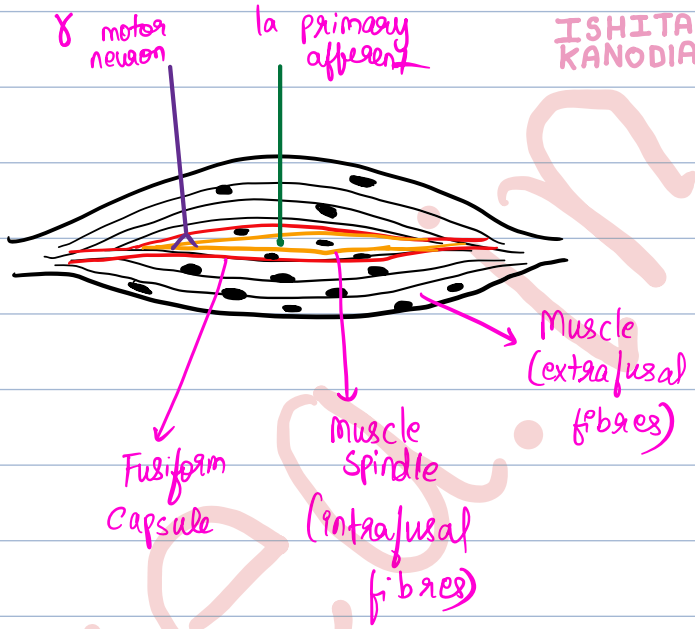
Syringomyelic Syndrome



Anterior spinal artery syndrome

Muscle Spindle:





Mechanism of muscle contraction in response to stimulation of γ motor neuron

Activation of γ motor neuron

↓

contraction of peripheral part of muscle spindle

↓

stretching of central part of spindle

↓

distortion of sensory nerve endings in nuclear bag fibre

↓

Generation of action potential in IA afferent fibers

↓

Stimulation of α motor neurons

↓

Muscle contraction

Golgi Tendon Organ:

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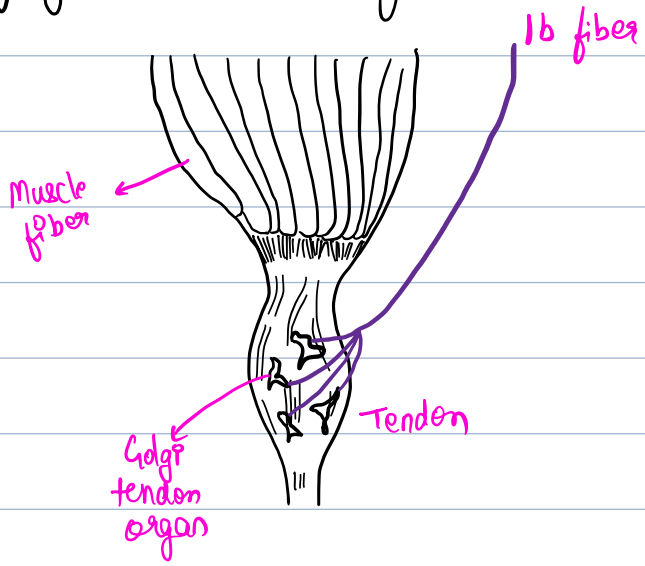
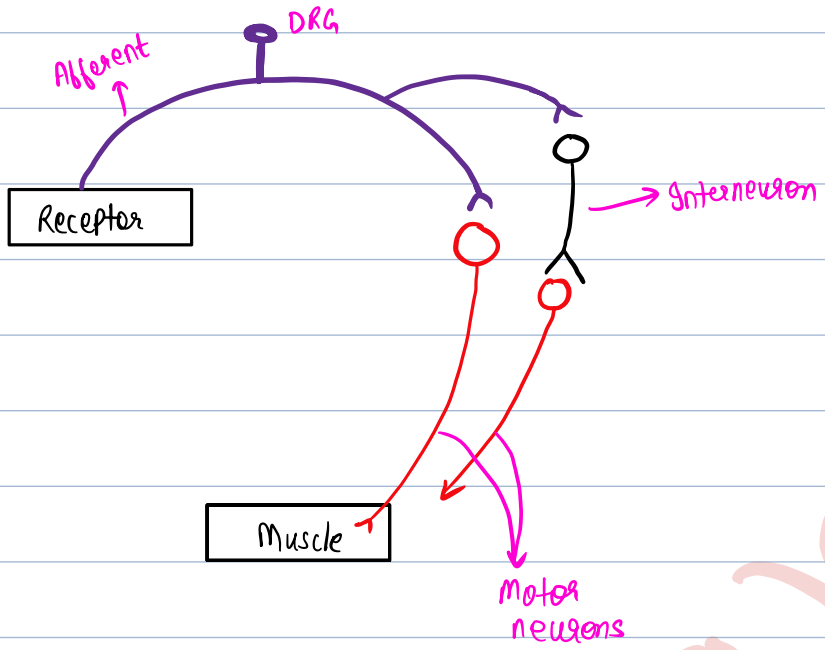


Components of Spinal Reflex:

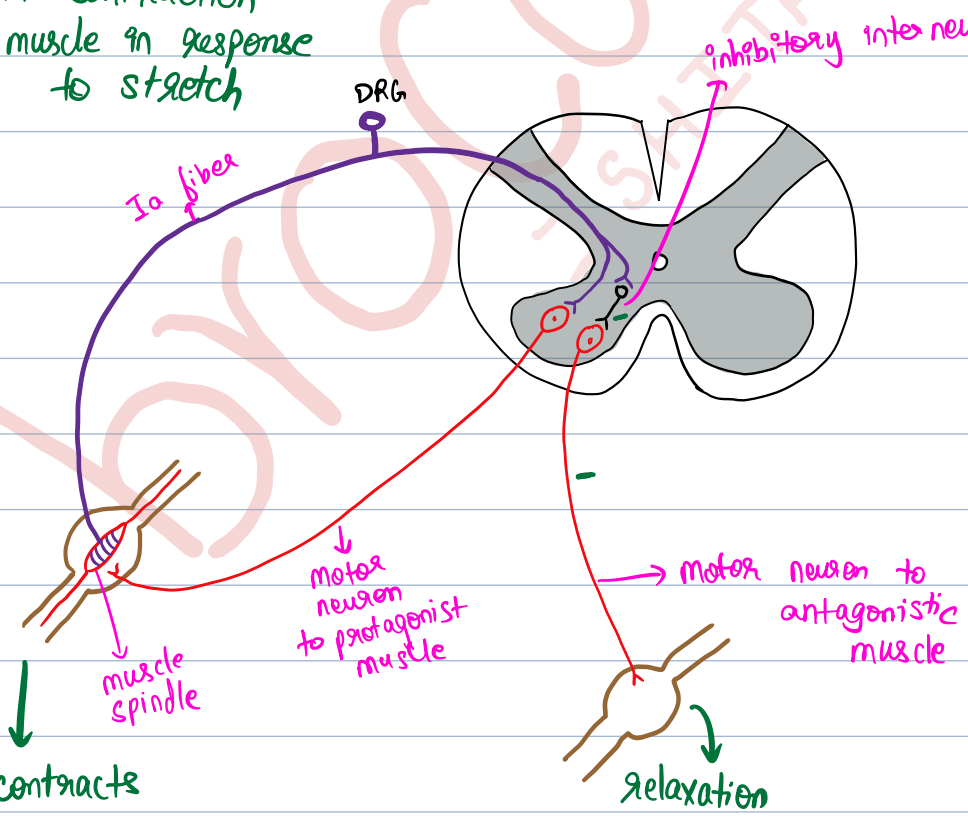


Stretch Reflex / Myotatic Reflex : (Monosynaptic)

reflex contraction of muscle in response to stretch

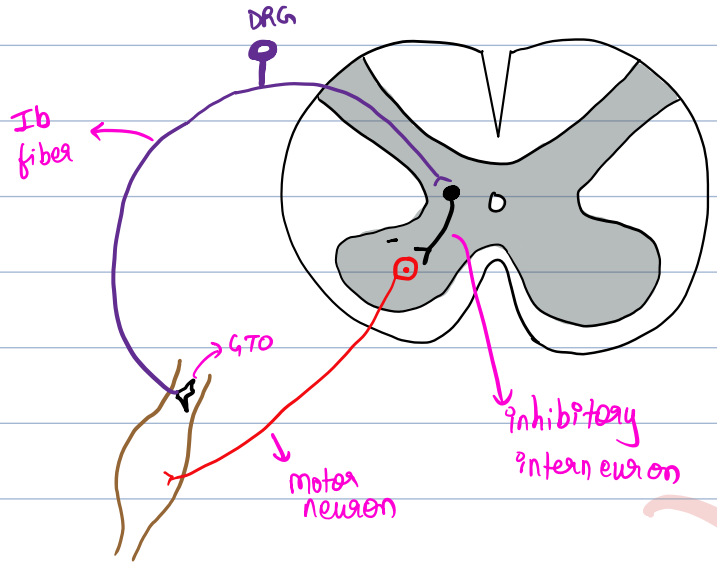
Phasic stretch reflex

tonic stretch reflex ⇒ during sustained stretch



Inverse Stretch / Inverse Myotatic Reflex : (disynaptic reflex)

reflex relaxation of muscle in response to strong stretch



Withdrawal Reflex : (polysynaptic)

(Crossed extensor / Phillipson's reflex)