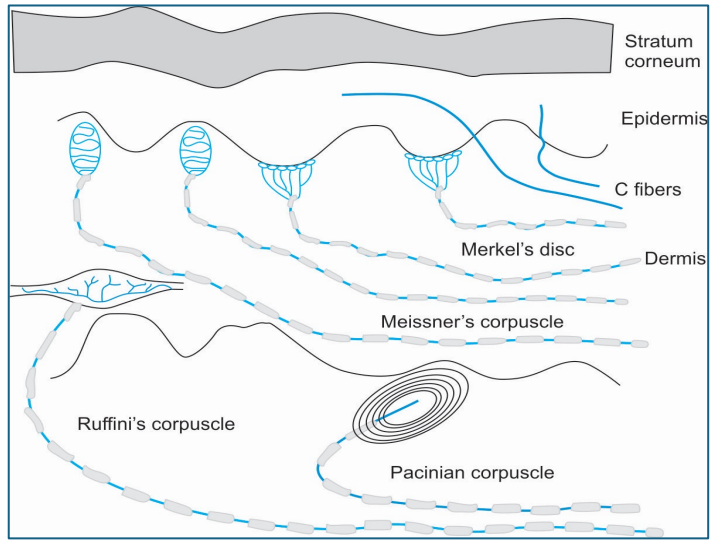
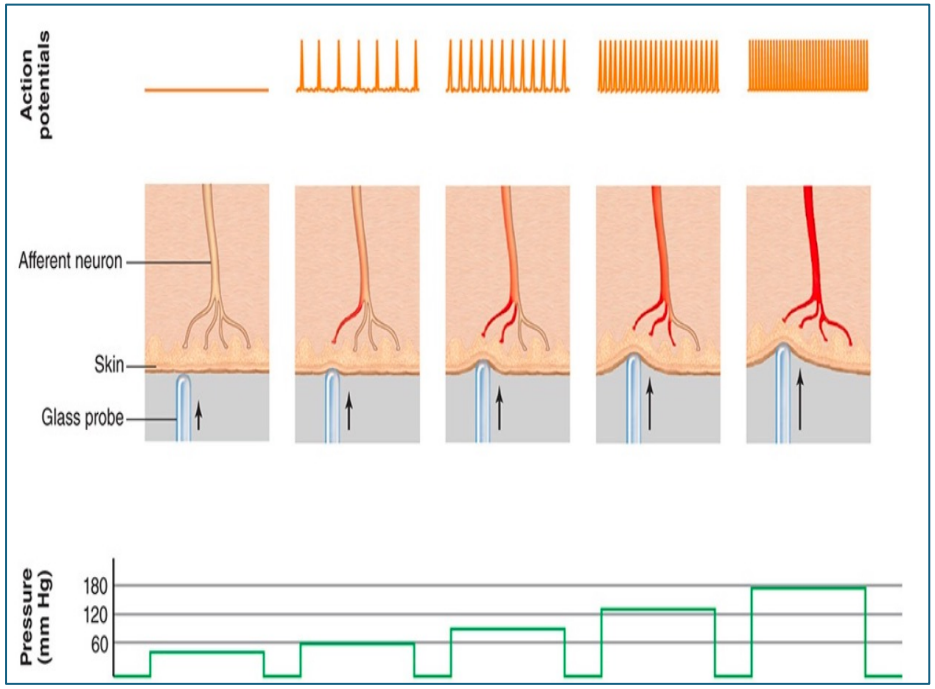
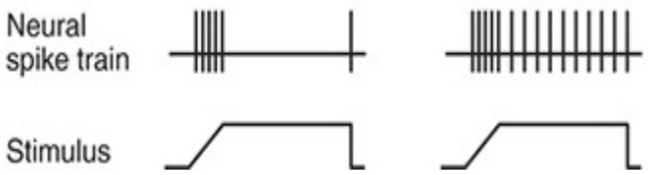
INTEGRATED NEUROLOGY

Sensory Receptors

RECEPTOR	ADAPTATION	REMARKS
	FAST	Most numerous Non-hairy skin only Fast moving touch, dynamic two-point discrimination, low frequency vibration
	FAST	Largest receptor Most sensitive HIGH FREQUENCY VIBRATION, Pressure
	FAST	Hair movement
	SLOW	Epidermis- Edge, static two-point discrimination BRAILLE
	SLOW	Skin stretch, pressure Maximum in joint capsule
	SLOW	Itching, Slow pain (Substance P)

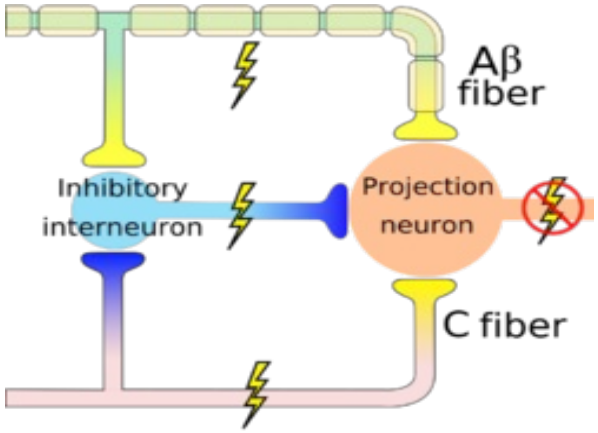






- Hyperalgesia
- Allodynia
- Gating theory of pain- Melzack/Wall

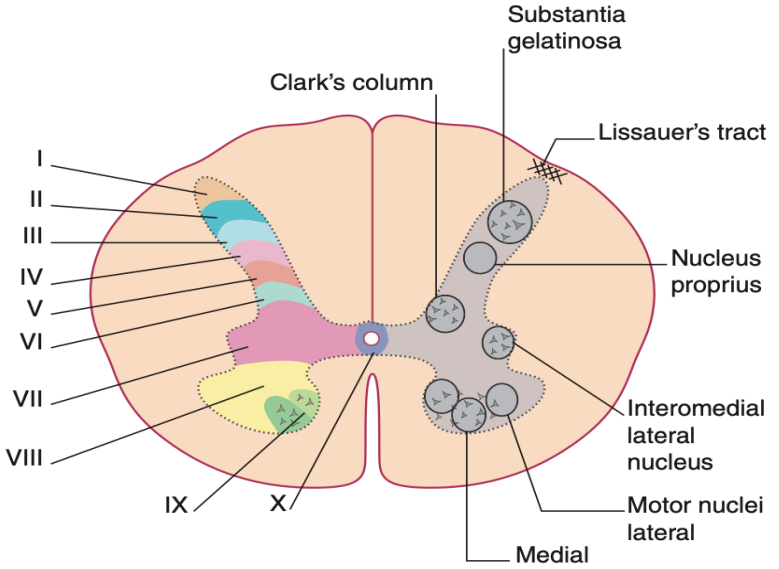
TENS / Accupuncture



Structure	PAIN INHIBITION
Periaqueductal gray (PAG)	Activates descending inhibition pathways
Nucleus raphe – 5HT	inhibits pain at spinal level
Locus ceruleus-NE	
Interneurons in dorsal horn	Release enkephalins, dynorphins

A 30-year-old female went on vacation and fell asleep while sitting on a beach. After some time she woke with sunburn. Later when she went back home, she experienced pain while taking a warm bath (40°C). Which of the following receptors is responsible for the pain?

A. Innocuous thermal receptor - allodynia
B. Innocuous thermal receptor - hyperalgesia
C. Thermal nociceptor - allodynia
D. Thermal nociceptor – hyperalgesia



Erlanger-Grasser: Nerve fibres

Fiber type		Functions	Conduction velocity (m/sec)	Diameter (µm)
A	Alpha	Proprioception; somatic motor	70-120	12-20
	Beta	Touch, pressure	30-70	8
	Gamma	Efferent to muscle spindles	15-30	5
	Delta	Fast Pain(Glu), temperature (cold)	12-30	2-5
B		Preganglionic autonomic	3-12	3
C	Unmyelinated	Slow Pain, temperature (warm), Postganglionic sympathetic	0.5-2	1

- Cold sensation:
- Warm, burning pain and freezing pain:
- Local anaesthetic: Aγ and Aδ>> Aα and Aβ >> B >>C
- Pressure:
- Hypoxia:

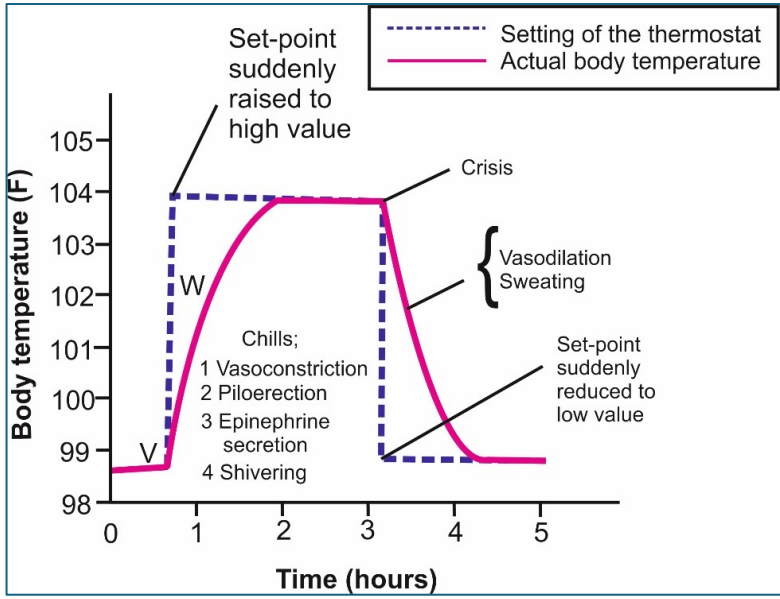
NT changes in diseases

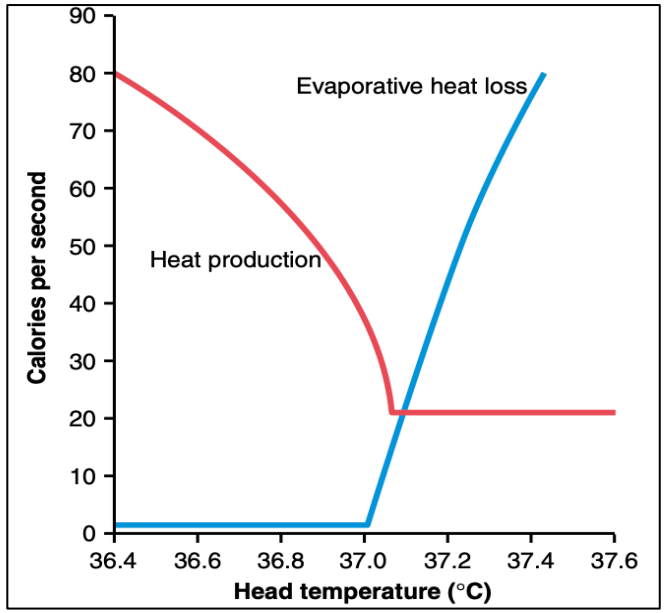
	Locations of synthesis	Anxiety	Depression	Mania	Schizophrenia	Alzheimer disease	Huntington disease	Parkinson disease
Acetylcholine	Basal nucleus of Meynert							
Dopamine	Ventral tegmentum, SNc							
GABA	Nucleus accumbens							
Norepinephrine	Locus ceruleus							
Serotonin	Raphe nuclei (medulla, pons)							

Hypothalamic nuclei

Lateral nucleus Stimulated by ghrelin
Ventromedial nucleus Stimulated by leptin
Anterior nucleus
Posterior nucleus
Suprachiasmatic nucleus
Supraoptic nucleus
Paraventricular nuclei
Preoptic nucleus
Arcuate nucleus

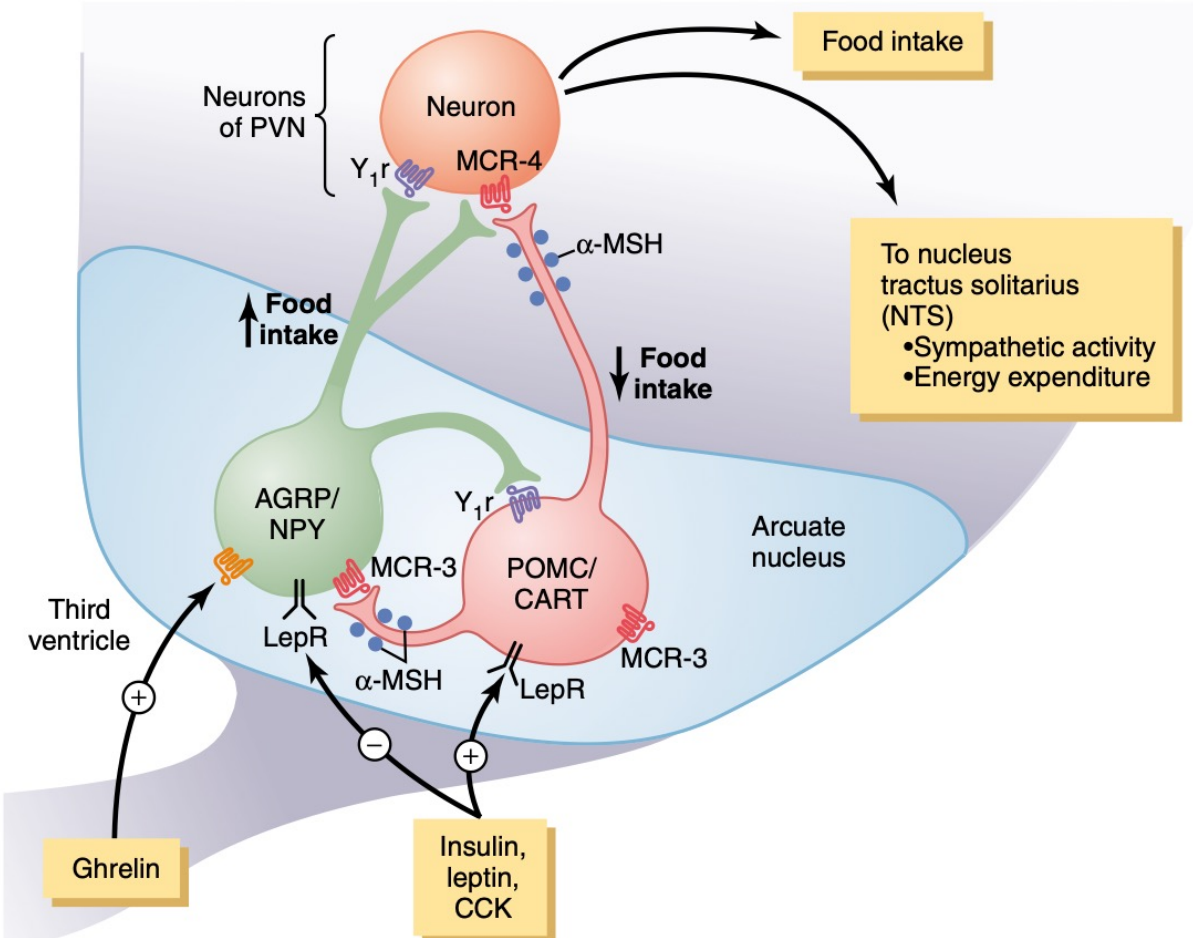
- Pulsatile release of GnRH-
- Permissive role in puberty-





Satiety

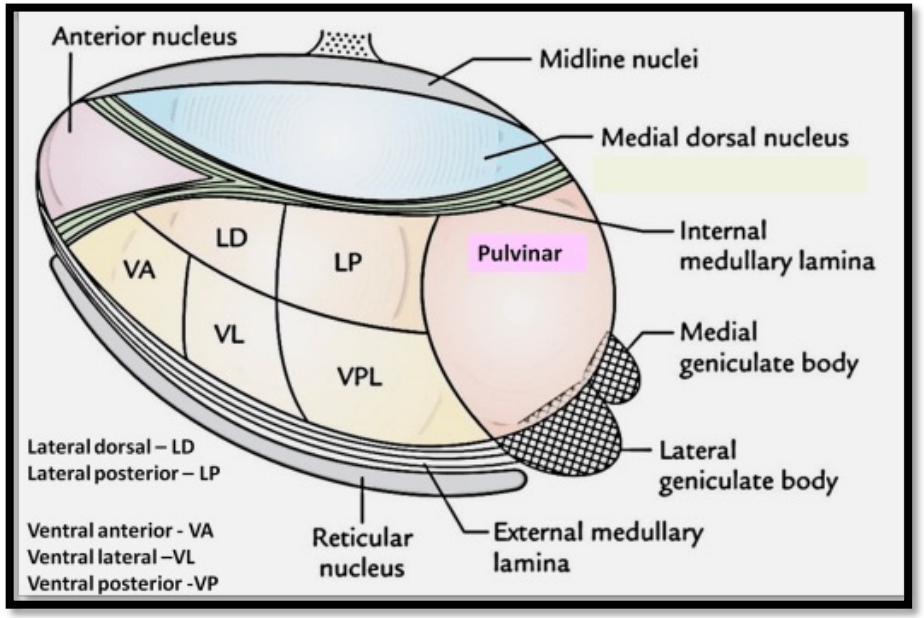
Decrease Feeding (Anorexigenic)	Increase Feeding (Orexigenic)
α-Melanocyte-stimulating hormone (α-MSH)	Neuropeptide Y (NPY)
Leptin	Agouti-related protein (AGRP)
Serotonin	Melanin-concentrating hormone (MCH)
Norepinephrine	Orexins A and B
Corticotropin-releasing hormone (CRH)	Endorphins
Insulin	Galanin (GAL)
Cholecystokinin (CCK)	Amino acids (glutamate and γ-aminobutyric acid)
Glucagon-like peptide (GLP)	Cortisol
Cocaine- and amphetamine-regulated transcript (CART)	Ghrelin
Peptide YY (PYY)	Endocannabinoids



Adiponectin:

Thalamic nuclei

Nuclei	Input	Senses	Destination
Ventral Postero-Lateral			
Ventral Postero-Medial			
Lateral geniculate nucleus			
Medial geniculate nucleus			
Ventral anterior/ lateral			



Memory

Declarative / Explicit Memory:

- Semantic (factual):
- Episodic (events):

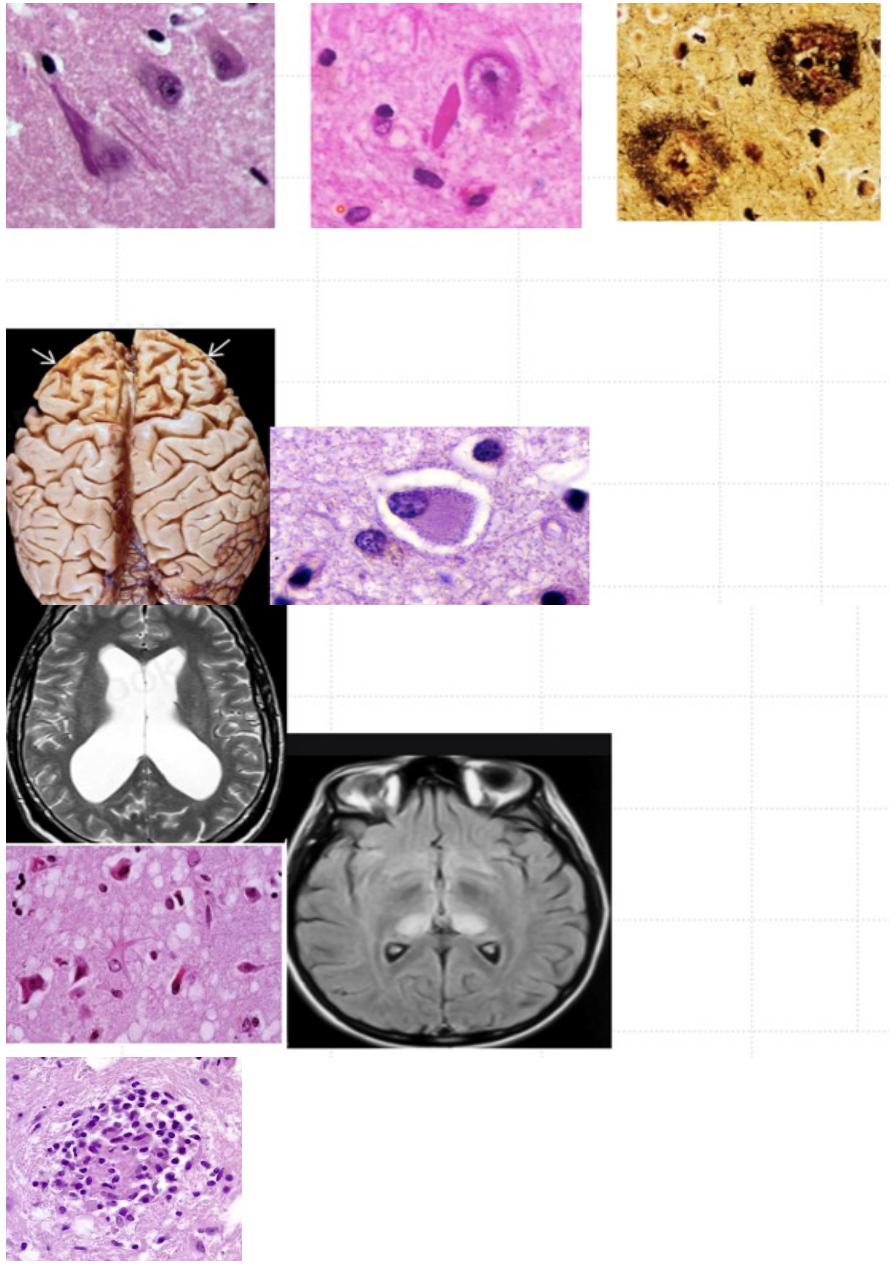
Nondeclarative / Implicit Memory:

- Procedural (skills, habits):
- Priming and perceptual:
- Associative learning (classical/ operant conditioning):
- Non-associative learning
- Habituation
- Sensitisation

Short term memory:
Long-term potentiation / depression

Dementia

	Early short-term memory loss, spatial disorientation -> personality changes Down syndrome (APP-Chr 21) Apo E2 Apo E4 Mild: Donepezil Severe: Memantine Lecanemab, Aducanumab Transdermal patch:
	Stepwise decline Deep white matter changes on neuroimaging
	Early personality changes Apathy, disinhibition & compulsive behavior
	Wet-Wacky-Wobbly Shuffling gait with preserved arm swing
	Behavioral changes, Myoclonus Rapidly progressive 14-3-3 in CSF, Periodic sharp wave EEG
	HIV + Global atrophy



Basal Ganglia

Caudate

Putamen

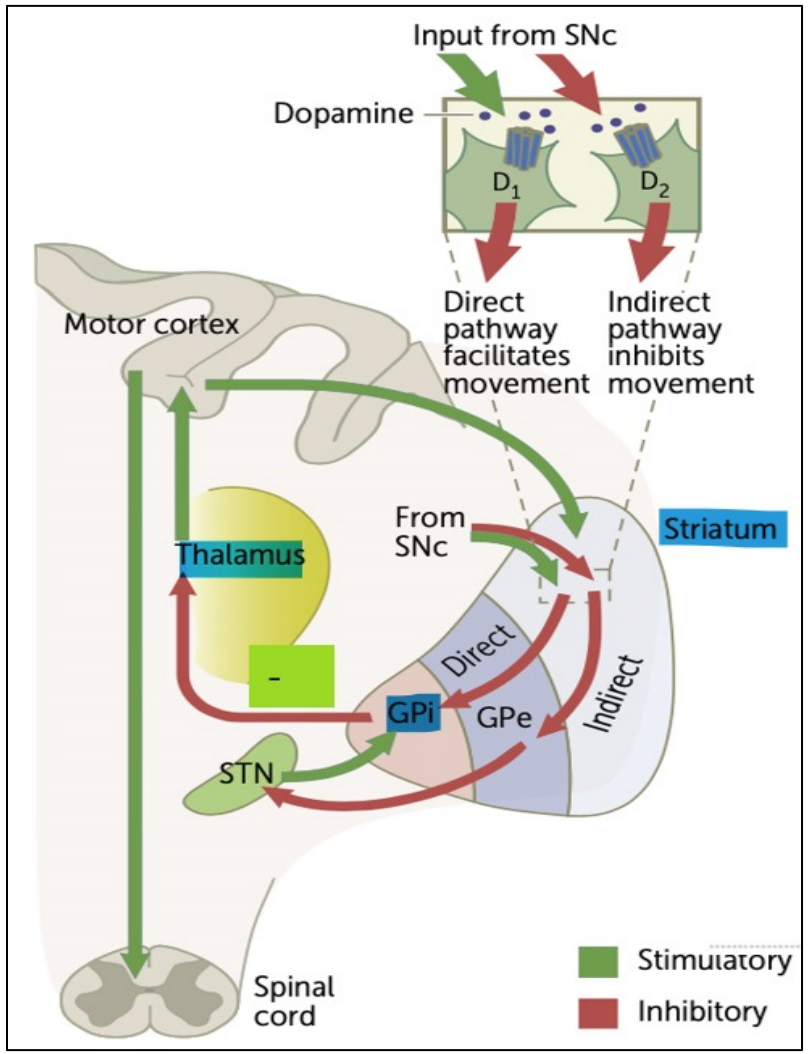
Gpi

Gpe

SNpr

SNpc

STN

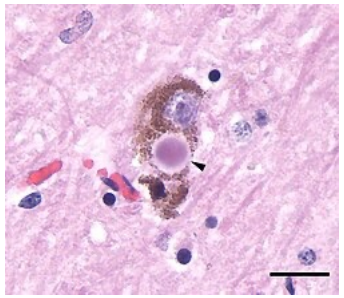


High-frequency tremor (6-10Hz) with sustained posture
Tremor increases with activity, anxiety
Decreases with alcohol
Familial
DOC:

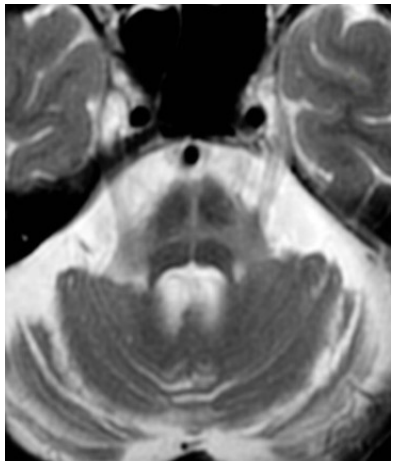
Movement disorders

Tremors (3-6Hz)
Rigidity
Akinesia
Postural instability
Micrographia
Mask like facies
Shuffling gait
Late-
Dementia, Depression

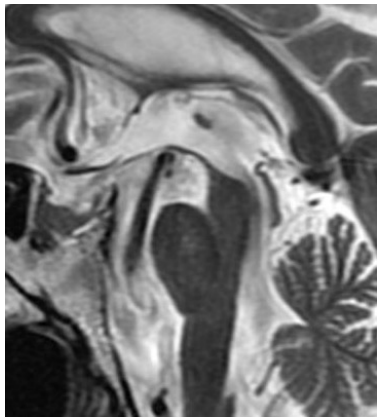
CORE:
- Fluctuating cognition
- Visual hallucinations
- REM sleep behavior disorder (RBD)
- Spontaneous Parkinsonism



Autonomic ++



Impaired downward gaze

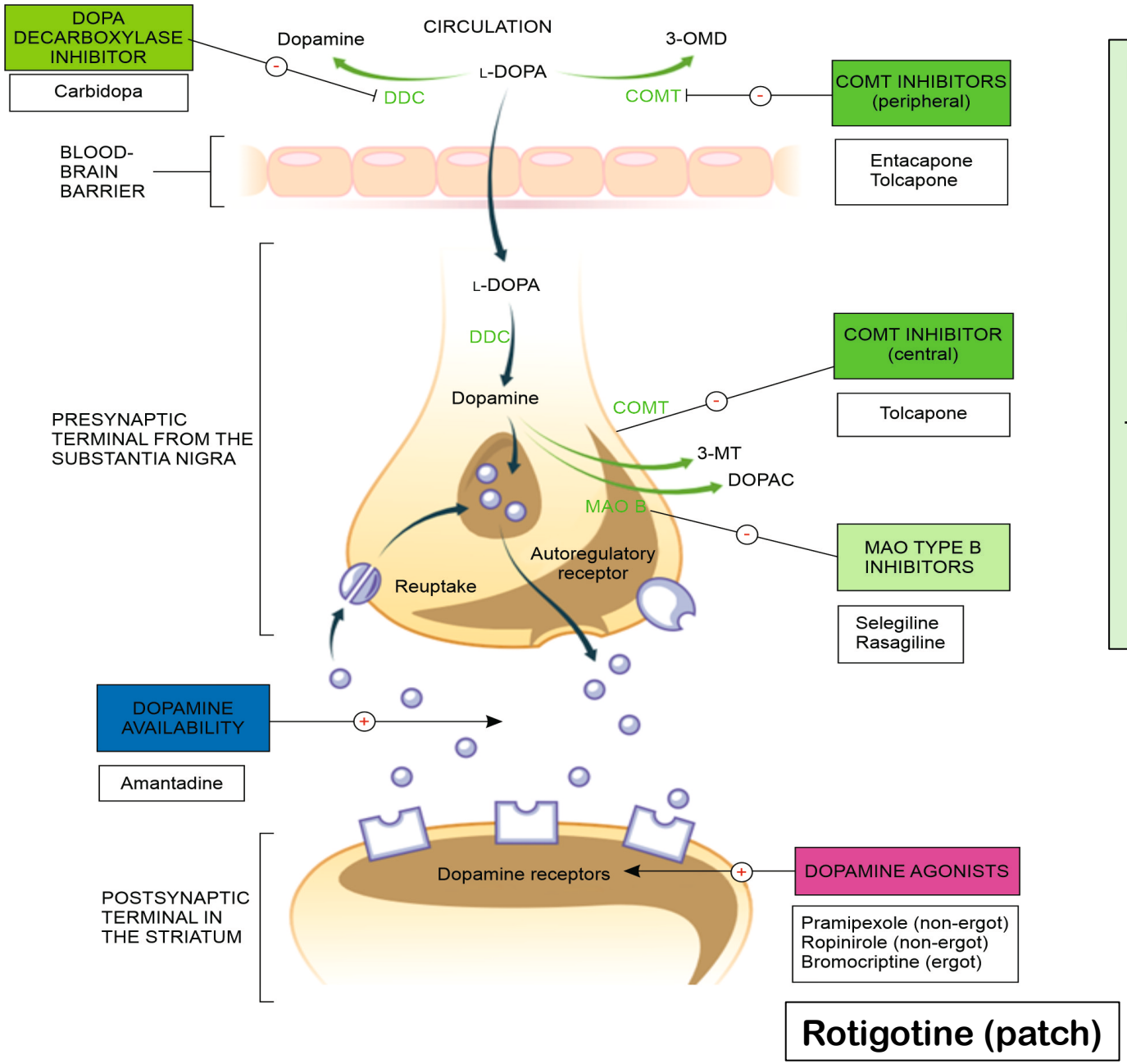


Alien limb phenomenon

Synucleinopathies:
•Parkinson's disease
•Dementia with Lewy bodies
•Multiple system atrophy

Tauopathies:
•Progressive supranuclear palsy
•Corticobasal degeneration
•Alzheimer's disease
•Pick's disease
•Chronic traumatic encephalopathy
•Pantothenate kinase-associated degeneration
•Subacute sclerosing panencephalitis (SSPE)

Parkinson Disease Mx



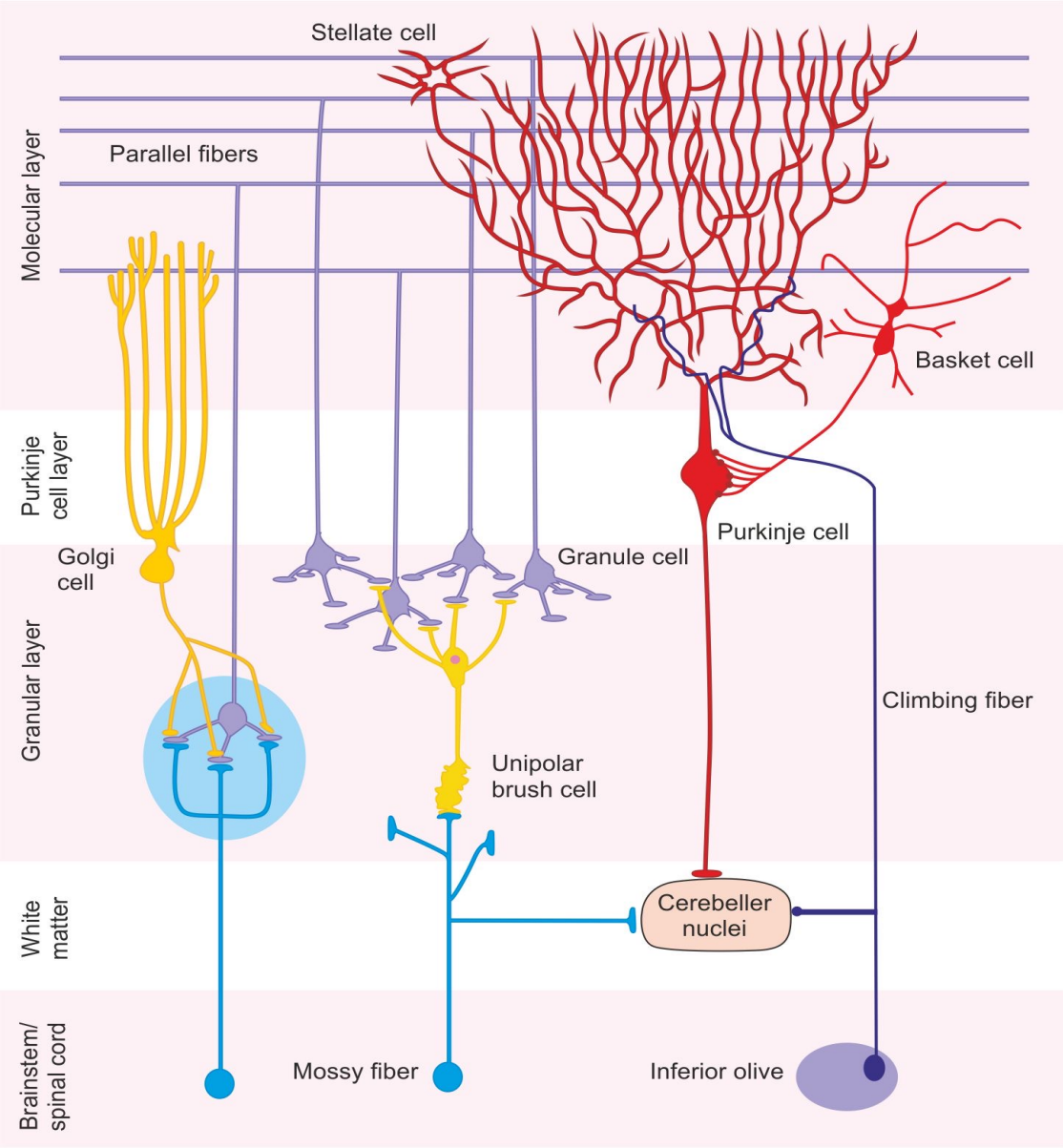
FIRST LINE:

FIRST LINE IN YOUNG:

<u>DOC for drug induced PD / tremors predominant:</u>
Benztropine, Trihexphenidyl

Istradefylline: Adenosine [A_{2A}] receptor antagonist
DBS:

Cerebellum



Cerebellar Part	Lesion Features
Vermis	Truncal ataxia, staggering gait, nystagmus Alcoholics +
Flocculonodular lobe (vestibulocerebellum)	
Anterior lobe (spinocerebellum)	
Dentate nucleus (lateral hemisphere / cerebro-cerebellum)	Dysmetria, intention tremor, dysdiadochokinesia

(Lateral to medial)
dentate, emboliform, globose, fastigial

APPROACH TO HEADACHE

UNILATERAL

BILATERAL

Pulsatile
4-72hrs
Nausea
AURA

Repetitive
Periorbital + lacrimation + Horner

Male > female
15min-3hrs

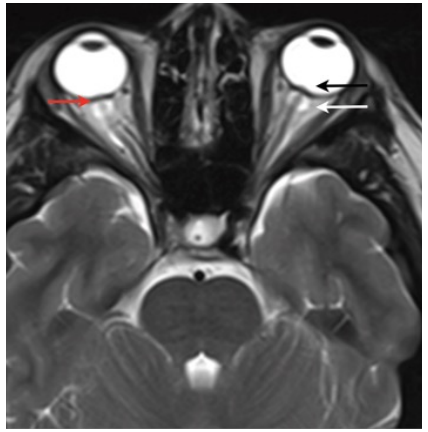
2-30min
Response to indomethacin

5-200s
Burning, stabbing pain

5-200s
V2/V3
Triggered by chewing/touch

Band-like
4-6hrs

Dull-aching
Papilledema
6th CN palsy
Tetracycline,Obesity
Vit A, Danazol



Short-lasting, Unilateral, Neuralgiform headache attacks with Conjunctival injection and Tearing

MIGRAINE
Acute attack: First line:
DOC: 5HT1B/1D+ :
S/e:
5HT1F + : LASMIDITAN (acute)
Prophylaxis:
DOC:
Topiramate / Valproate
CGRP-: RimeGEPANT, AtoGEPANT (oral-acute/prophylaxis)
ERENUMAB, GALANEZUMAB, FREMANEZUMAB, EPTINEZUMAB

CLUSTER HEADACHE
DOC:
Prophylaxis:

TENSION HEADACHE
DOC:
Prophylaxis:

Weight loss, acetazolamide, invasive procedures

Meningitis

	Colour	WBC (cells/ul)	Glucose (mg/dl)	Protein (mg/dl)	Opening Pressure (mm Hg)
Normal	Clear	0-5	40-70	<40	50-180
Bacterial					
TB					
Viral					
Fungal					
GBS					
MS					

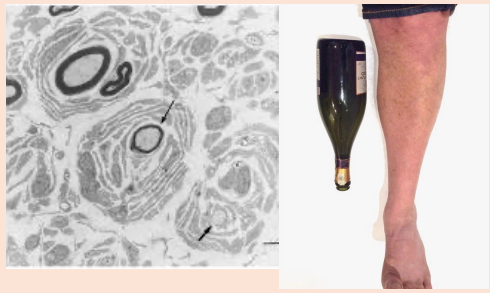
h/o prior GI / STD
B/L Acute ascending Flaccid paralysis + Areflexia
Monophasic course <4weeks
>8 weeks/3 or more relapses:
Anti GM1 antibodies
Brighton criteria
MCC of death-
Vital Capacity < 20 mL/kg
Maximal Inspiratory Pressure (MIP) < –30 cm H_2O
Maximal Expiratory Pressure (MEP) < 40 cm H_2O
Rx:

Miller fisher syndrome (MFS):

Ophthalmoplegia, ataxia, areflexia

Anti GQ1b antibodies (90%)

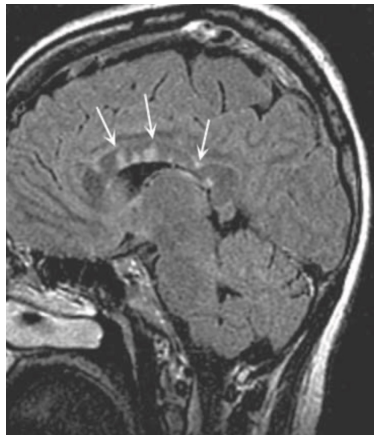
Hereditary SM demyelinating
AD CMT1A-PMP22
•Distal muscle weakness and atrophy
•Areflexia
•Foot drop
•Pes cavus/ Hammer toes

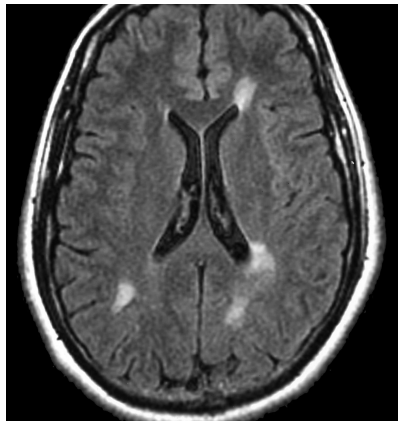


NCV studies
Demyelination: Conduction velocity reduced,
Distal latencies
Axonal: Low amplitude

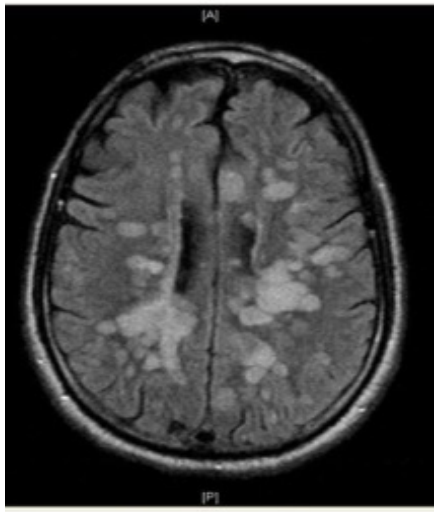
Demyelinating disorders

20-40yrs, Females MC
Away from equator, Low Vit D
RELAPSING REMITTING
McDonald criteria
Charcot triad:
Lhermitte sign
Uthoff sign
ON : U/L, asymmetrical
Spinal cord: Short segment
Rx: Acute-steroids
RRMS: β-interferon, Natalizumab, Mitoxantrone, Fingolimod, Alemtuzumab
PPMS (ORATORIO Trial):



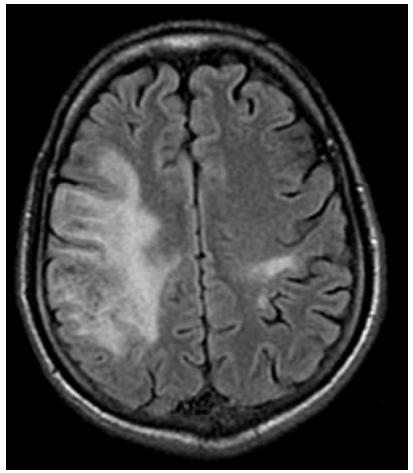


<20yrs
Antecedent infection
Monophasic
ON : B/L
Spinal cord: Long segment

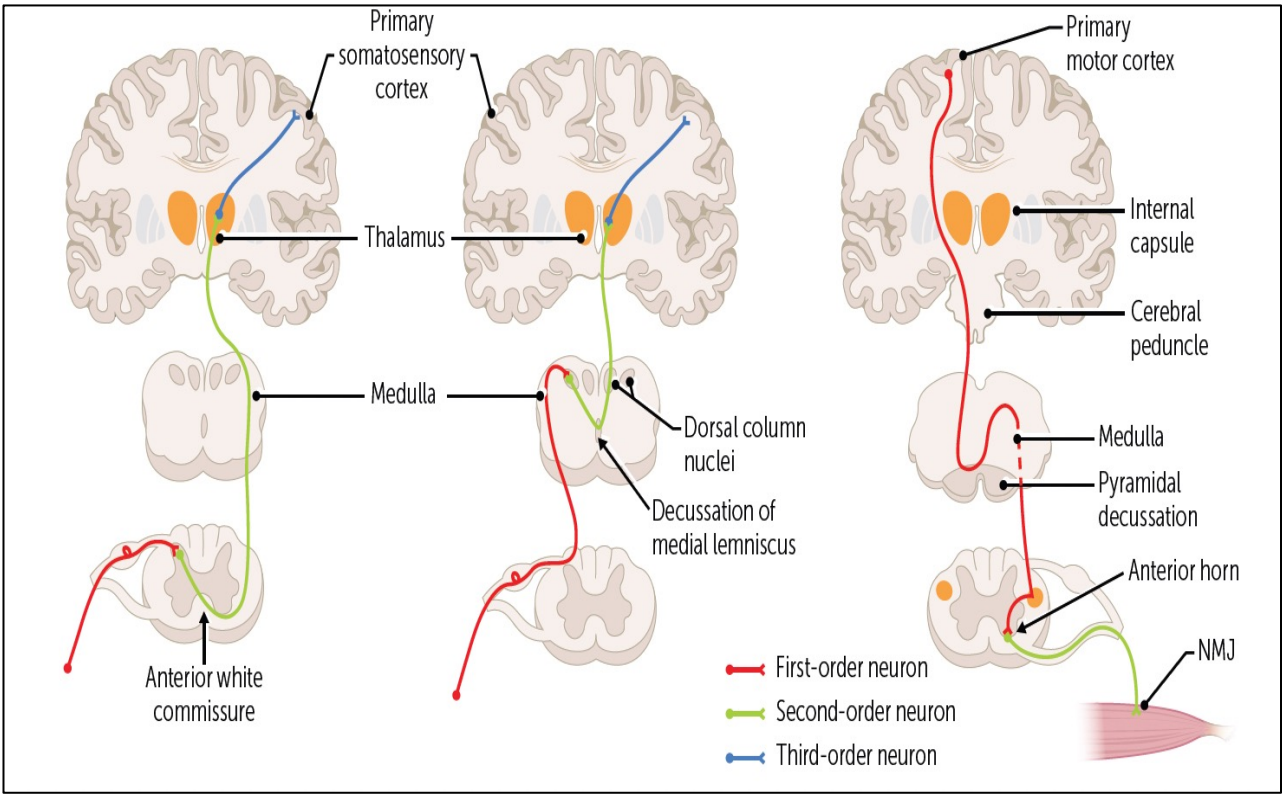


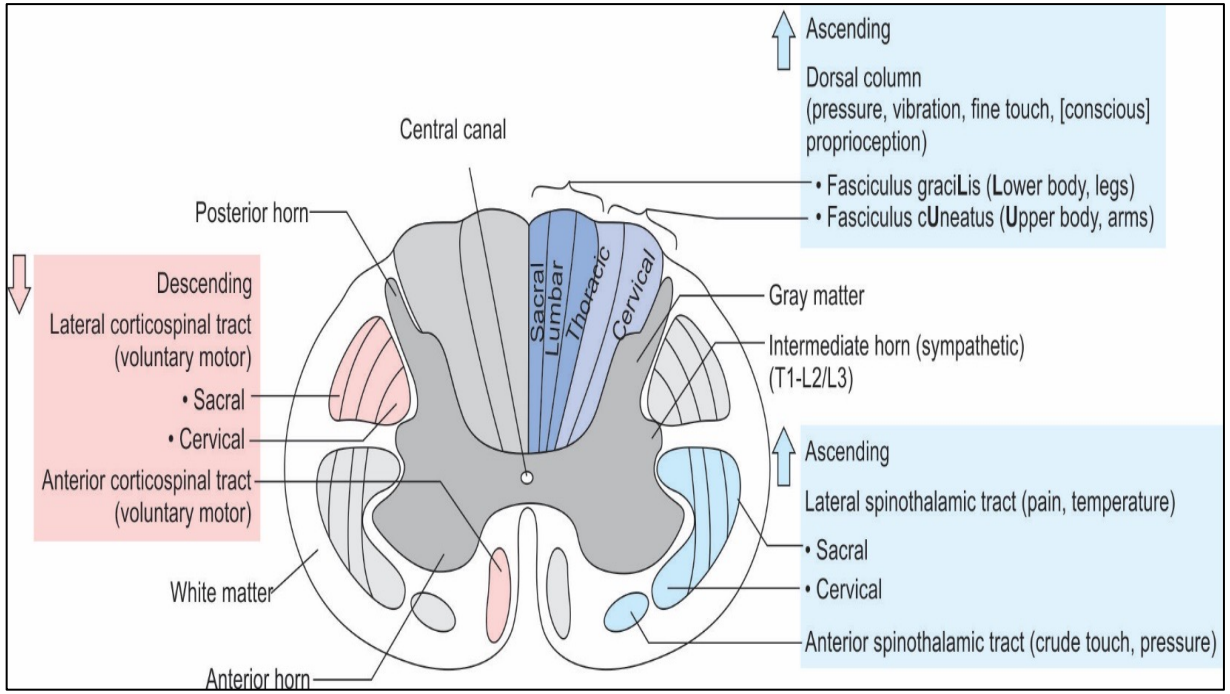
20-40yrs
ON: B/L
Spinal cord:
Antibody:Anti-Aqp4
Area prostema syndrome
Diencephalon syndrome
Acute myelitis
ON

HIV +
Asymmetric



Spinal cord tracts

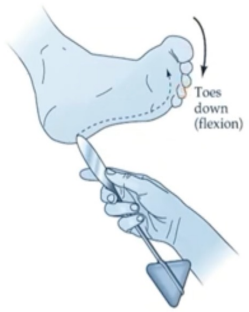


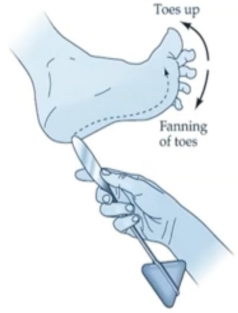


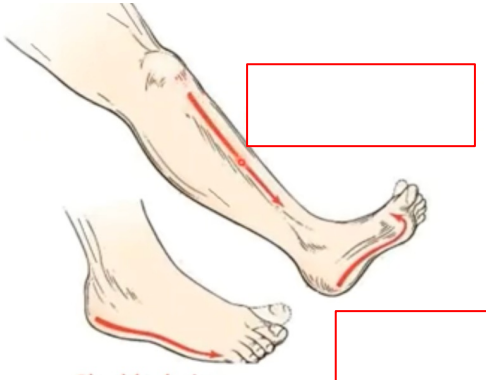
UMN VS LMN

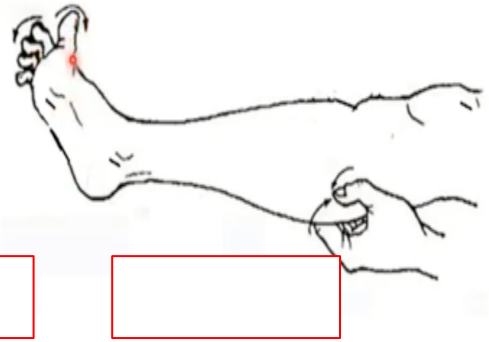
	Pseudobulbar (UMN: 5,7,10,11,12)	Bulbar (LMN: 9,10,11,12)
Gag reflex		
Jaw jerk		
Tongue		
Speech	Laboured/spastic	Nasal twang Nasal regurgitation

SIGN	UMN	LMN
Weakness	+	+
Reflexes	↑	↓
Tone	Spastic	Flaccid
Babinski	+	-
Atrophy Fasciculations	-	+

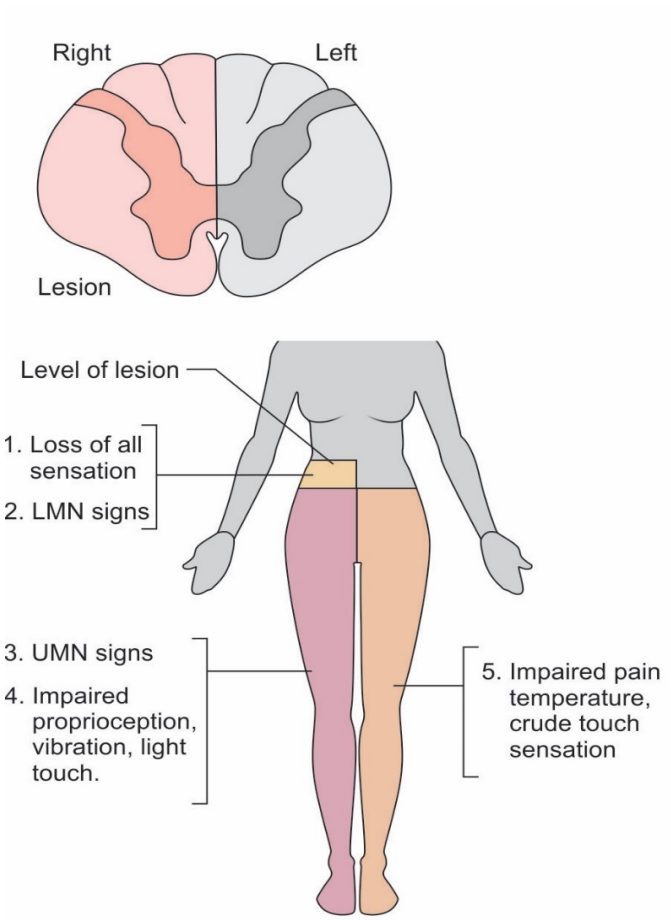


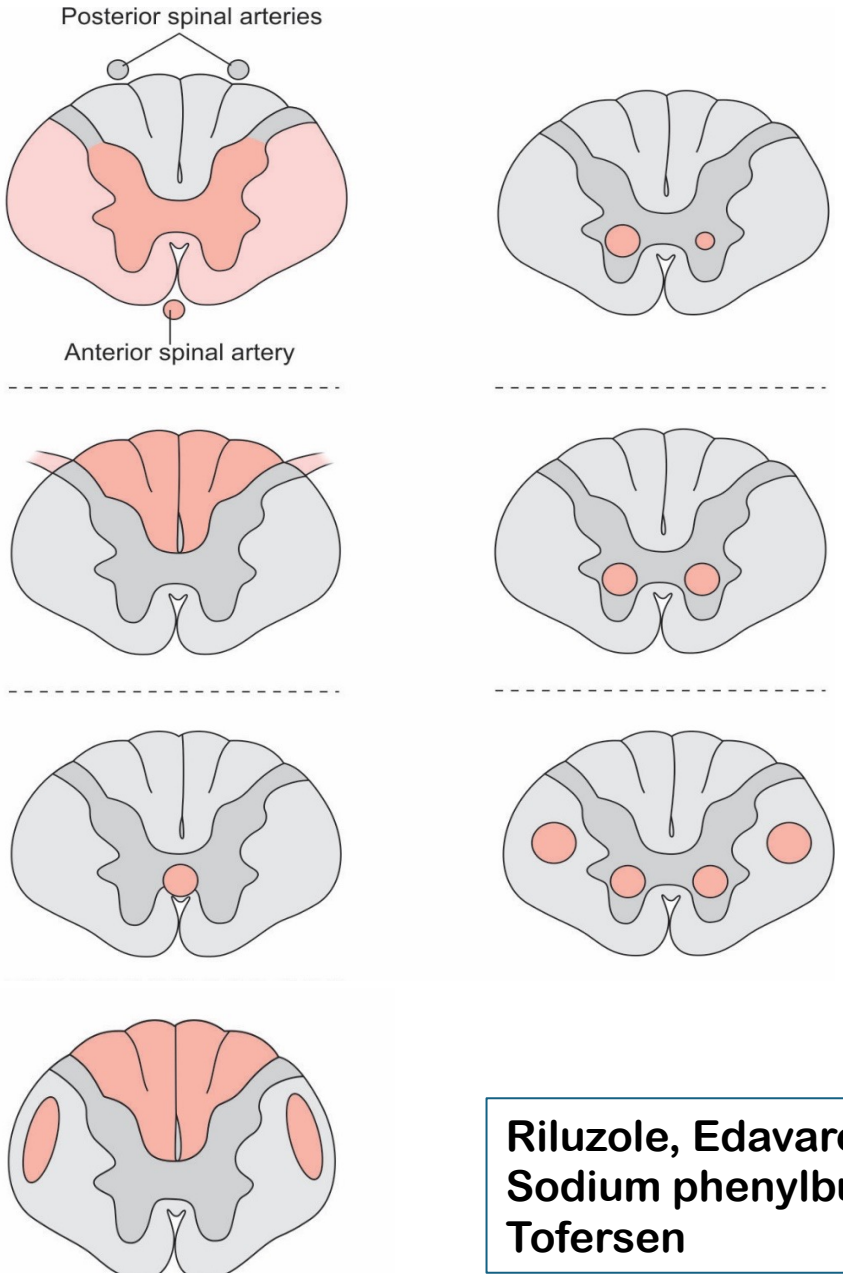


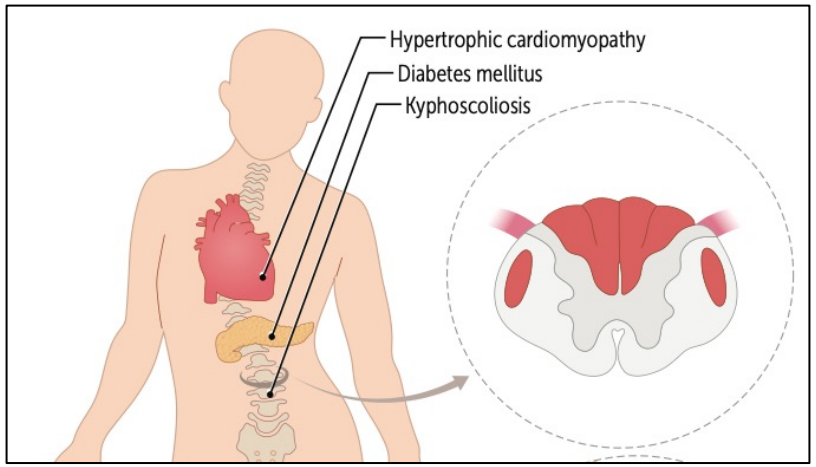




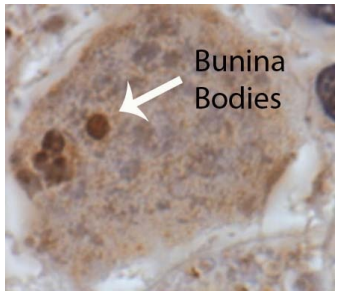
SPINAL CORD LESIONS







Nusinersen / Onasemnogene/ Zolgensma/ Risdiplam



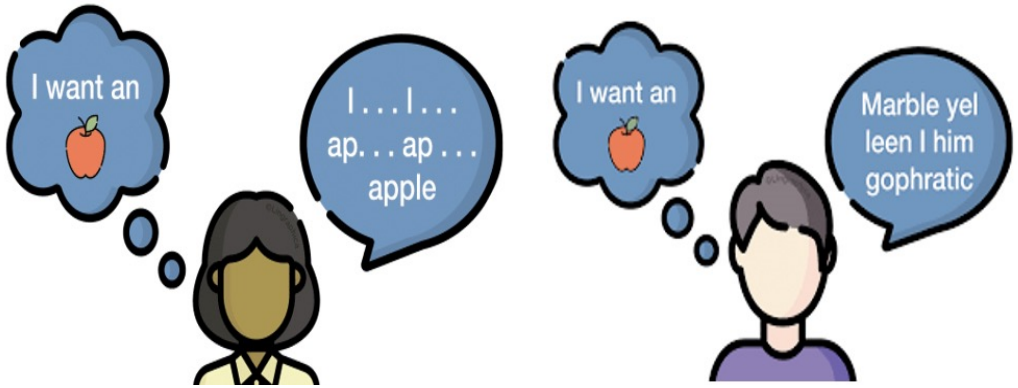
Riluzole, Edavarone
Sodium phenylbutyrate-Tursodiol
Tofersen

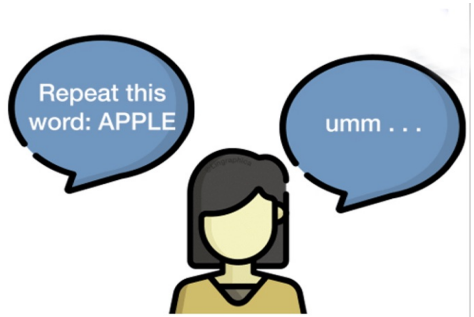
Myasthenia gravis

Weakness, ptosis, diplopia more in evening
Improves with rest
Sensory/ Autonomic/ DTR/ Bowel bladder/ Pupil
Ice-pack improvement
IOC:
Repetitive nerve stimulation
VS LEMS:

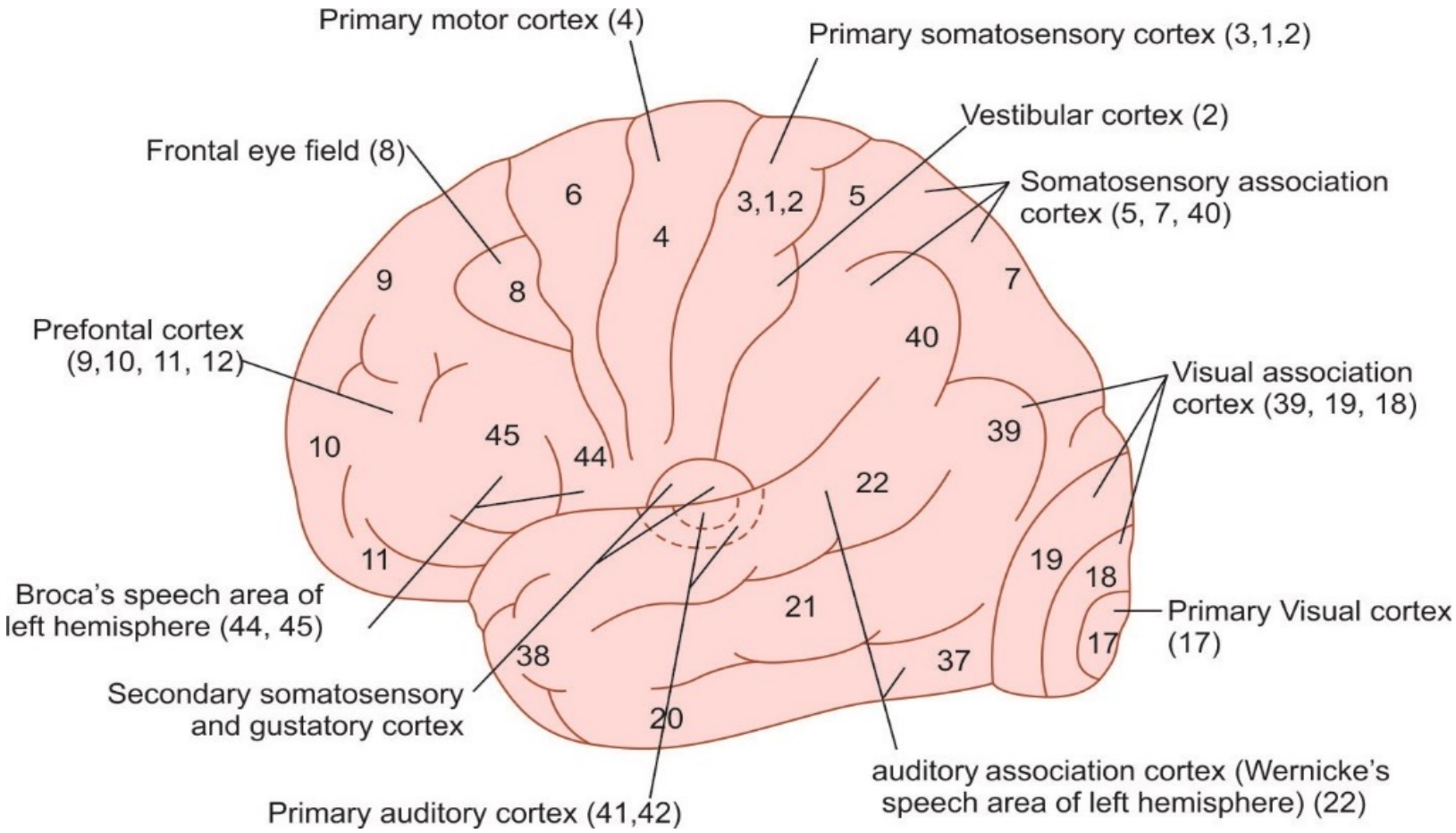
DOC: AchE-: Pyridostigmine
IVIG/ plasmapharesis in crises
Rozanolixizumab
Avoid Bblocker, CCB, FQ, Blactams, Aminoglycosides
D/D: Critical illness myopathy/ neuropathy
(proximal muscle/axonal degeneration)

Aphasia





Brodmann areas

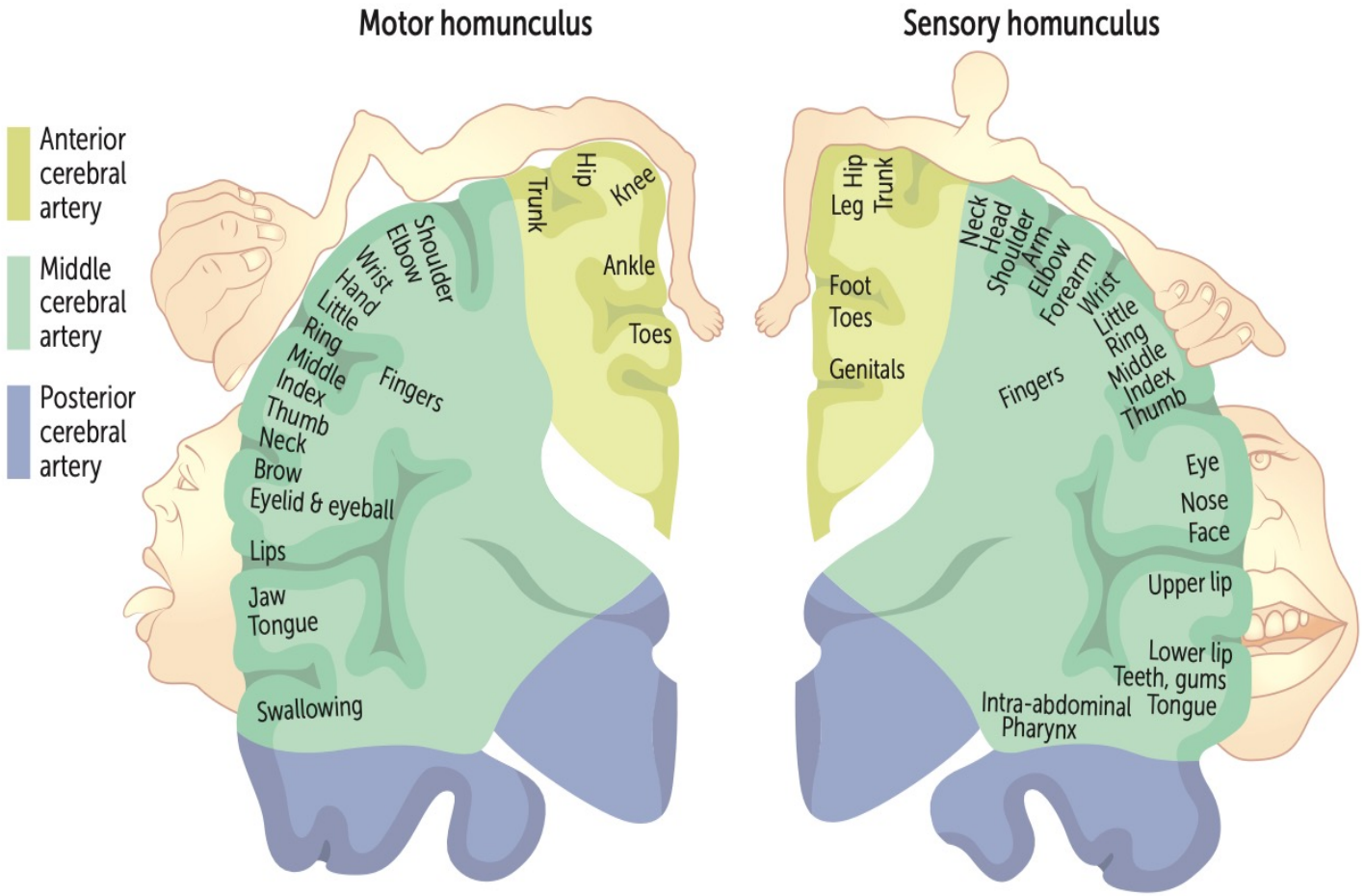


Agraphia, acalculia, finger agnosia, R-L disorientation

Phantom limb pain

Law of projection: Sensory perception is always projected to the site of the receptor, even if stimulation occurs elsewhere along the sensory pathway.

Cortical plasticity-Reorganization of the primary somatosensory cortex S1

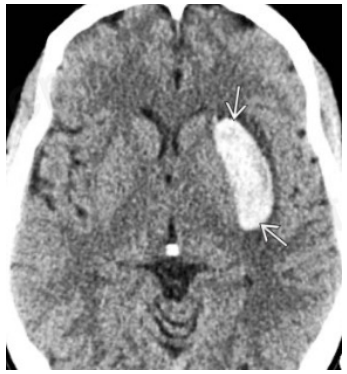

Motor homunculus
Sensory homunculus
Anterior cerebral artery
Middle cerebral artery
Posterior cerebral artery
Hip
Knee
Trunk
Ankle
Toes
Shoulder
Elbow
Wrist
Hand
Little
Ring
Middle
Index
Thumb
Fingers
Neck
Brow
Eyelid & eyeball
Lips
Jaw
Tongue
Swallowing
Hip
Trunk
Leg
Foot
Toes
Genitals
Neck
Head
Shoulder
Arm
Elbow
Forearm
Wrist
Little
Ring
Middle
Index
Thumb
Fingers
Eye
Nose
Face
Upper lip
Lower lip
Teeth, gums
Tongue
Intra-abdominal
Pharynx

STROKE-APPROACH

FACE – One side of face drooping
ARMS – Weakness in arm
SPEECH – Slurred speech
TIME – Time to call EMS

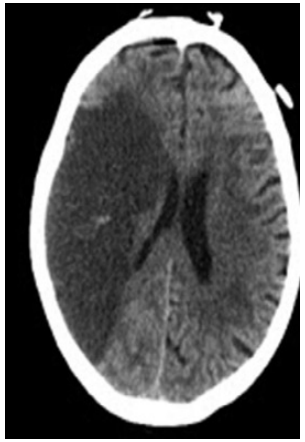
Focal neurological deficit

1st:
Best/ Most sn:



Hemorrhage

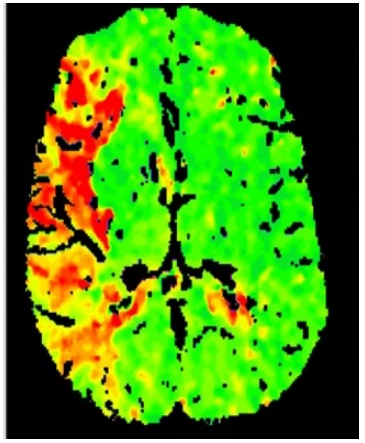
Ischemic



BP > 185/110
Bleeding diathesis
Recent head injury or ICH
Major surgery in last 2 weeks
GI bleed in 3 weeks
Recent MI

Window:
CI to thrombolytic?

Dose (alteplase):



Brief, reversible with normal MRI

Penumbra+ major vessel:

- **Age ≥ 60 years** – 1 point
- **BP ≥ 140/90 mmHg** at initial evaluation – 1 point

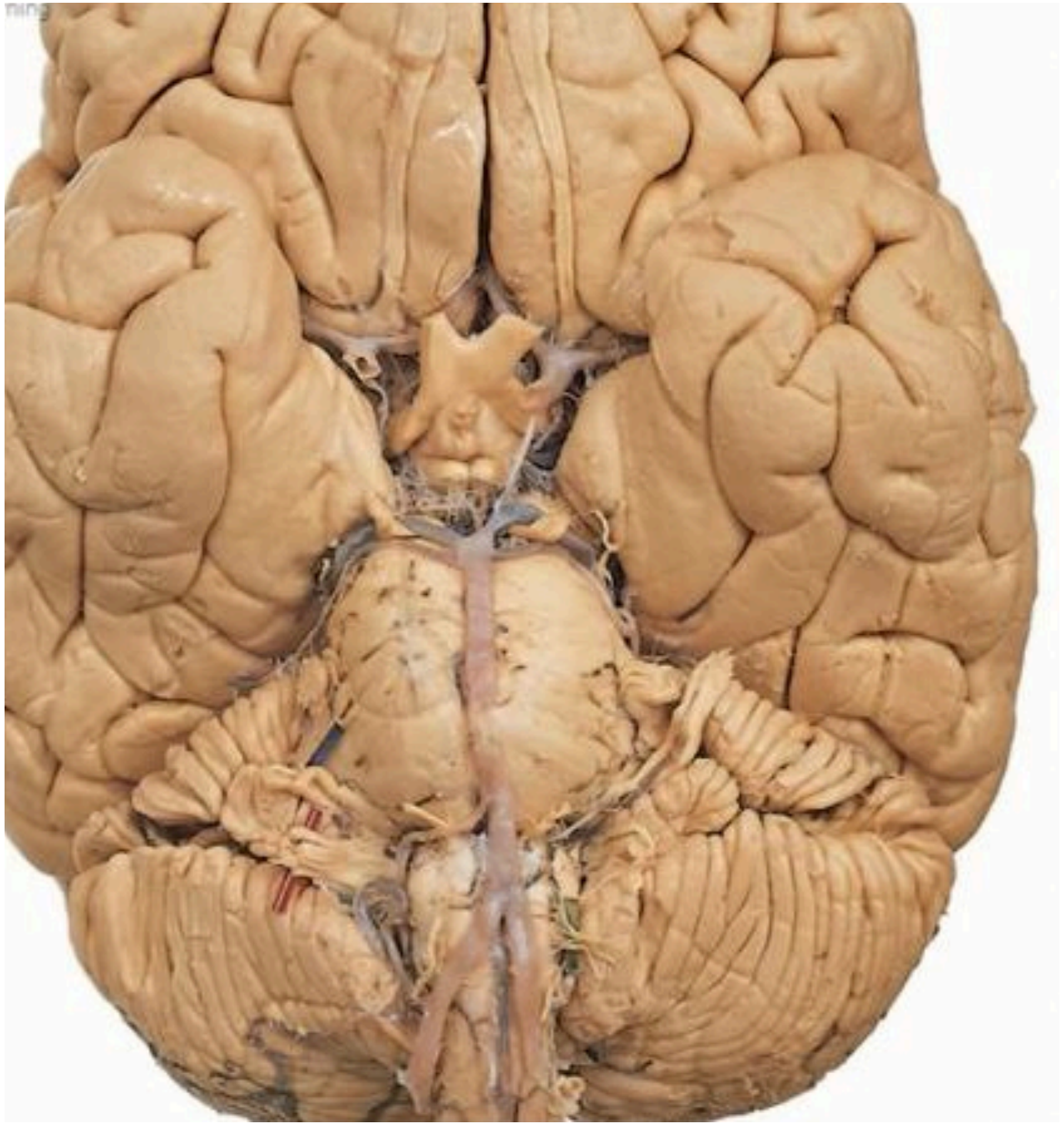
Clinical features of TIA

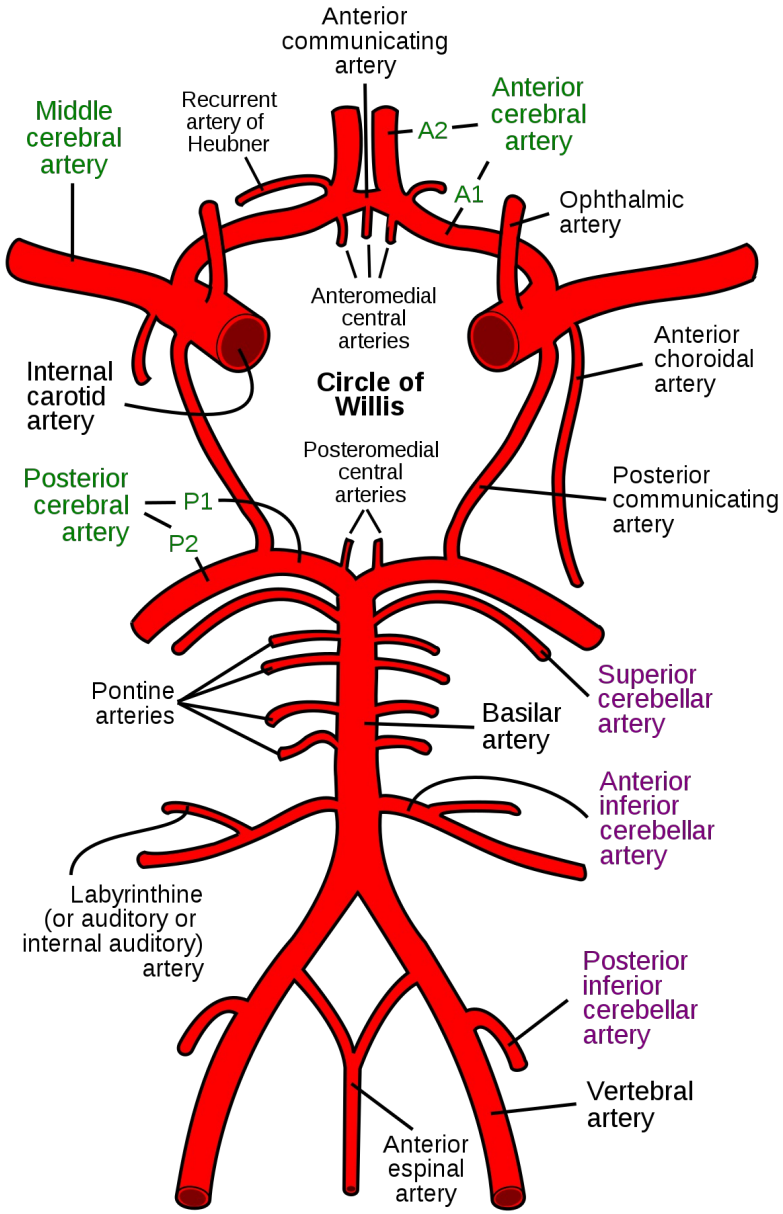
- Speech disturbance without weakness – 1 point
- Unilateral weakness – 2 points

Duration of symptoms

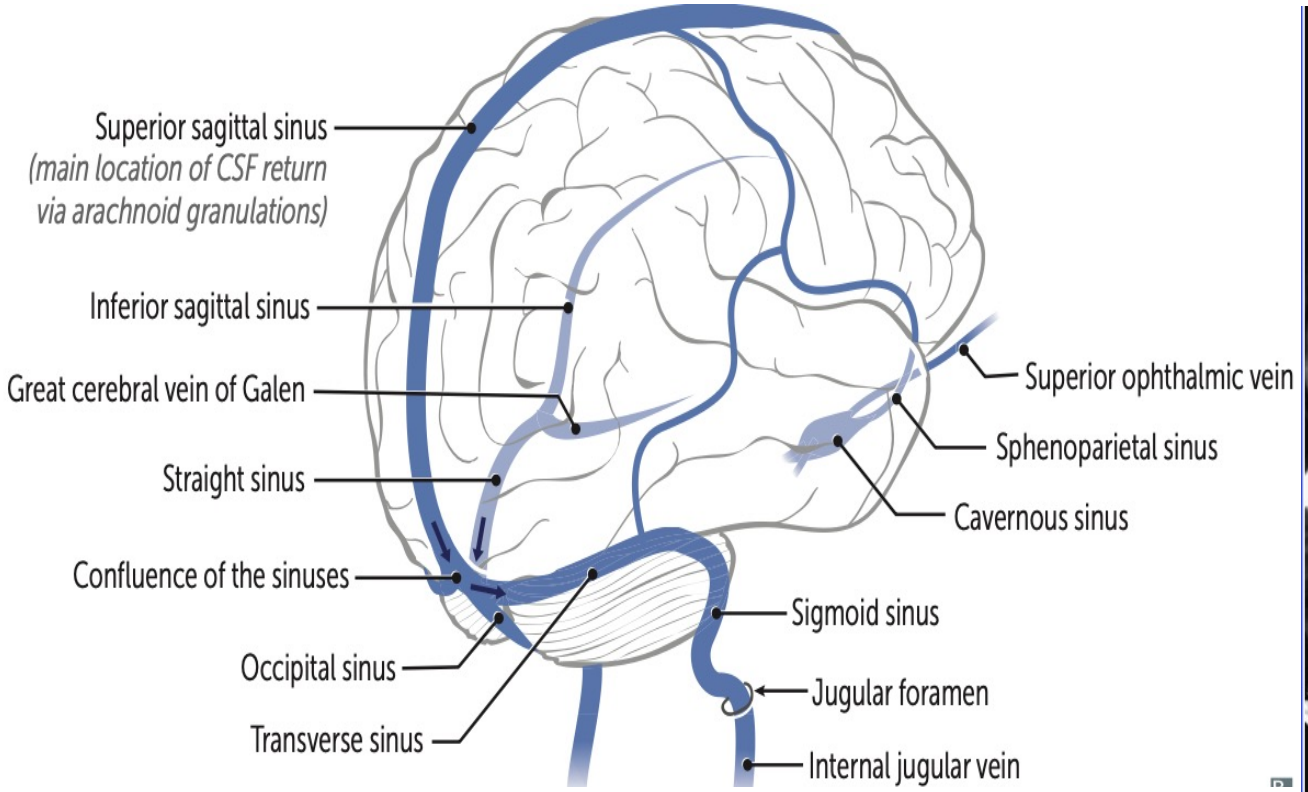
- 10–59 minutes – 1 point
- ≥ 60 minutes – 2 points
- **Diabetes mellitus** in patient's history – 1 point

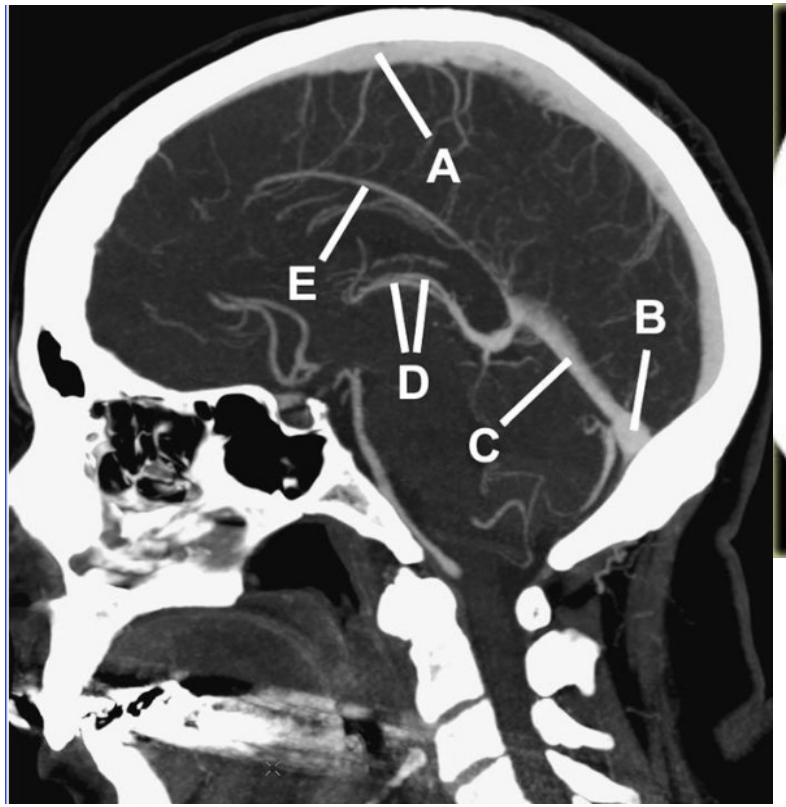
VASCULAR ANATOMY OF BRAIN

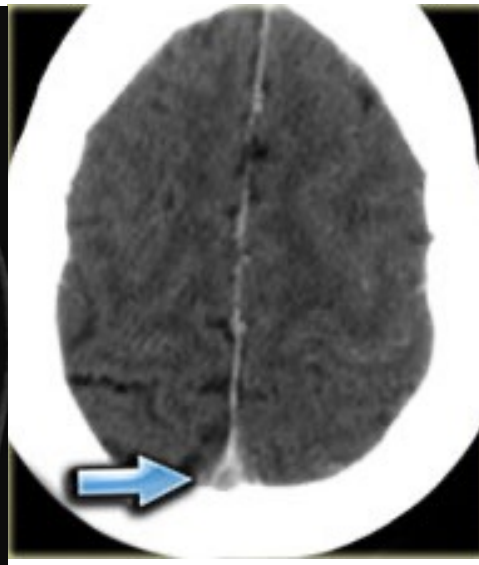




Dural venous sinuses





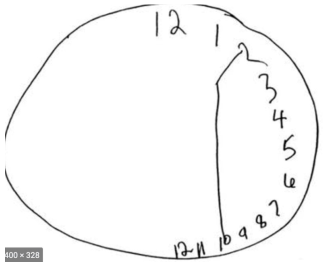


STROKE LOCALISATION

C/L paralysis and sensory loss: lower limb + Urinary incontinence + Personality changes

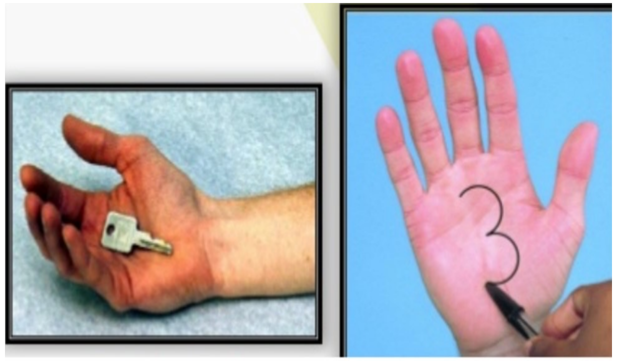
C/L paralysis and sensory loss: face and upper limb + Aphasia

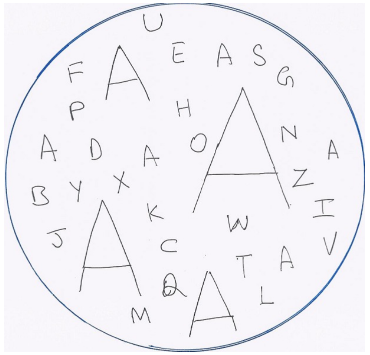
C/L paralysis and sensory loss: face and upper limb +

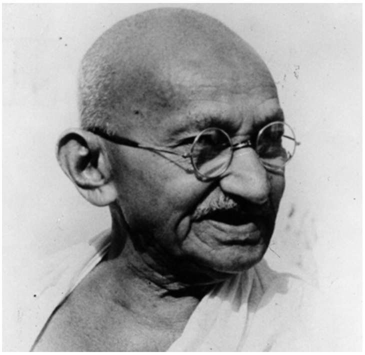


C/L hemianopia + Denial of blindness + Alexia without agraphia (Dominant)

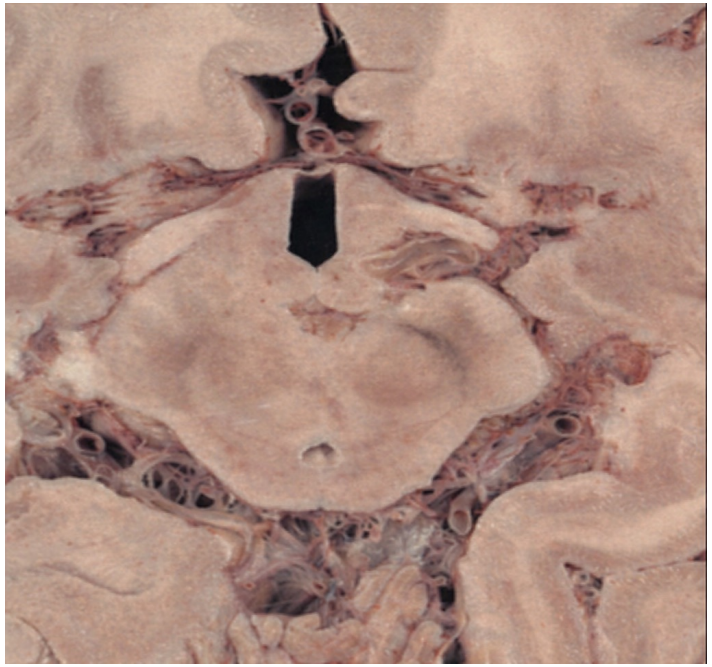
C/L hemisensory loss followed by an agonizing, burning pain in the affected areas

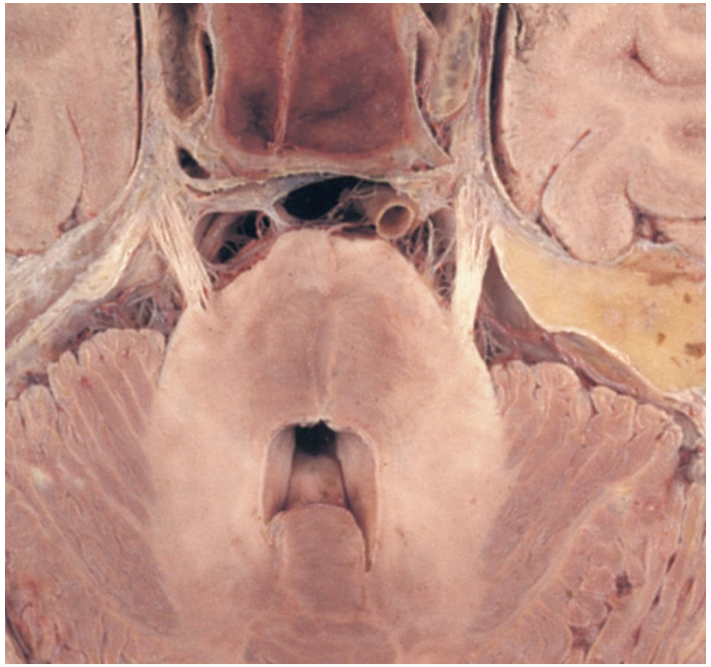


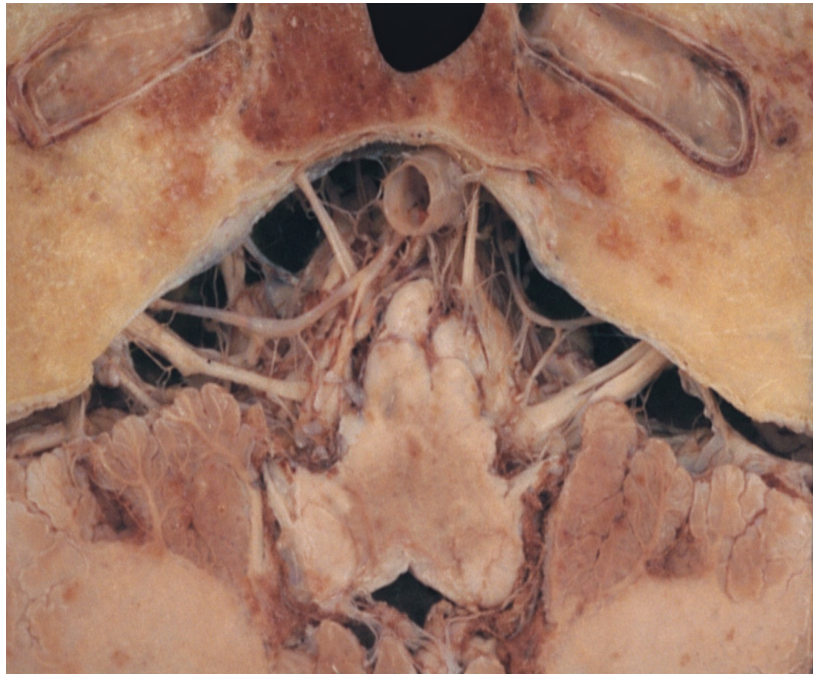


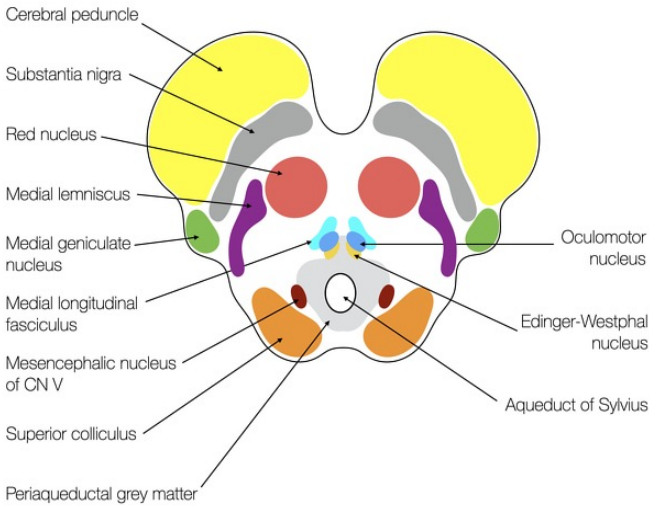


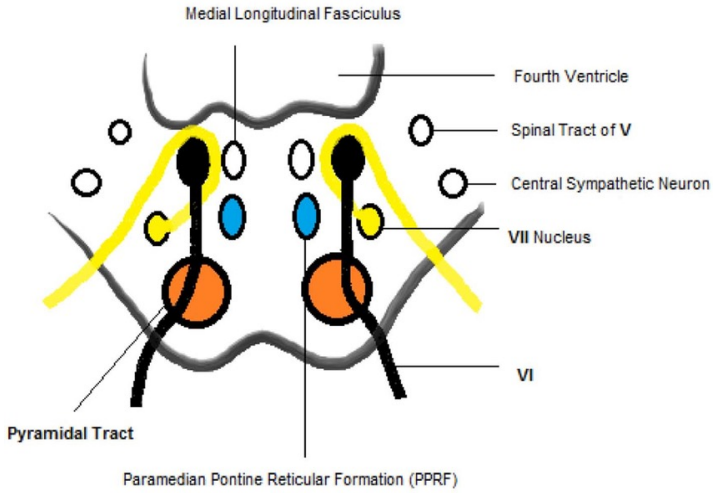
BRAINSTEM-ANATOMY

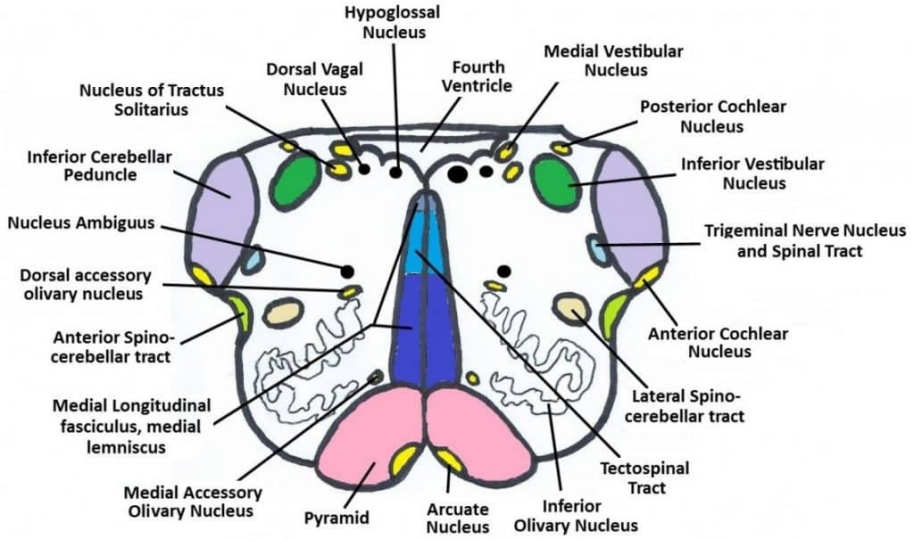




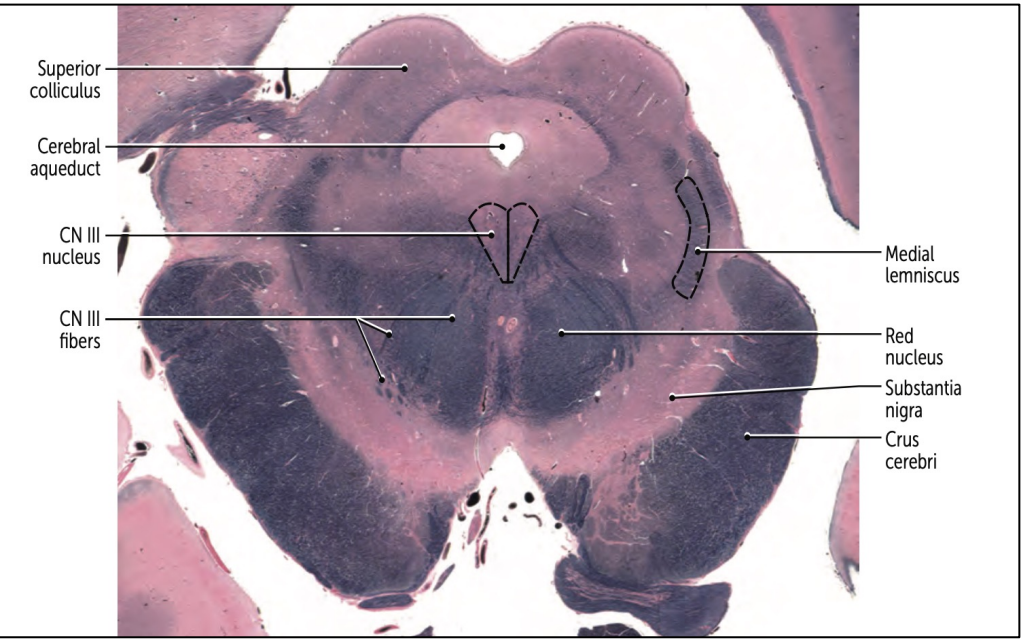


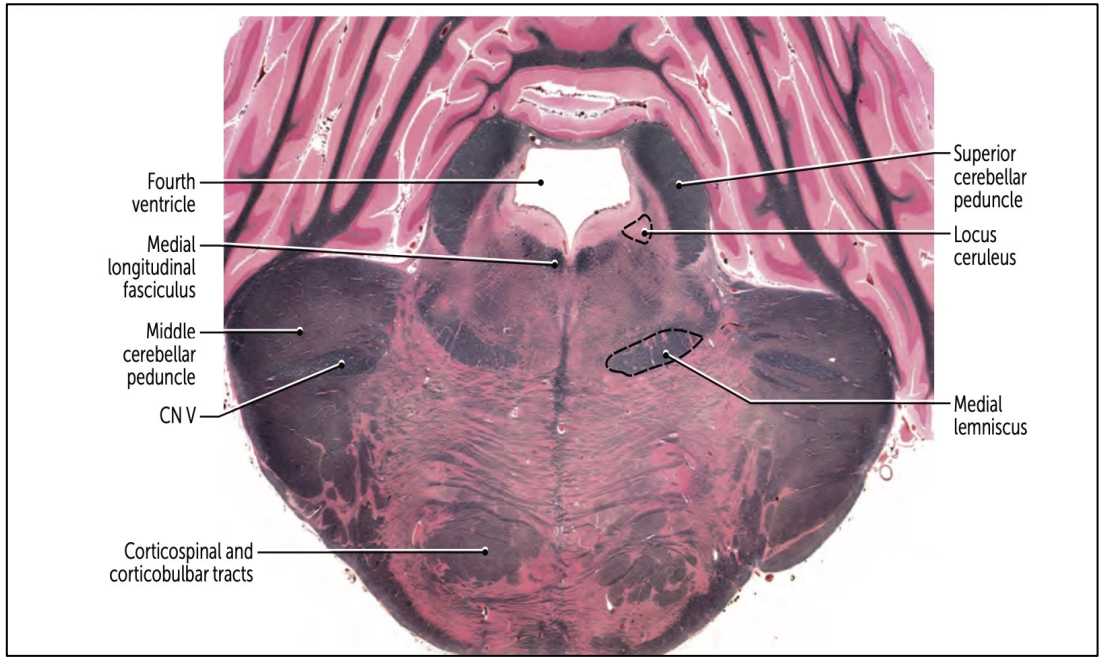


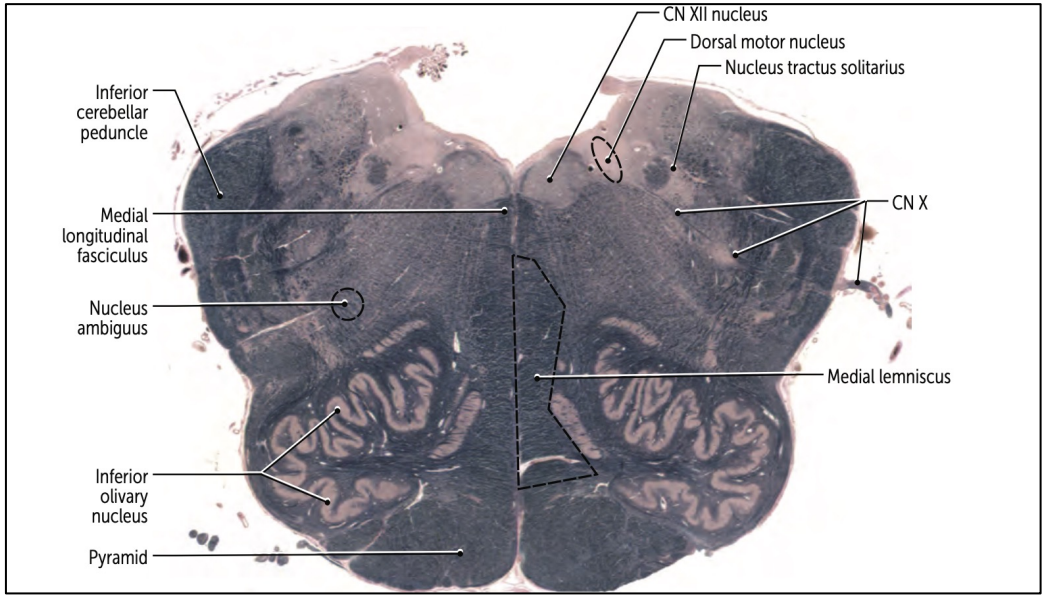




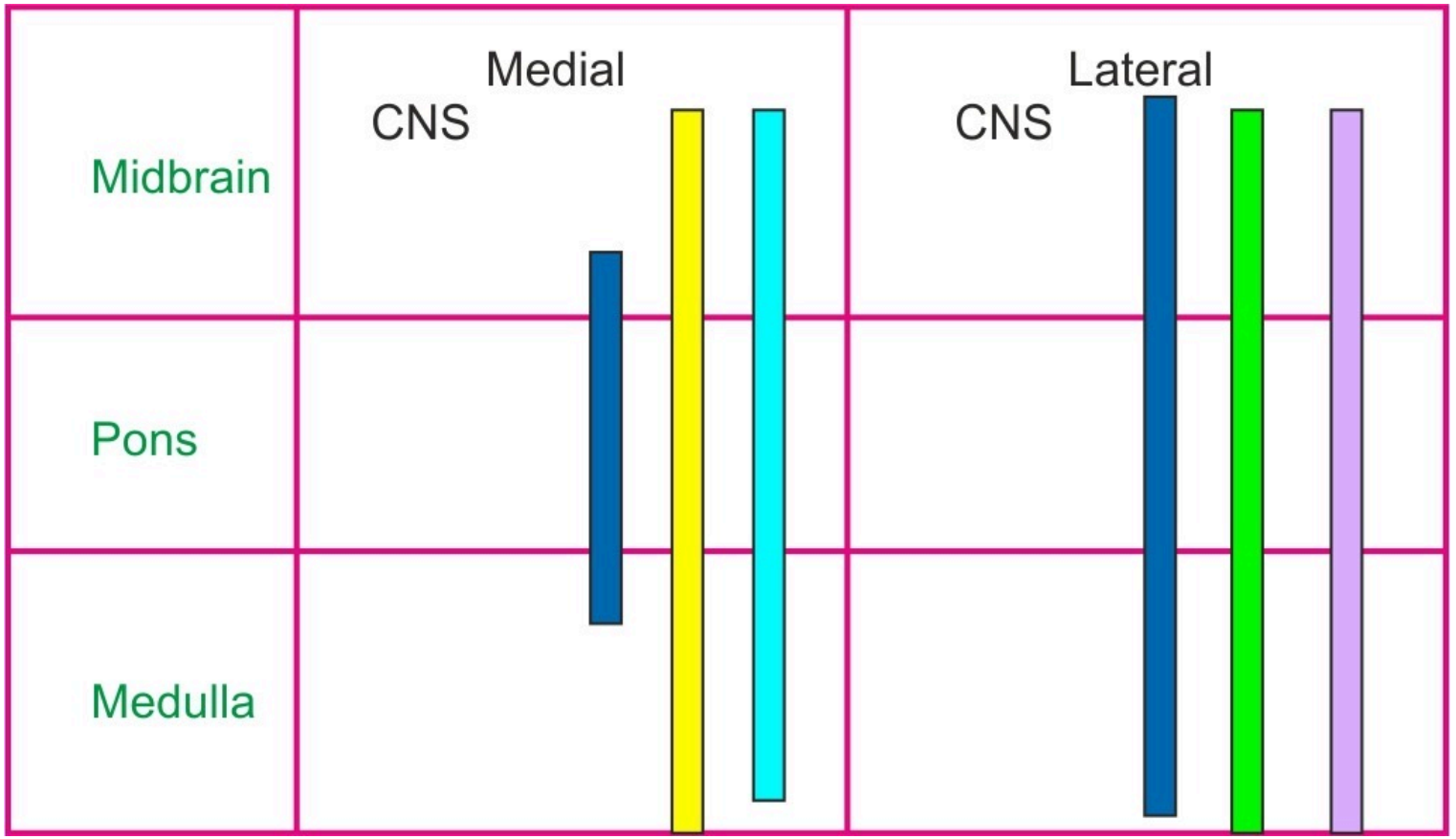
BRAINSTEM-HISTOLOGY







BRAINSTEM STROKE



BRAINSTEM STROKE SYNDROMES

C/L hemiplegia + I/l down and out pupil

C/l hyperkinesis, chorea, tremor (red n)+ i/l down and out pupil

I/L cerebellar ataxia + i/l down and out pupil

C/L hyperkinesis, chorea, tremor + ataxia + i/l down and out pupil

Upward gaze palsy + Collier sign-eyelid retraction

C/l hemiplegia+ i/l CN 6 + 7

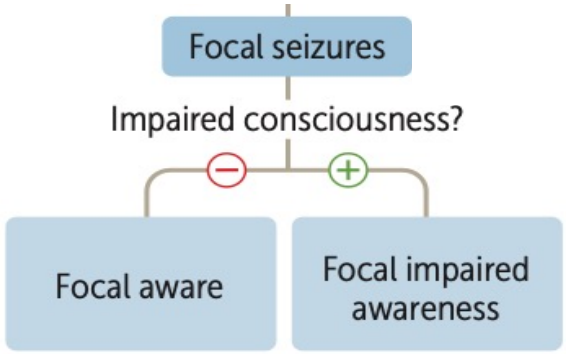
C/l hemiplegia, hemisensory loss+ i/l CN 6 + 7 + 8 CN palsy + Horizontal gaze palsy

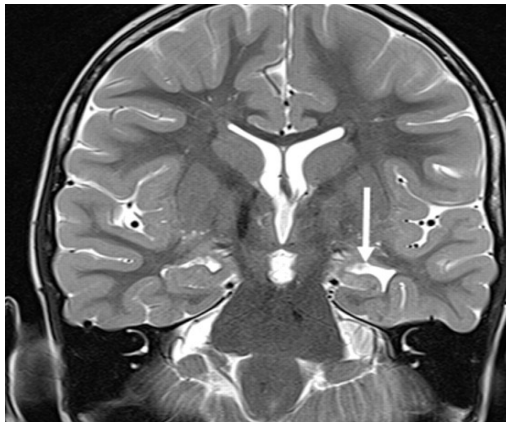
C/l hemiplegia+ i/l CN 6 palsy

C/l hemiplegia + i/l tongue deviation

Loss of pain, temp from c/l body, i/l face, Horner's, Dysphagia, hoarseness, loss of gag

Seizures

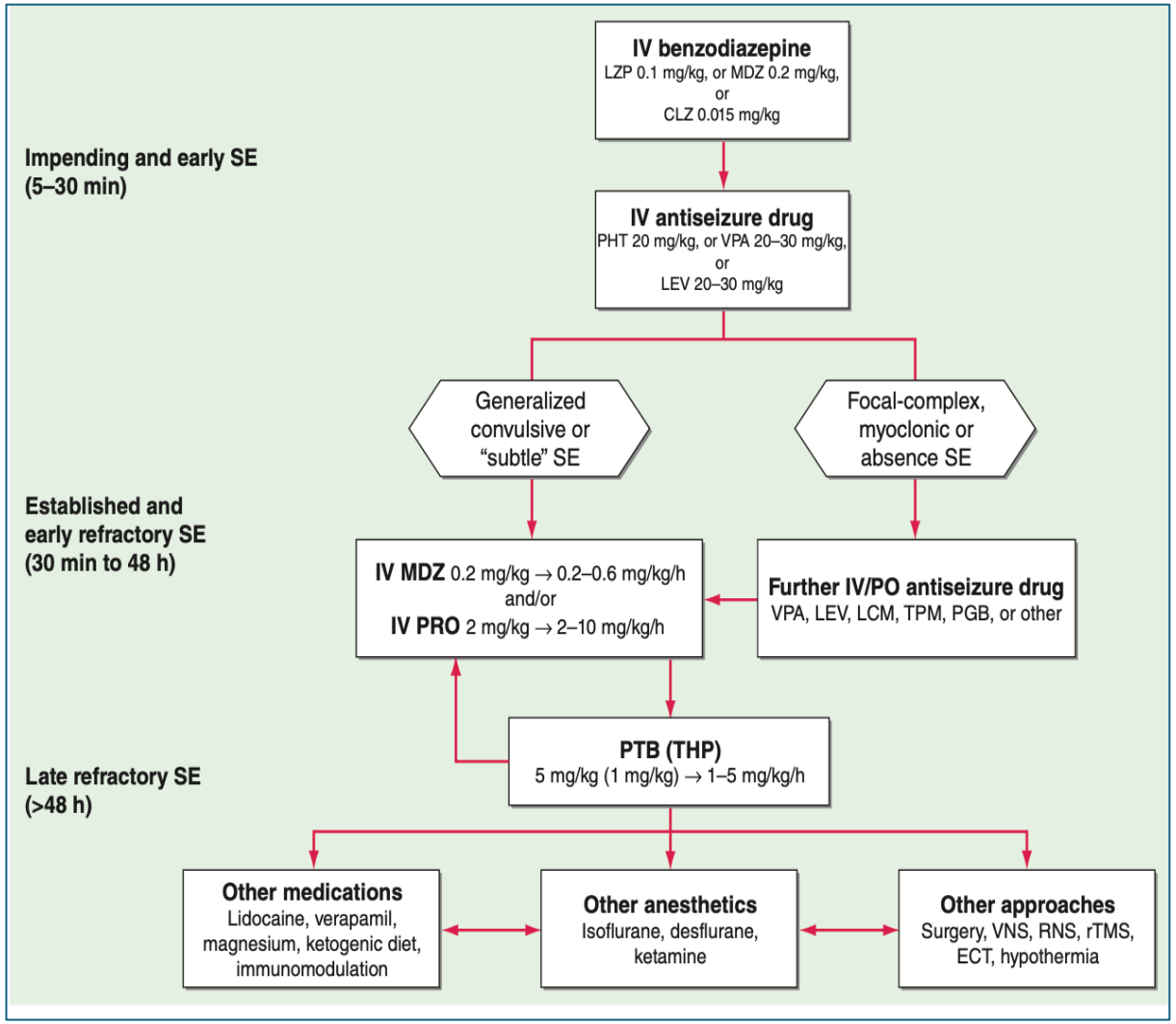




Jacksonian march
Todd palsy
DOC focal seizure
DOC focal seizure in elderly

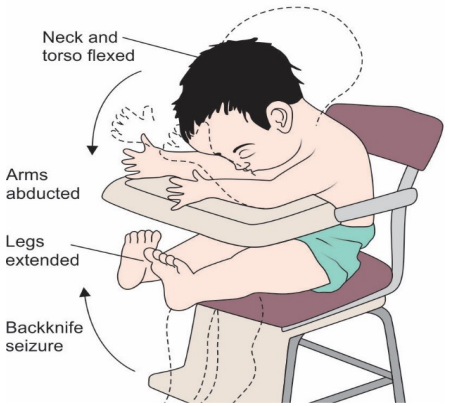
When to discontinue:
Seizure freedom > 2 years
Poor prognosis:
- Age ≥ 16 years
- More than one AED required
- Seizures after starting AED therapy
- History of generalized tonic–clonic seizures
- History of myoclonic seizures / JME
- Abnormal EEG in the prior year

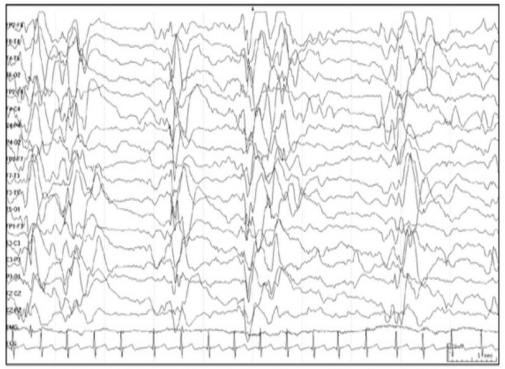
Status epilepticus — continuous seizures lasting ≥ 5 minutes or recurrent seizures without return to baseline consciousness between episodes



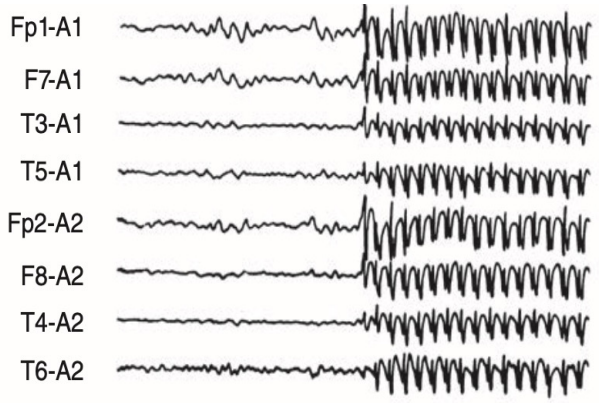
EPILEPSY SYNDROMES

Infant + Global developmental delay
DOC:
DOC in TSC:

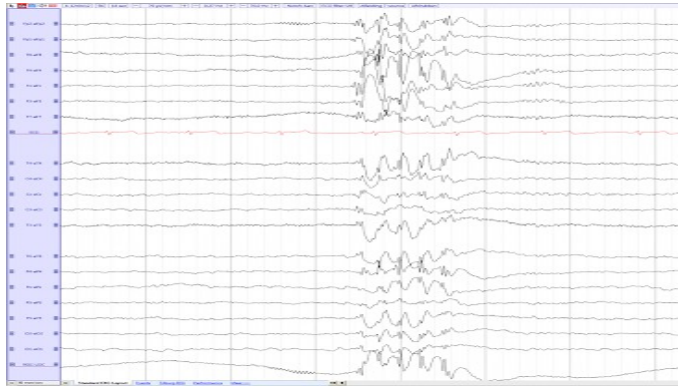




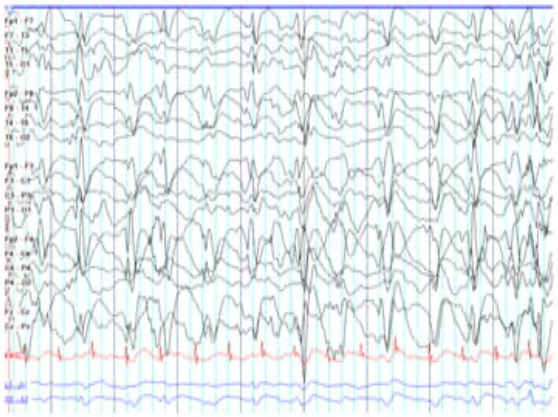
-Transient loss of consciousness (1-2s)
-No loss of postural control
-3Hz Spike and slow wave pattern
DOC Typical:
DOC Atypical:



MC in Adolescent
Early morning "clumsy"
3-6 Hz generalized polyspike and wave discharge
GABRA1,CLCN2
DOC:



Multifocal sz
1-2Hz spike and wave pattern
DOC:
BZD approved:



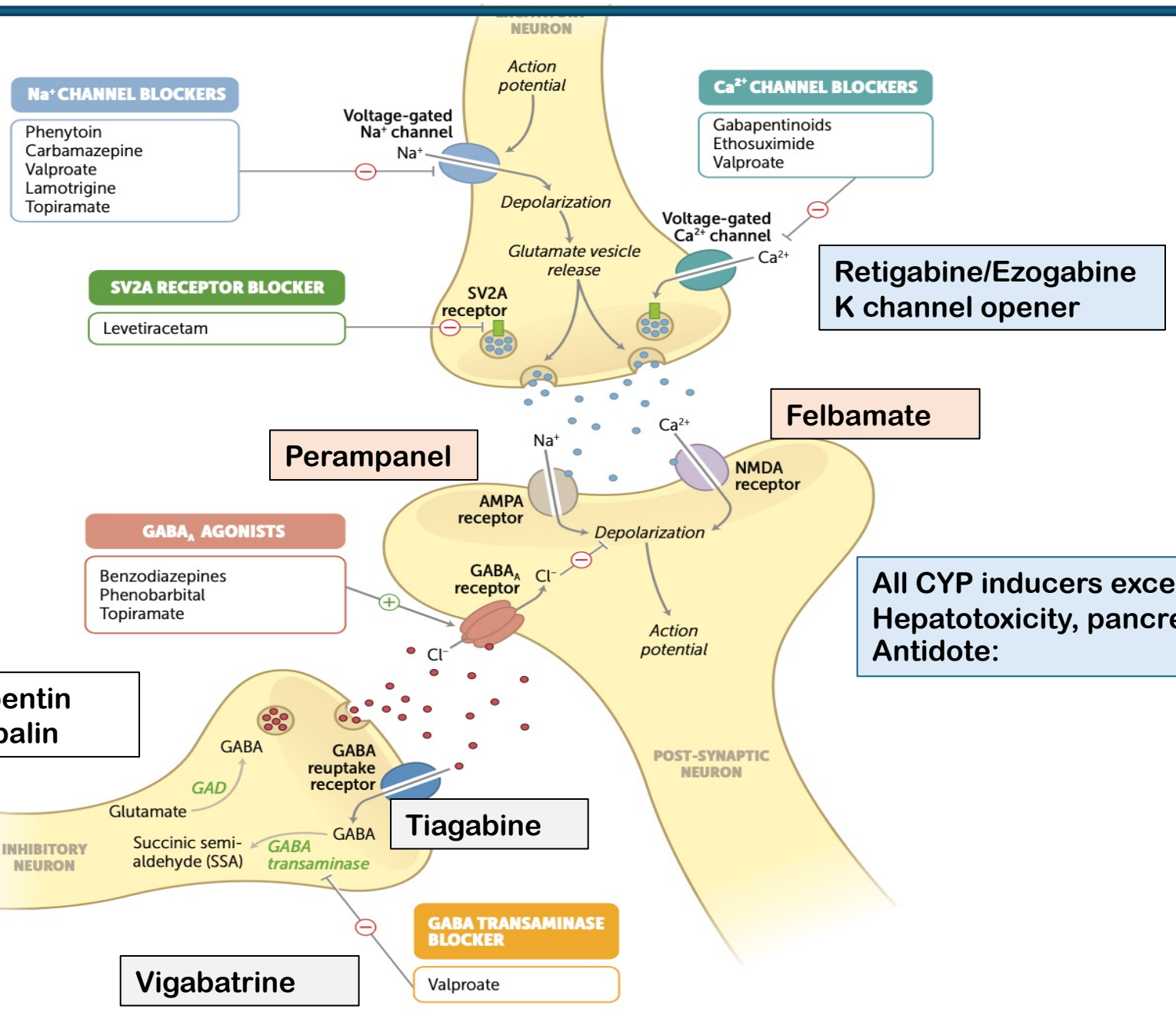
SLC2A1: GLUT1
SCN1A: Dravet syndrome

ANTI-EPILEPTIC DRUGS

s/e Agranulocytosis, SJS
SIADH
Stones / ACG/ wt loss:

Cerebellar toxicity, gingival hypertrophy, hirsutism, hepatotoxicity, osteoporosis, NTD, Purple glove Sx, Pseudo-lymphoma, megaloblastic anemia

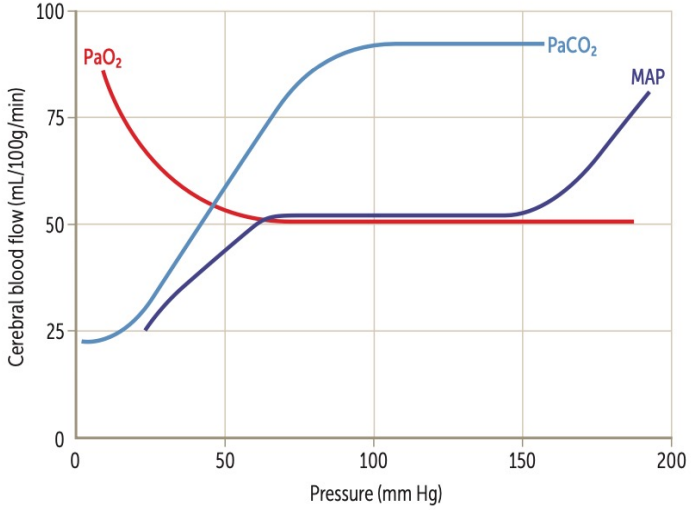
Lacosamide

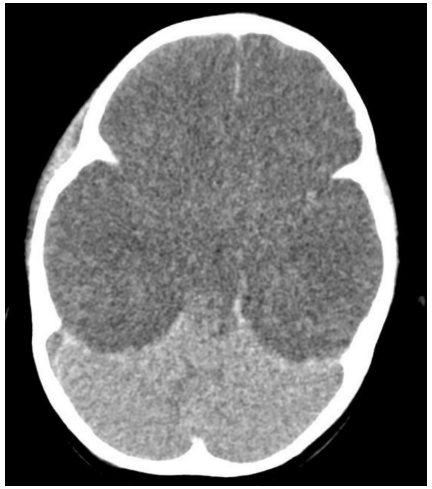


Raised ICP – Brain death

Cushing triad:
CPP=MAP-ICP
Target: ICP<20mm and CPP >60mm

1. Elevate head end
2. Ventriculostomy
3. Mannitol
4. Steroid –CI in head trauma / stroke/ hemorrhage –Use in tumor, abscess
5. Hyperventilation
6. Vasopressors





GCS 3/15
Apnea test
(Preoxygenate -> pCo2 >60mm)
Brainstem reflex:
Spinal reflex:
No motor function or posturing
EEG silent

Purposeful blinking, vertical gaze
Quadriparesis
Self-awareness+
Normal respiration/EEG/metabolism

Posture	Level of lesion	Tracts affected
Decorticate	Above red nucleus (midbrain)	C/S disrupted Rubrospinal tract active
Decerebrate	At or below red nucleus	C/S and rubrospinal tracts disrupted (vestibulospinal dominance)