

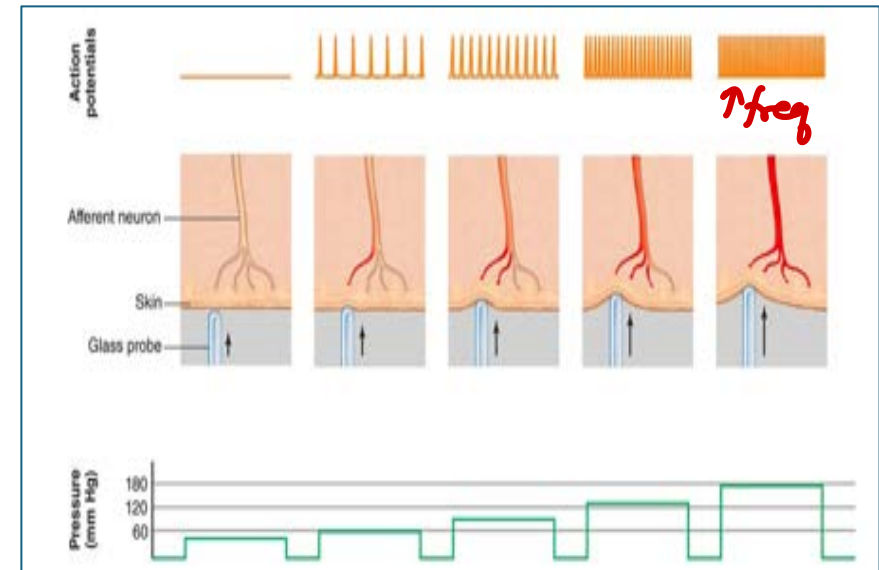
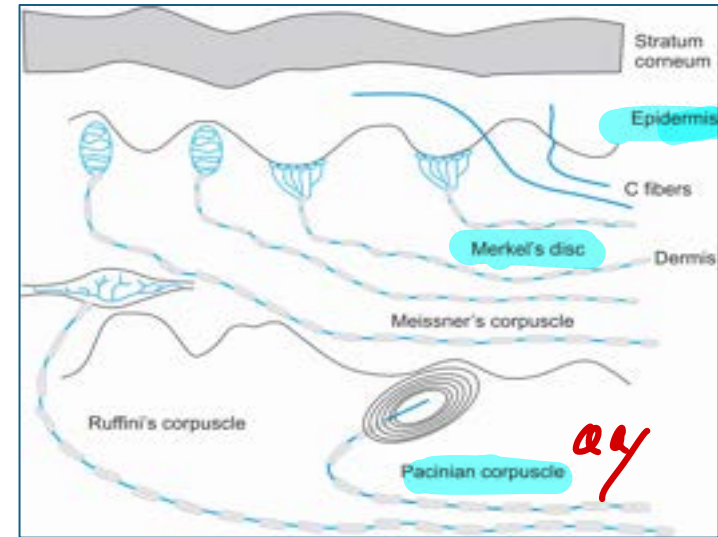
INTEGRATED NEUROLOGY



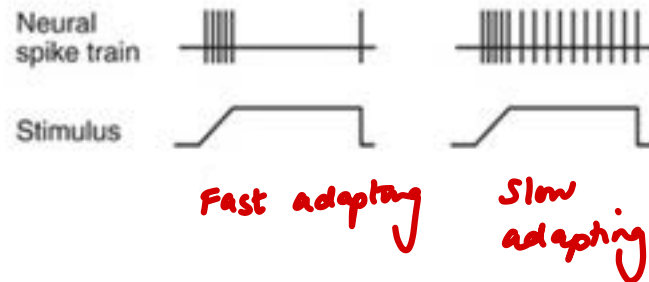
Sensory Receptors

RECEPTOR	ADAPTATION	REMARKS
Meissner	FAST	Most numerous Non-hairy skin only Fast moving touch, two-point discrimination
Pacinian	FAST	Largest receptor Most sensitive HIGH FREQUENCY VIBRATION
Hair end	FAST	Hair movement
Merkel	SLOW	Epidermis- Edge BRAILLE
Ruffini	SLOW	Skin stretch, pressure Maximum in joint capsule
type c	SLOW	Itching, <u>Slow pain</u> (Substance P)

max: lips
min: back



freq coding law = Weber-Fencher law
↑ stimulus ↑ perception



(unmyelinated)

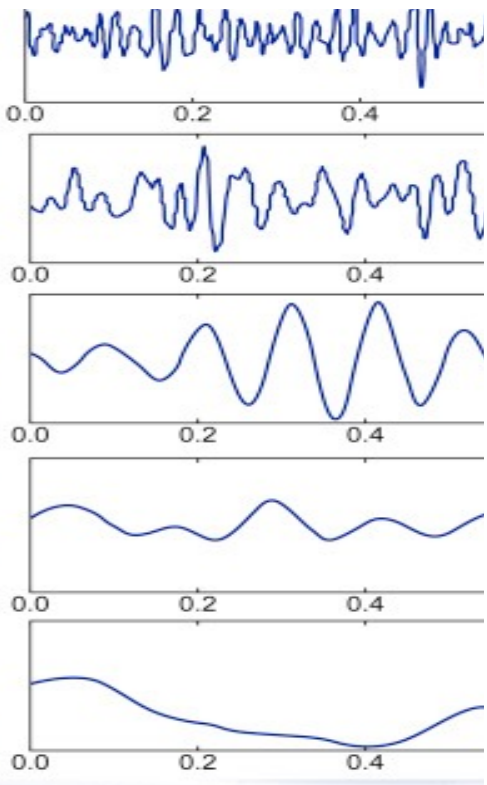
Erlanger-Grasser: Nerve fibres

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, 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: $A\delta$
- Warm, burning pain and freezing pain: C
- Local anaesthetic: $A\gamma$ and $A\delta \gg A\alpha$ and $A\beta \gg B \gg C$ "GAD"
 Least sm
- Pressure: $A > B > C$
- Hypoxia: $B > A > C$

SLEEP PHYSIOLOGY

Good BAT Dance



Gamma → problem solving
 = meditator
 B → awake, eyes open
 α → awake, eyes closed
 θ → light sleep
 δ → deep sleep

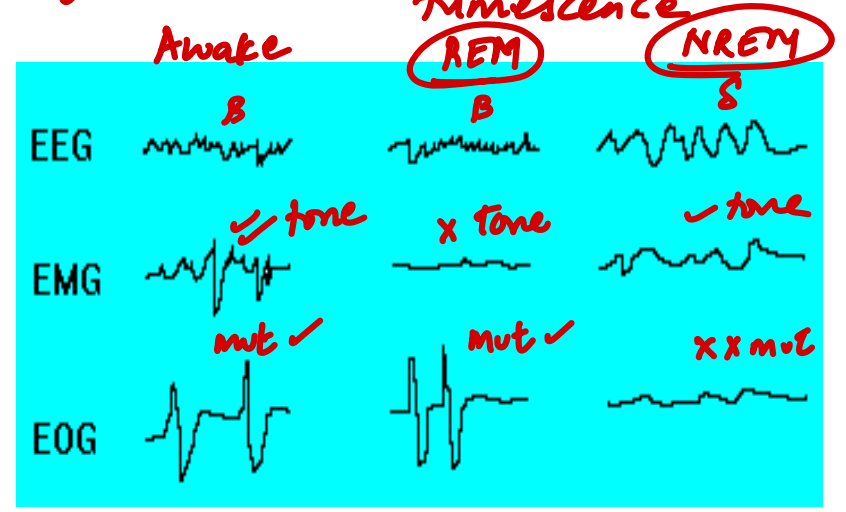
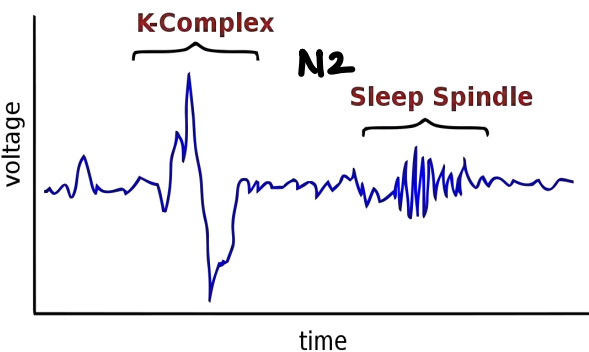
Awake (eyes open)	Beta	
Awake (eyes closed)	Alpha	
Stage N1 (5%)	Theta	
Stage <u>N2</u> (45%)	<u>Sleep spindles, K complexes</u>	<u>Bruxism</u>
Stage N3 (25%)	Delta	<u>Bedwetting, sleepwalking, Night terrors</u>
<u>REM sleep</u> (25%)	Beta, <u>PGO</u>	<u>Nightmares</u>

BZD ↓

Paradoxical

loss of motor tone / penile tumescence

Reduced REM Latency:
 - Depression - Narcolepsy
Elderly: Low REM, Low N3



Hypothalamic nuclei

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

⊕ → Hunger, Angry

⊕ → Satiety, Reward centre

"AC" ⊕ → Cooling → vasodilⁿ / Sweating

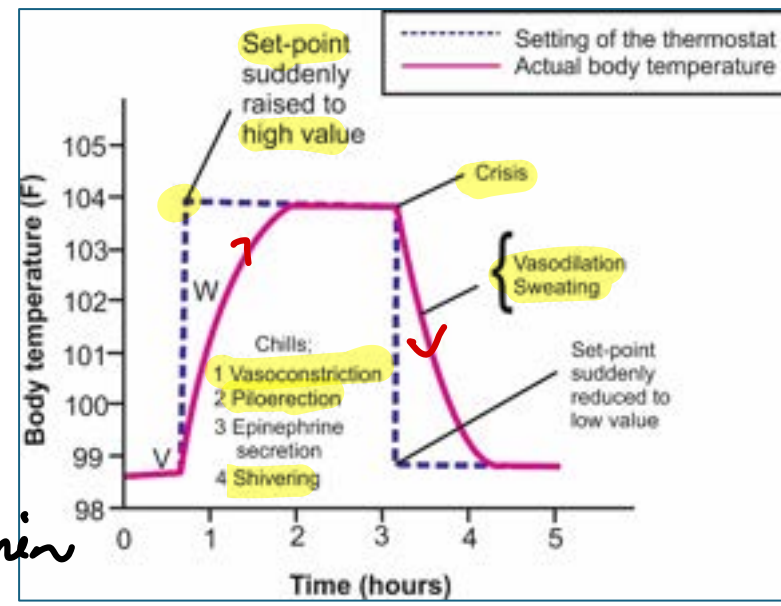
⊕ → Δ → VC / shivering

- circadian rhythm - Pineal: melatonin

→ ADH

→ oxytocin

→ Mint, sexual fn, GnRH



T_{1w}
 |
 post pit
 hot spot

↓ x
Kallman Sx

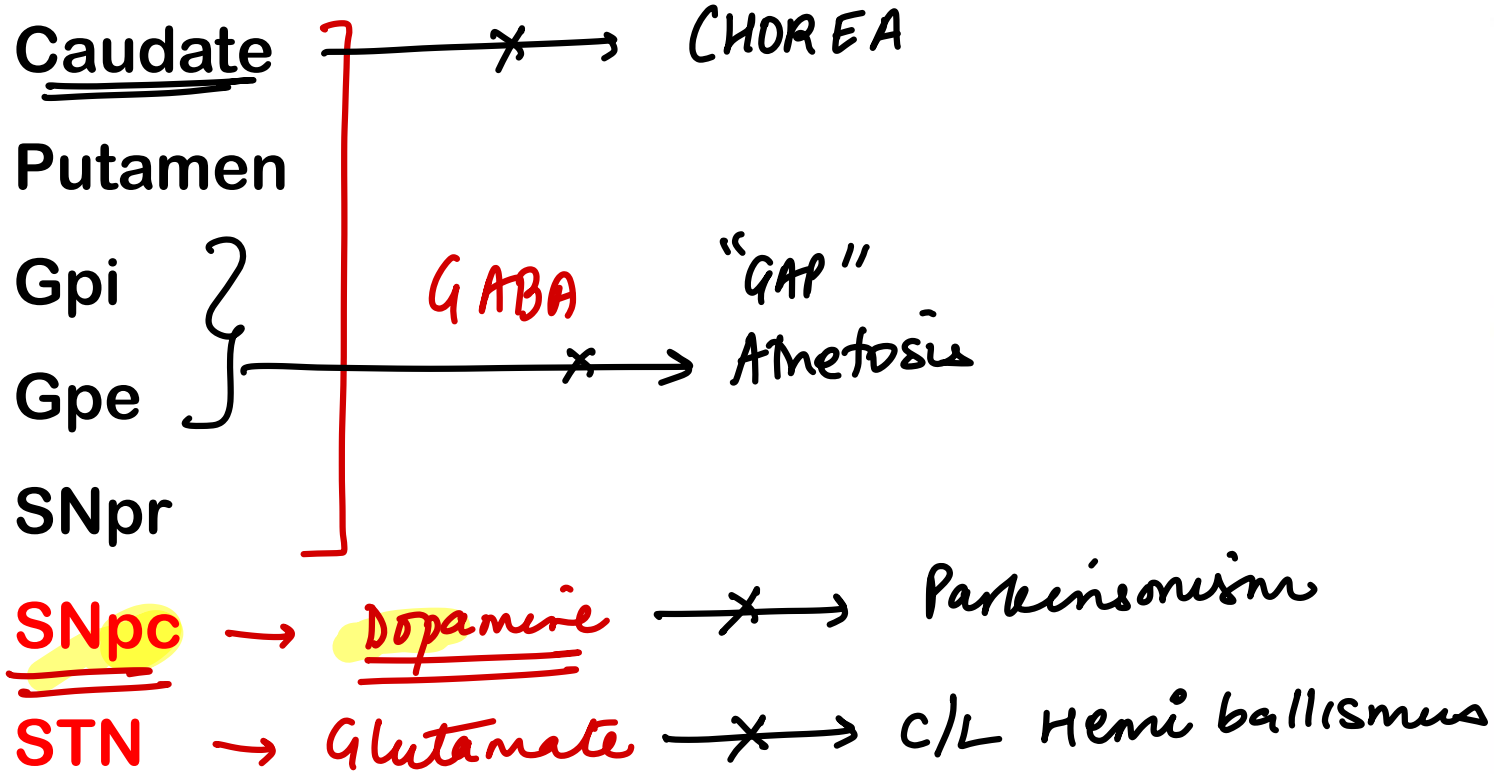
Thalamic nuclei

Nuclei	Input	Senses	Destination
Ventral Postero-Lateral (limbs)	SN → <u>DC</u> / <u>ST</u>	jt sense / propri / pain temp	3, 1, 2
Ventral Postero-Medial	SN → face	taste / SN face	3, 1, 2
Lateral geniculate nucleus	SC / optic radn / tract	①	vision → 17
Medial geniculate nucleus	IC	hearing	auditory → 41, 42
Ventral anterior / lateral	<u>BG</u> / <u>cerebellum</u>	Motor	1° motor ④

EECOLIMA
 // // // //

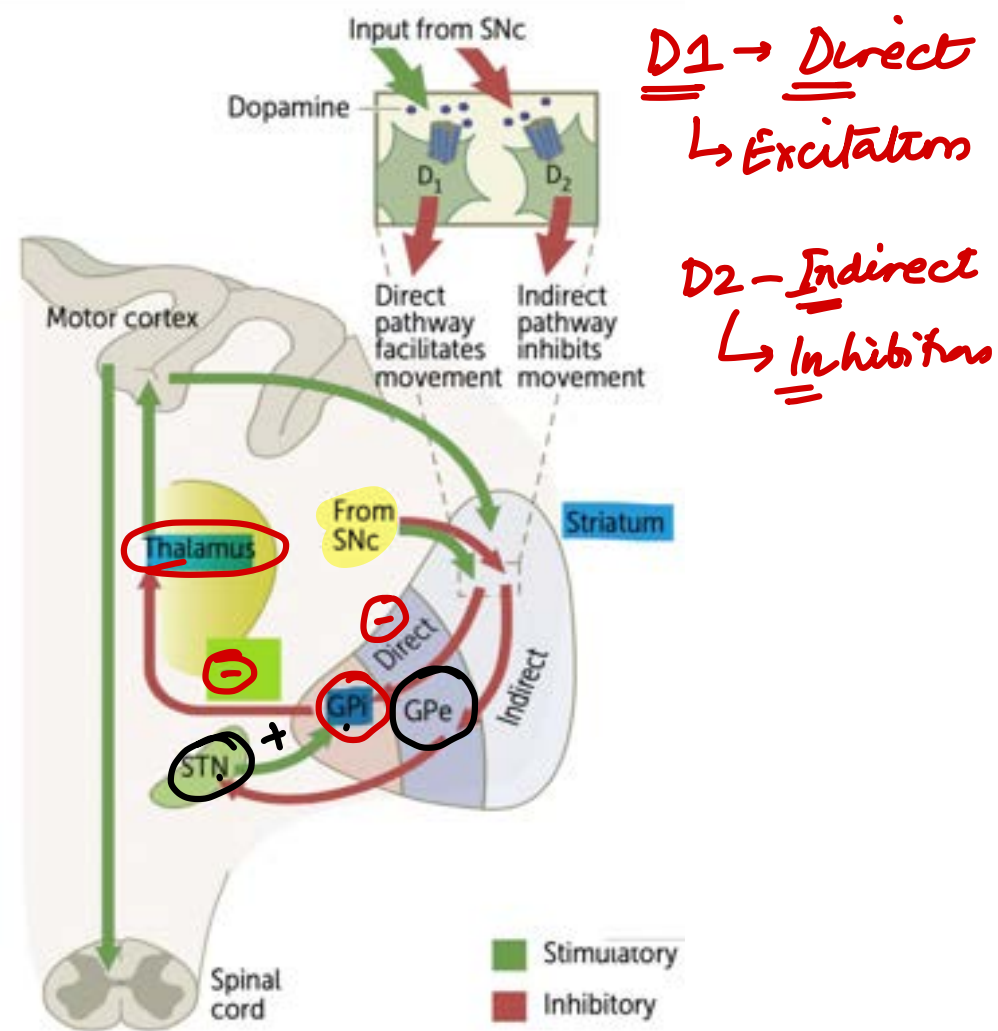
taste → ④③

Basal Ganglia



Essential tremor

High-frequency tremor with sustained posture
 Tremor increases with activity, anxiety
 Decreases with alcohol
 Familial
 DOC: Propranolol



Movement disorders

Parkinsonism

- Tremors *Rest, pill rolling*
- Rigidity
- Akinesia/bradykinesia
- Postural instability
- Micrographia
- Mask like facies
- Shuffling gait
- Late-Dementia, Depression

R₁ → Dopa ↑

Lewy body dementia

PSNP

Visual hallucinations + Dementia

Impaired downward gaze



Hummingbird

MSA-C

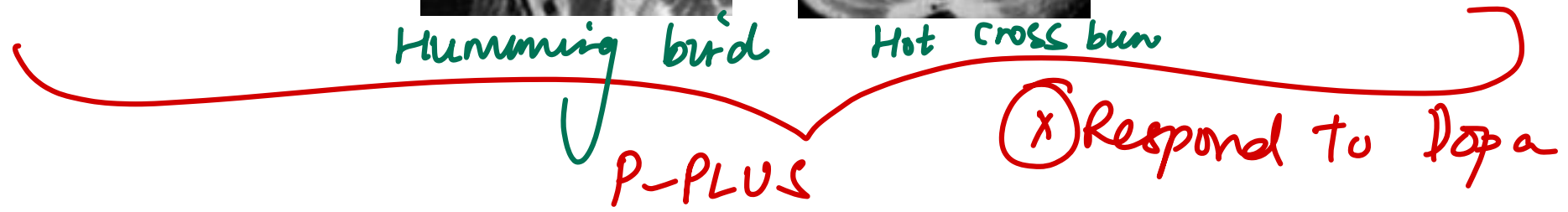
Autonomic ++



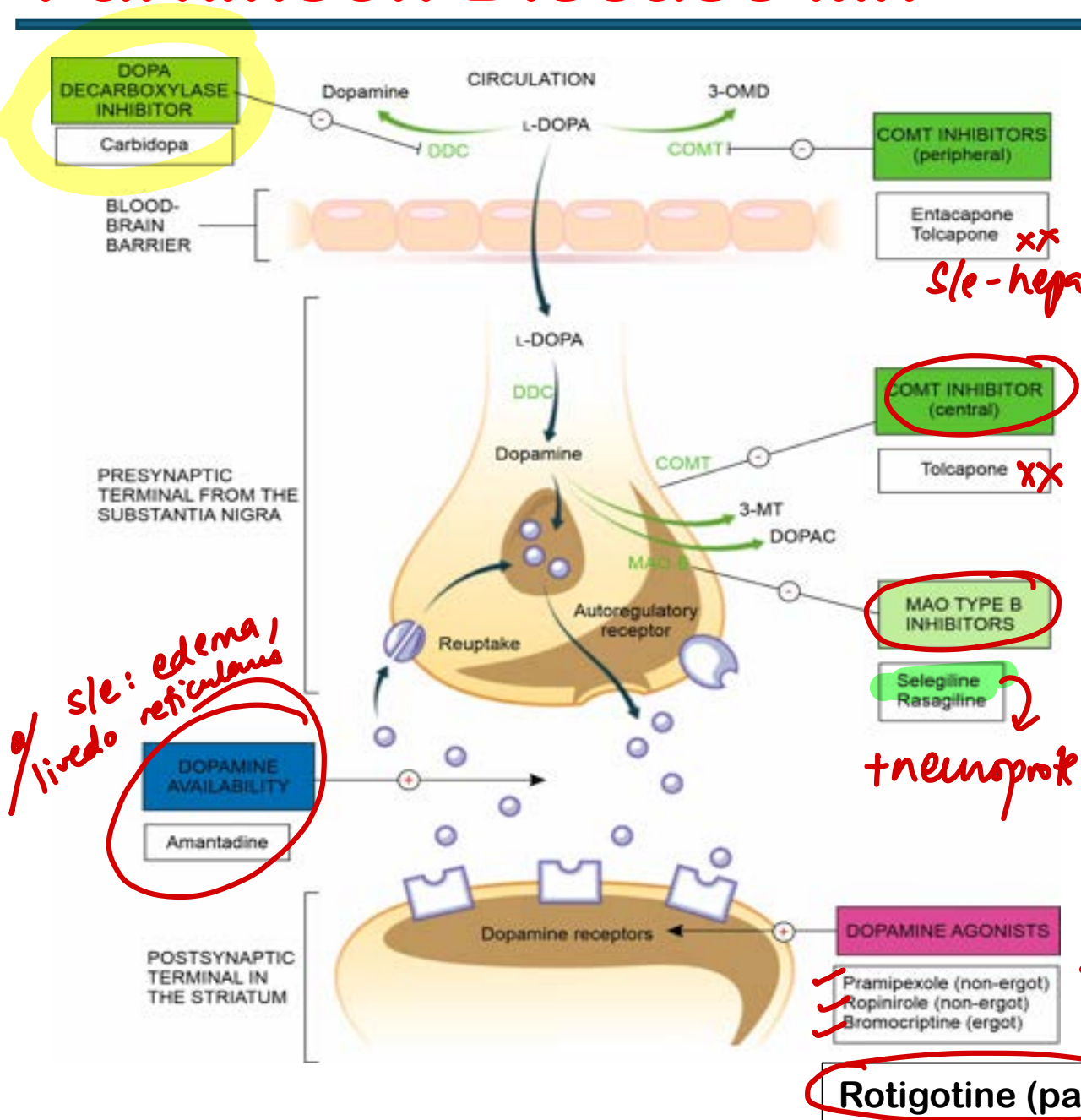
Hot cross bun

Cortico basal degeneri

Alien limb phenomenon



Parkinson Disease Mx



FIRST LINE:
 elderly → Levodopa - Carbidopa: Syndopa
 ↓
 On-off phenomenon → Levodopa induced dyskinesia
 ↓
 COMT(-) / MAO-B → Amantadine

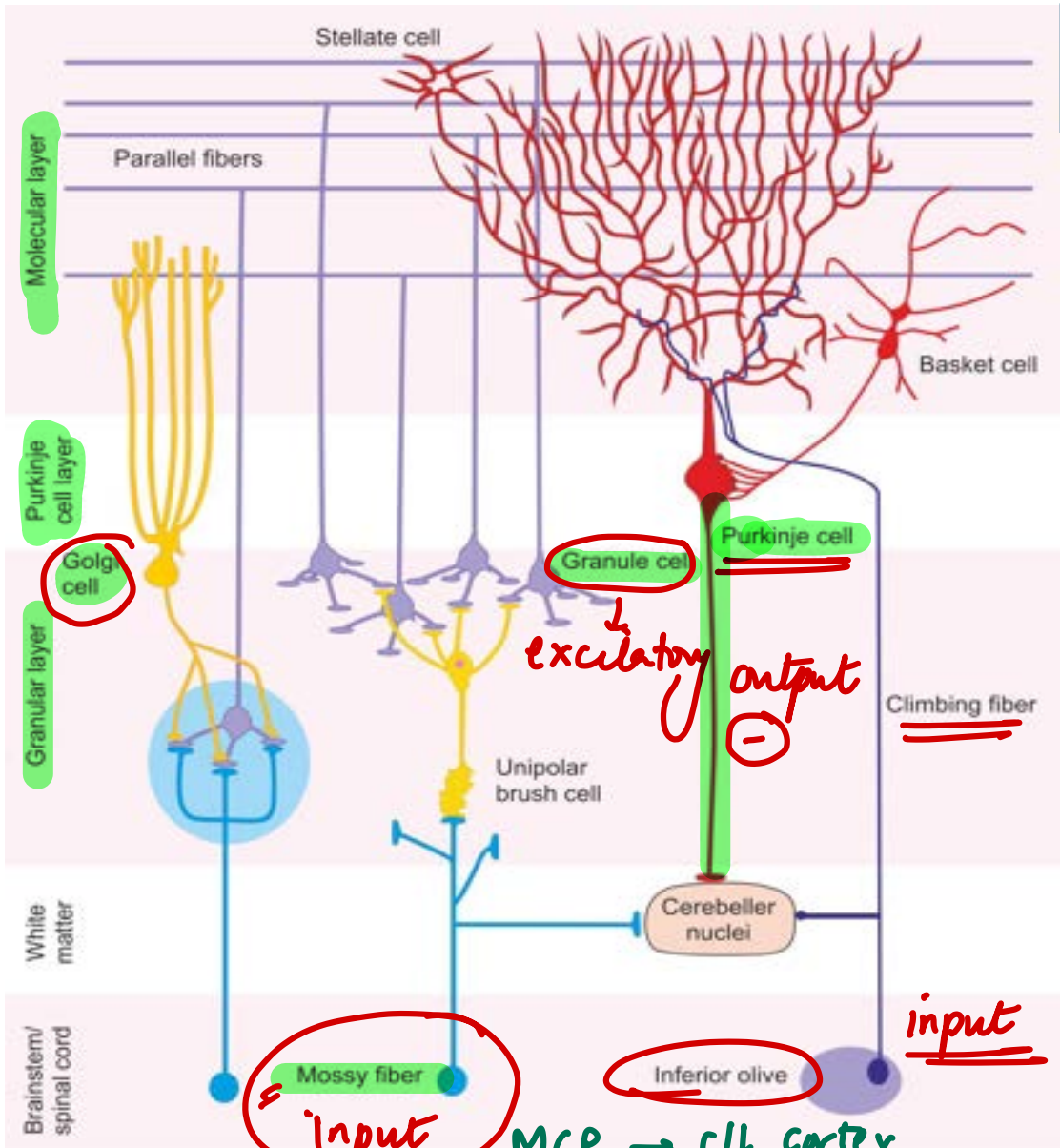
FIRST LINE IN YOUNG: Dopa (+)

DOC for drug induced PD / tremors predominant:
 Benztropine, Trihexphenidyl
anticholinergic

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

DBS: STN > Gpi

Cerebellum



Medial cerebellum-vermis: truncal ataxia / prox limb
 Lateral cerebellar hemisphere: 1/L limbs - distal

Intention tremor
 Dysdiadochokinesia
 Pendular knee jerk

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

SCP → Cortex

MCP → c/l cortex
 LCP → s/c

NT changes in diseases

	Locations of synthesis	Anxiety	Depression	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)	↓	↓	-	-	-	-

CAG

Dementia

Alzheimer's disease

MC

Early short-term memory loss, spatial disorientation -> personality changes
 Down syndrome (APP-Chr 21)
 Apo E2 (happy face) Apo E4 (sad face)
 Mild: Donepezil (AChE ⊖)
 Severe: Memantine (NMDA ⊖)
 Lecanemab, Aducanumab
 Transdermal patch: Rivastigmine

Vascular dementia

Stepwise decline
 Deep white matter changes on neuroimaging

FTD = Pick's D

Early personality changes
 Apathy, disinhibition & compulsive behavior

Lewy body dementia

Visual hallucinations
 Spontaneous parkinsonism (subcortical)
 Fluctuating cognition, REM behaviour disorder

NPH

Wet-Wacky-Wobbly Hakim's Δ
 Shuffling gait with preserved arm swing

Prion D
 CJD

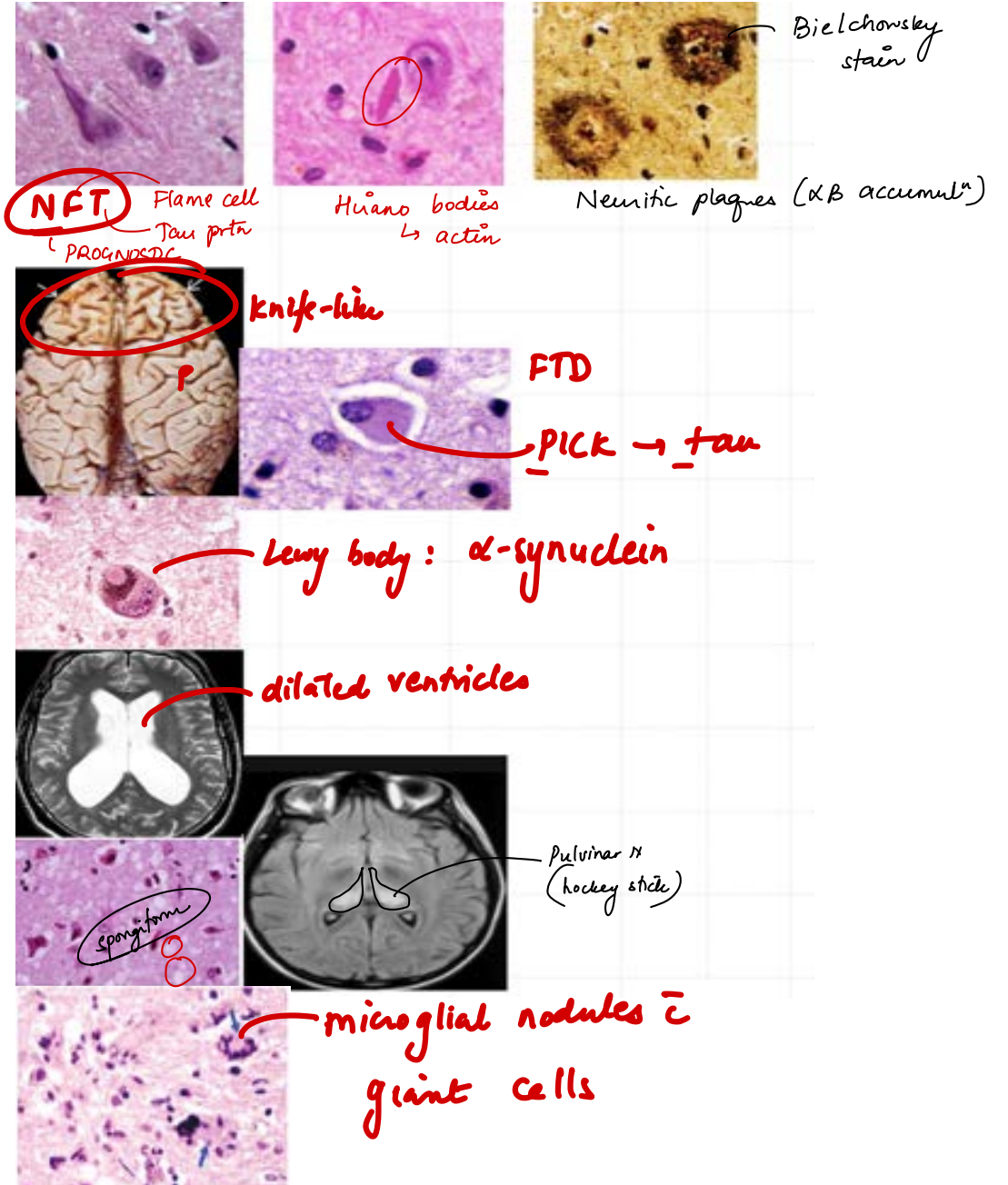
PrP^C → PrP^{Sc} (B-pleated sheets → proteases)

Behavioral changes, Myoclonus
 Rapidly progressive
 14-3-3 in CSF, Periodic sharp wave EEG

HAND

HIV ass neurocogn

HIV +
 Subcortical dysfunction



APPROACH TO HEADACHE

UNILATERAL

Repetitive
Periorbital + lacrimation + Horner

Male > female
15min-3hrs

2-30min
Response to
indomethacin

5-200s
Burning,
stabbing pain

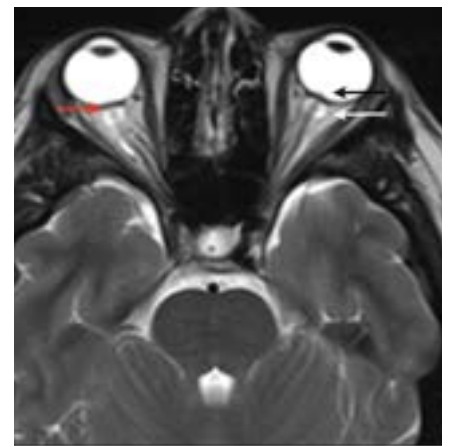
5-200s
V2/V3
Triggered by
chewing/touch

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

BILATERAL

Band-like
4-6hrs

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



*Idiopathic
hypertension
Intracranial*

*tension
headache*

*Trigeminal
neuralgia
↓
Rx- Carbamazepine
Lx
Gamma knife*

Pulsatile
4-72hrs
Nausea
AURA

Migraine

• CLUSTER

*Paroxysmal
hemicrania*

SUNCT

MIGRAINE
First line: NSAIDs
DOC: 5HT1B/1D+ : triptans
Prophylaxis: Propranolol
5HT1F + : LASMIDITAN
CGRP-: RimeGIPANT
ERENUMAB, GALANEZUMAB

*→ VC → CI in
angina*

CLUSTER HEADACHE
DOC: 100% O₂ + Triptans
Prophylaxis: Verapamil

TENSION HEADACHE
DOC: NSAIDs
Prophylaxis: TCA

Weight loss,
acetazolamide, invasive
procedures → LP/
Optic fenestrⁿ

Meningitis

	COLOUR	WBC (cells/ul)	GLUCOSE (mg/dl)	PROTEIN (mg/dl)	OPENING PRESSURE mm H2O
Normal	Clear	0-5	40-70	<40	50-180
Bacterial	turbid	↑↑ (N)	↓↓	↑↑	↑↑
TB <i>Cobweb coagulum</i>	turbid	↑↑ (L)	↓↓	↑↑	↑↑
Viral	clear	↑ (L)	(N)	↑	(N)
Fungal	clear	↑ (L)	↓	↑	(N) - ↑ <i>Cryptococcal</i>
GBS	-	(N)	-	(↑)	-
MS	oligoclonal bands				

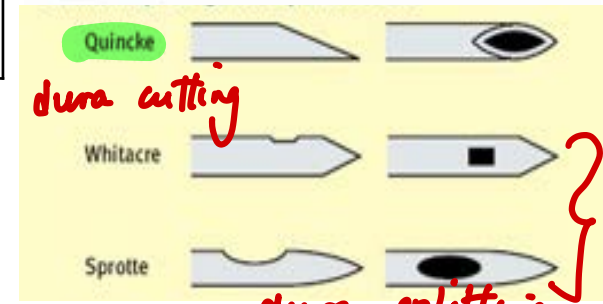
albumino cytological dissociation

Indications of CT before LP:

FAILS - P: FND / Altered mental status / ic / lesion / seizure / Papilledema

Layers punctured for LP:

Skin - Subcut fat → SSP → ISP



Conservative post dural puncture headache (↓) → ↑ on ambulaⁿ

↓ x autologous blood patch

1. Adult spinal cord - Lower border of L1
2. Spinal cords in infants - Upper border of L3
3. A/D/Subarachnoid space - Lower border of S2

Demyelinating disorders

Acute Inflan Deny

MULTIPLE SCLEROSIS

ADEM

NMO = Devic's D

GBS = AIDP

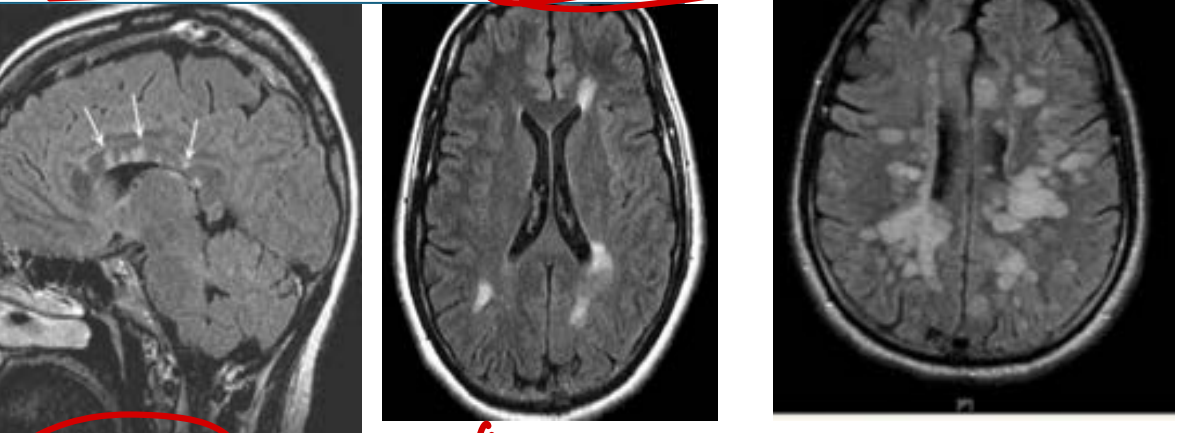
20-40yrs, Females MC
 Away from equator, Low Vit D
 RELAPSING REMITTING MC
 McDonald criteria → *dissemⁿ time/space*
 Charcot triad: SIN
 Lhermitte sign *scanning speech*
 Uthoff sign *"hot bath" Intention tremor*
 ON: U/L, asymmetrical *RAPD INO*
 Spinal cord: Short segment
 Rx: β-interferon, Natalizumab,
 Mitoxantrone *-most effect*
 (Acute-steroids) *s/e: PML*

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

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

BRIGHTON CRITERIA
 h/o prior GI / STD *Campylobacter*
 B/L Acute ascending
 Flaccid paralysis, Areflexia
 Anti GM1 antibodies
 Rx: ~~Steroids~~
 IVIG / Plasmapheresis

Miller fisher syndrome
 (MFS) Ophthalmoplegia,
ataxia, areflexia
 Anti GQ1b antibodies (90%)

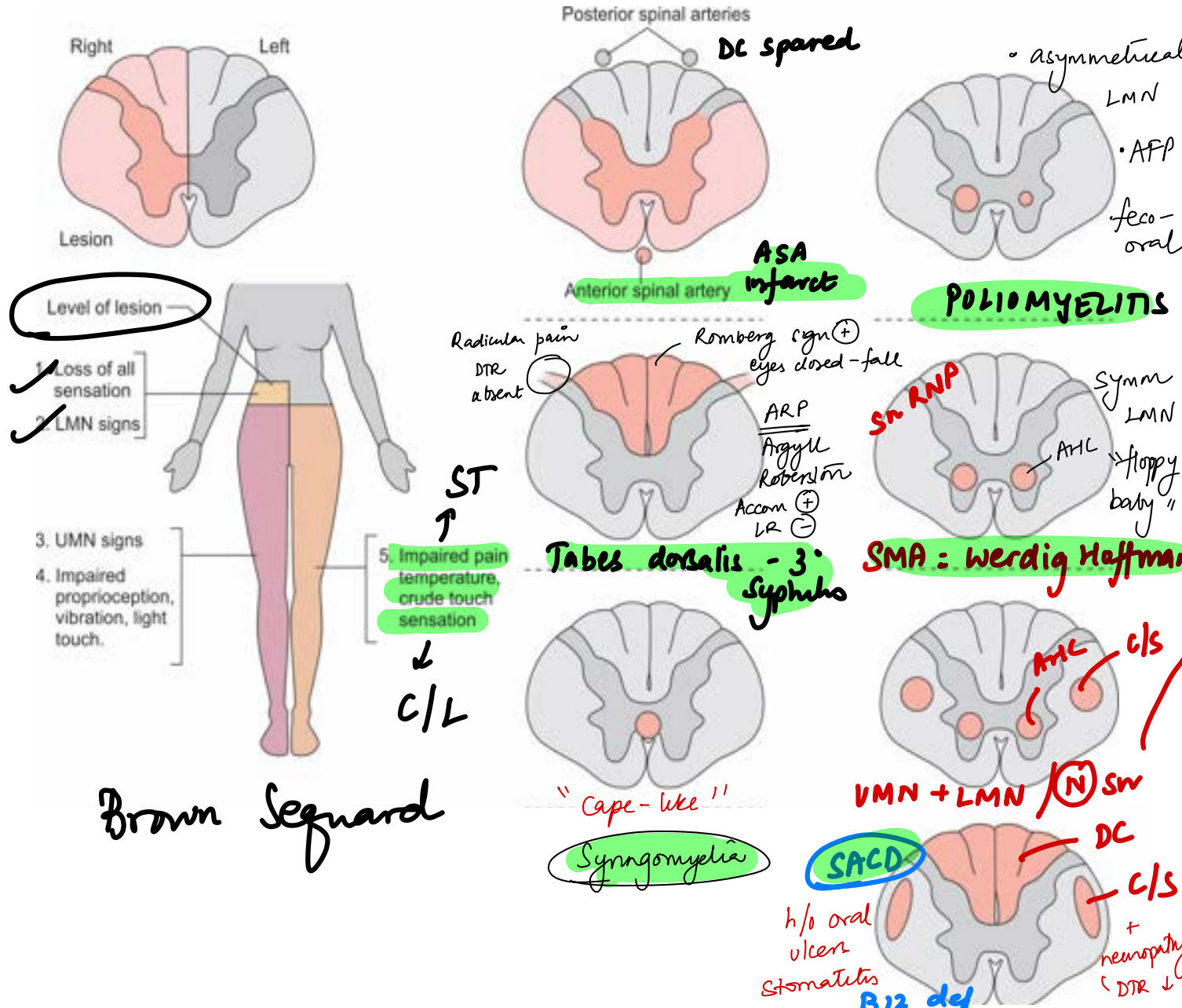


FLAIR Dawson fingers
 Periventricular



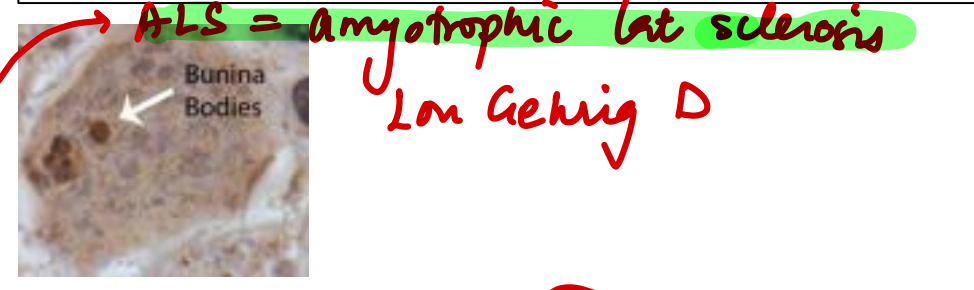
Demyelination: Conduction velocity reduced, Distal latencies
Axonal: Low amplitude

SPINAL CORD LESIONS



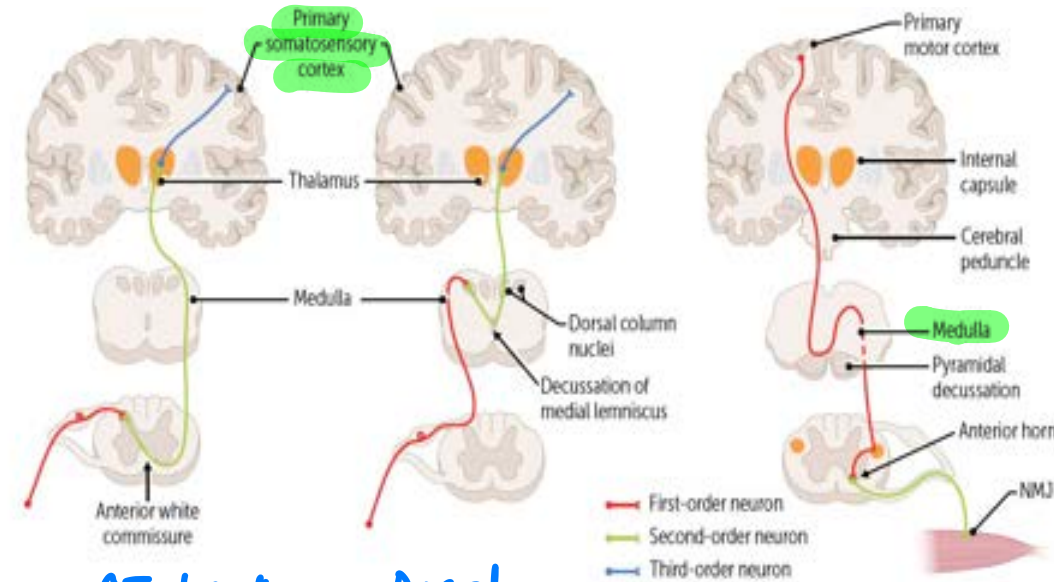
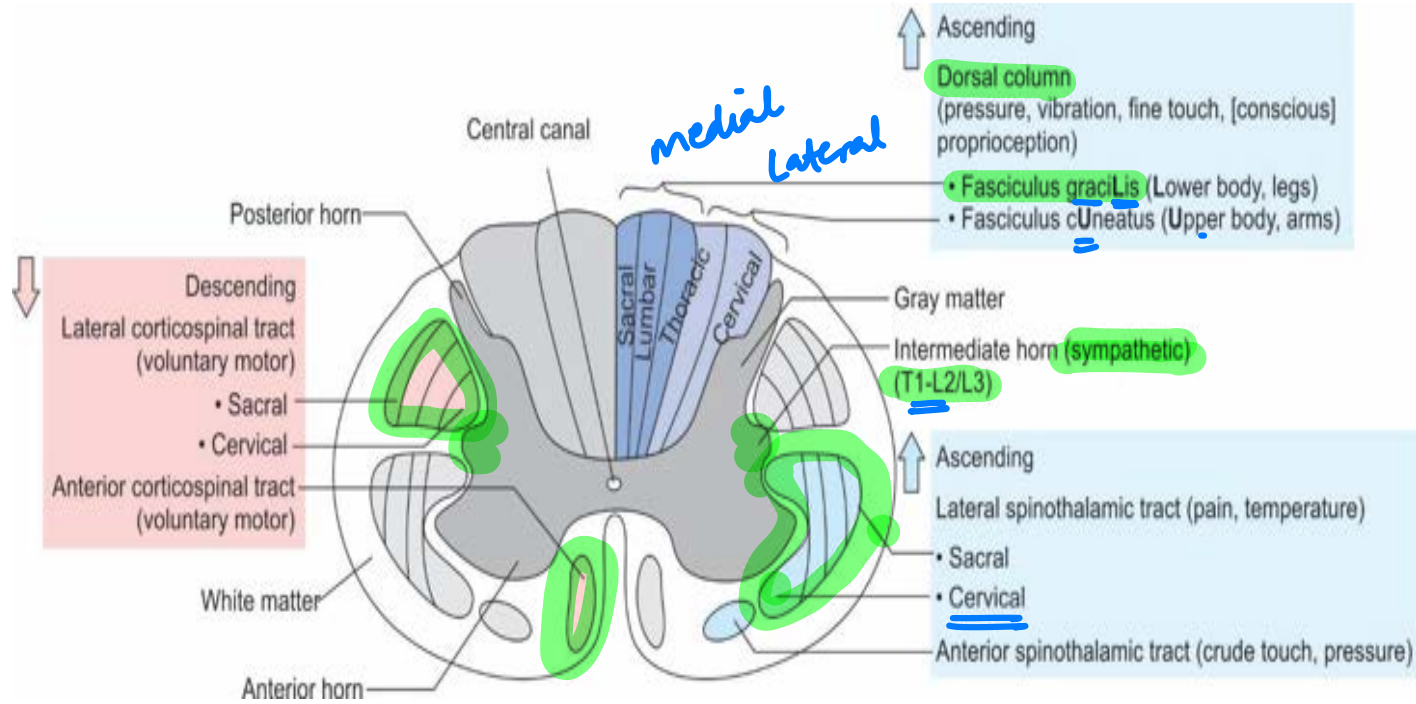
SIGN	UMN LESION	LMN LESION
Weakness	+	+
Atrophy	-	+
Fasciculations	-	+
Reflexes	↑	↓
Tone	↑	↓
Babinski	+	-
Spastic paresis	+	-
Flaccid paralysis	-	+
Clasp knife spasticity	+	-

Nusinersen / Onasemnogene / Zolgensma / Risdiplam



Riluzole, Edavarone (R), Sodium phenylbutyrate-Turursodiol, Tofersen

SPINAL CORD TRACTS



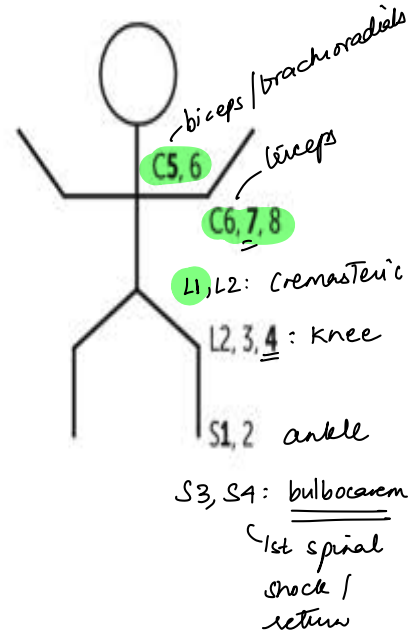
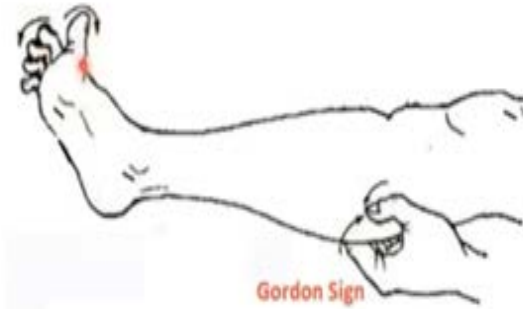
ST tract
↓
Crude touch
pain temp

Dorsal column
↓
fine touch,
proprioception
vibrations

CST



Babinski (+) VMN
 (N) → infants



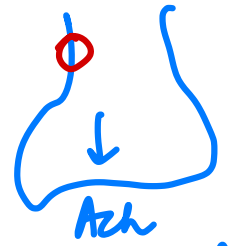
NIMJ

Weakness, ptosis, diplopia more in evening
 Improves with rest
 Sensory/ Autonomic/ DTR/ Bowel bladder/ Pupil
 Ice-pack improvement
 IOC: Anti-AchR / Anti-Musk-ocular MG
 Repetitive nerve stimulation → decremental response
 VS LEMS: Anti-Ca²⁺
 Small cell Ca lung → incremental → improve \bar{c} activity
 DOC: AchE: Pyridostigmine
 IVIG/ plasmapheresis in crises myasthenic
 Avoid Bblocker, CCB, FQ, Blactams, Aminoglycosides

Myasthenia gravis

(N)

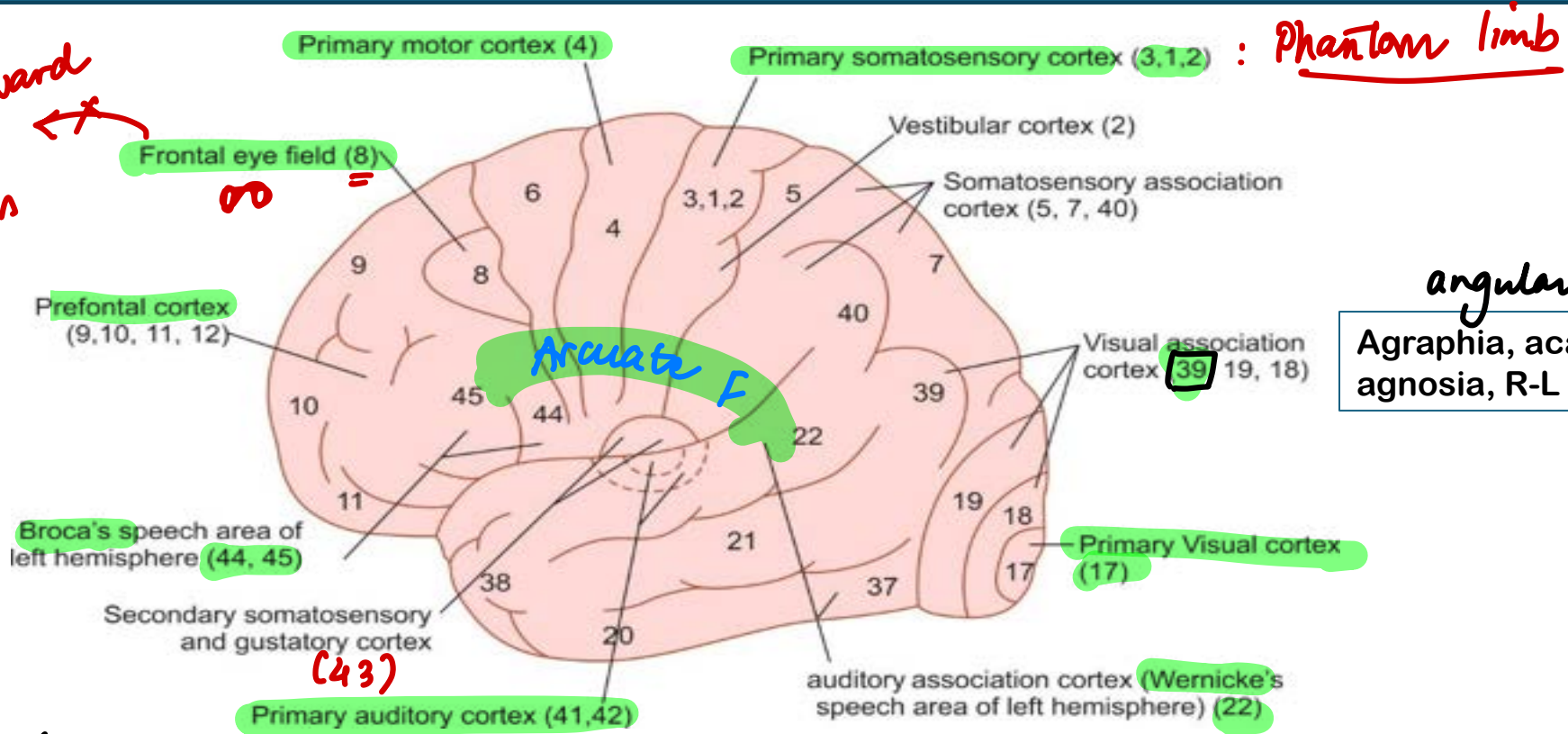
THYMOMA



Anti-AchR
 Type II / V hyson

Ptosis
 (N) LR → MG
 miosis → Homer
 mydriasis → 3rd CN

Brodmann areas



look toward side of lesion

PPRF

away from side of lesion

1/5

angular gyrus - Gertmann

Agraphia, acalculia, finger agnosia, R-L disorientation

BROCA'S

I want an

I...I...
ap...ap...
apple

Wernicke's

I want an

Marble yel
leen I him
gophratic

"neologism"
word salad

Conduction

Repeat this word: APPLE

umm ...

Repetition-LOST

BROCA'S

44

inf frontal gyrus

↓x

"Broken"

WERNICKE'S

22

sup temp gyrus

↓x

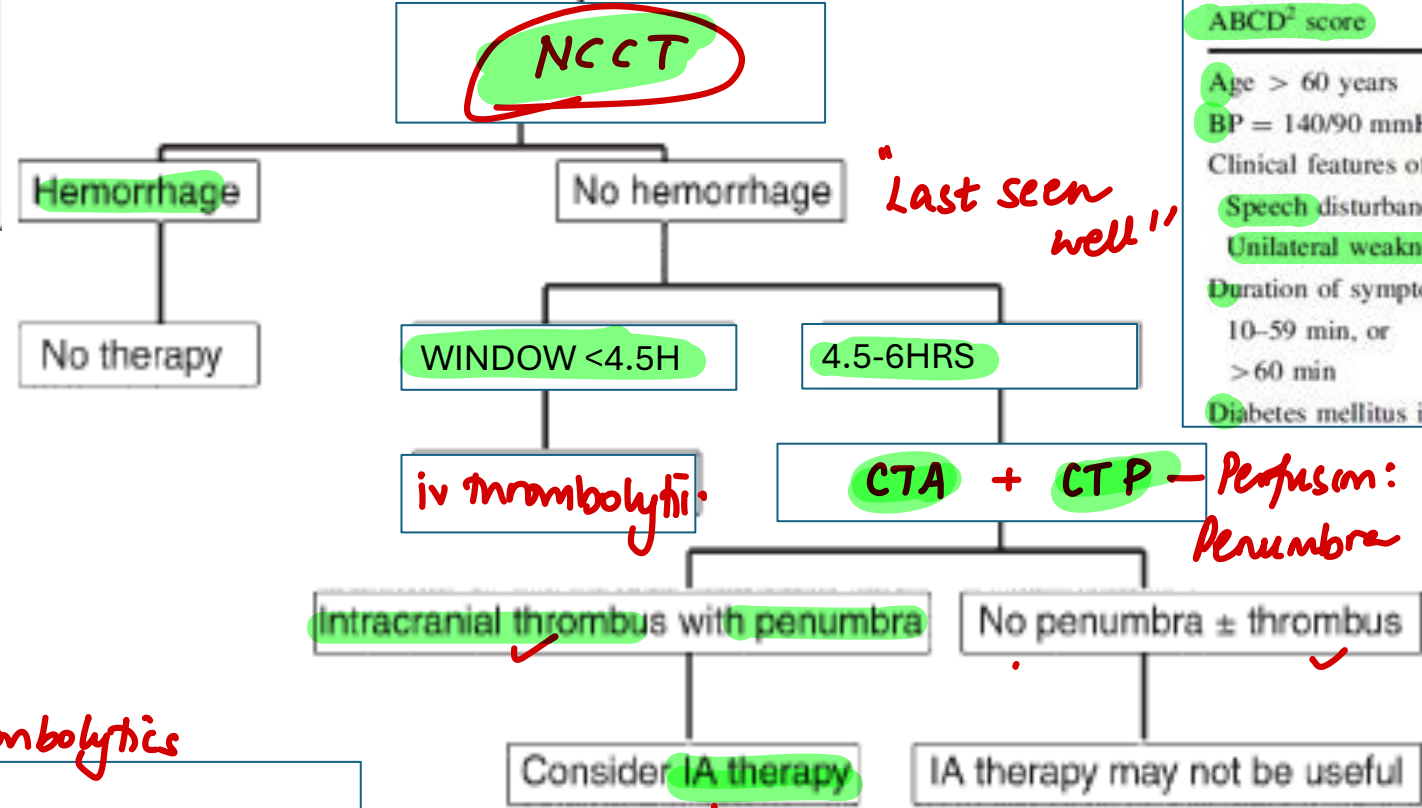
(x) comprehension

STROKE-APPROACH

TIA

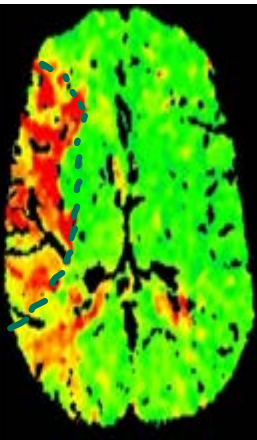
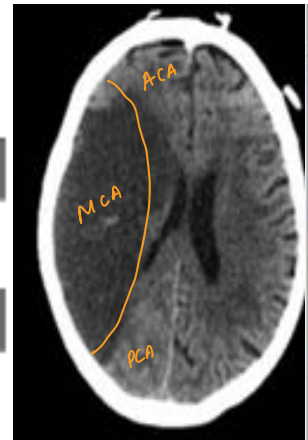


FOCAL NEUROLOGICAL DEFICIT
IRREVERSIBLE



Brief, reversible with normal MRI

ABCD ² score	Points
Age > 60 years	1
BP = 140/90 mmHg at initial evaluation	1
Clinical features of the TIA	
Speech disturbance without weakness, or Unilateral weakness	1
Duration of symptoms	2
10-59 min, or >60 min	1
>60 min	2
Diabetes mellitus in patient's history	1



Ischemic stroke

CT Perfusion
CBV
CBF

CI to thrombolytics

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

- ia thrombolytic
- Mechanical thrombectomy

STROKE LOCALISATION

Paracentral lobule

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

ACA

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

MCA Dominant / Lt

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



RE MCA Nondominant



Hemineglect
↓
Nondominant Rt parietal

Anton Sx

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

↳ splenium

PCA

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

Thalamic / Djerine-Roussy Sx



Stereognosis

Graphemesia

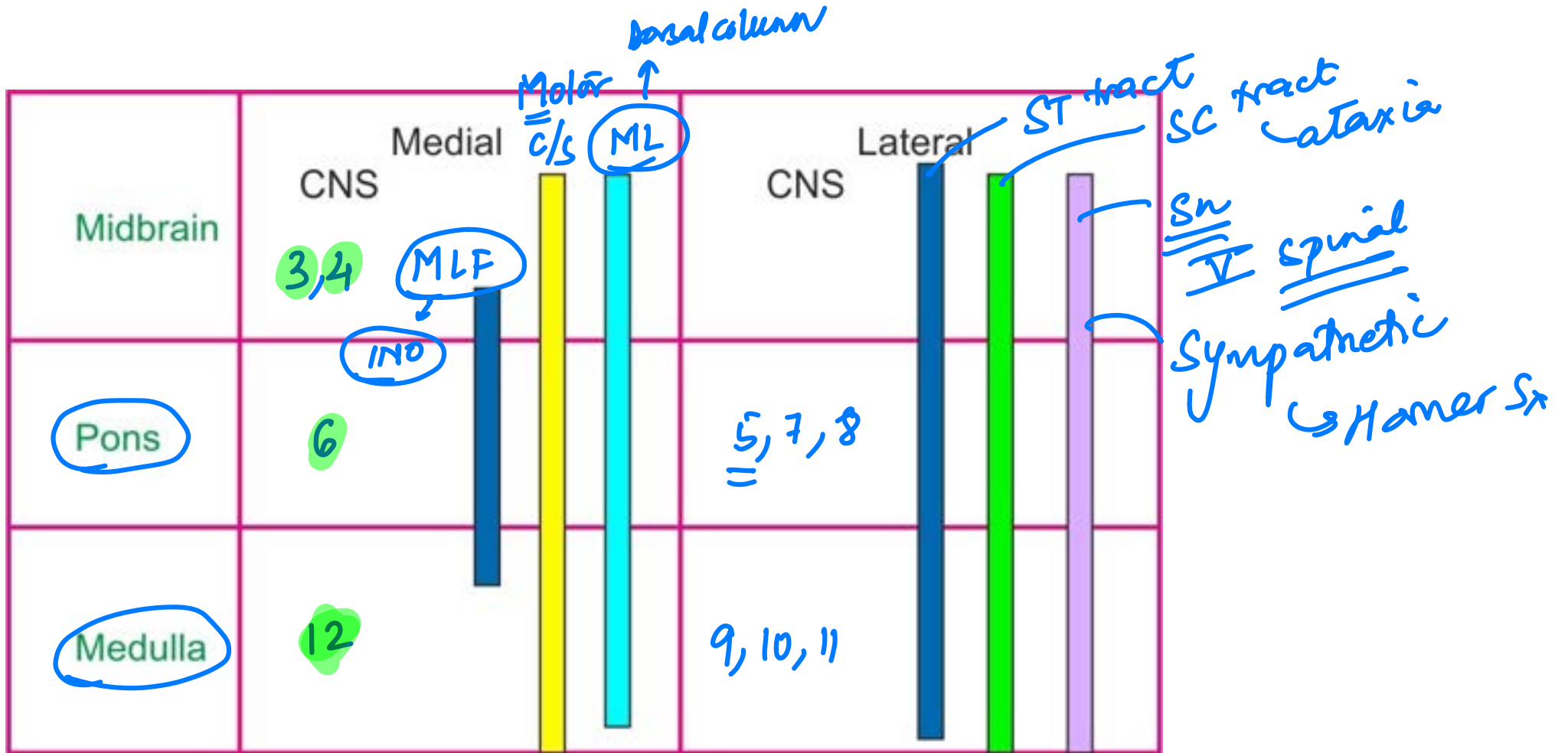
Simultagnosia

Prosopagnosia

PARIETAL LOBE

↳ fusiform - temporal - occipital

BRAINSTEM STROKE



BRAINSTEM STROKE SYNDROMES

C/L hemiplegia + I/I down and out pupil *Weber Sx*
Red N

C/L hyperkinesia, chorea, tremor + I/I down and out pupil *Benedict Sx*

C/L hemiataxia + C/L hyperkinesia, chorea, tremor + I/I down and out pupil *Claude Sx*

Upward gaze palsy + Collier sign-eyelid retraction *Painaud Sx* - *pontine lesions* - dorsal MB

C/L hemiplegia + I/I CN 6 + 7 *Millard - Gubler* ^{Q/}

C/L hemiplegia, hemisensory loss + I/I CN 6 + 7 + 8 CN palsy + INO *Foville*

C/L hemiplegia + I/I CN 6 palsy *Raymond Sx*

C/L hemiplegia + I/I tongue deviation *Medulla medial* = *Djerine Sx*

Loss of pain, temp from c/l body, Horners, Dysphagia, hoarseness, loss of gag

IX / X

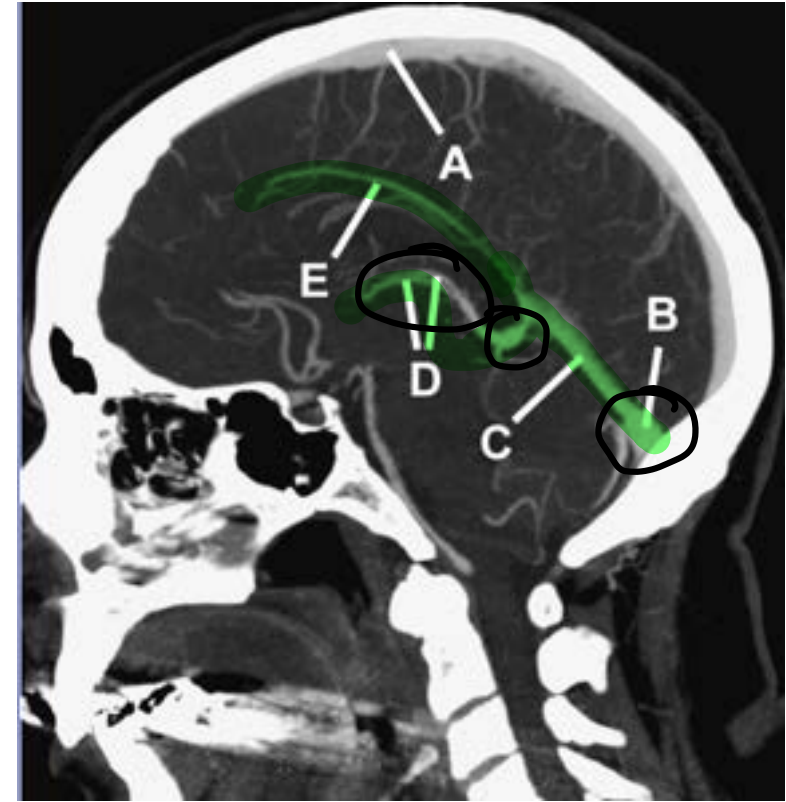
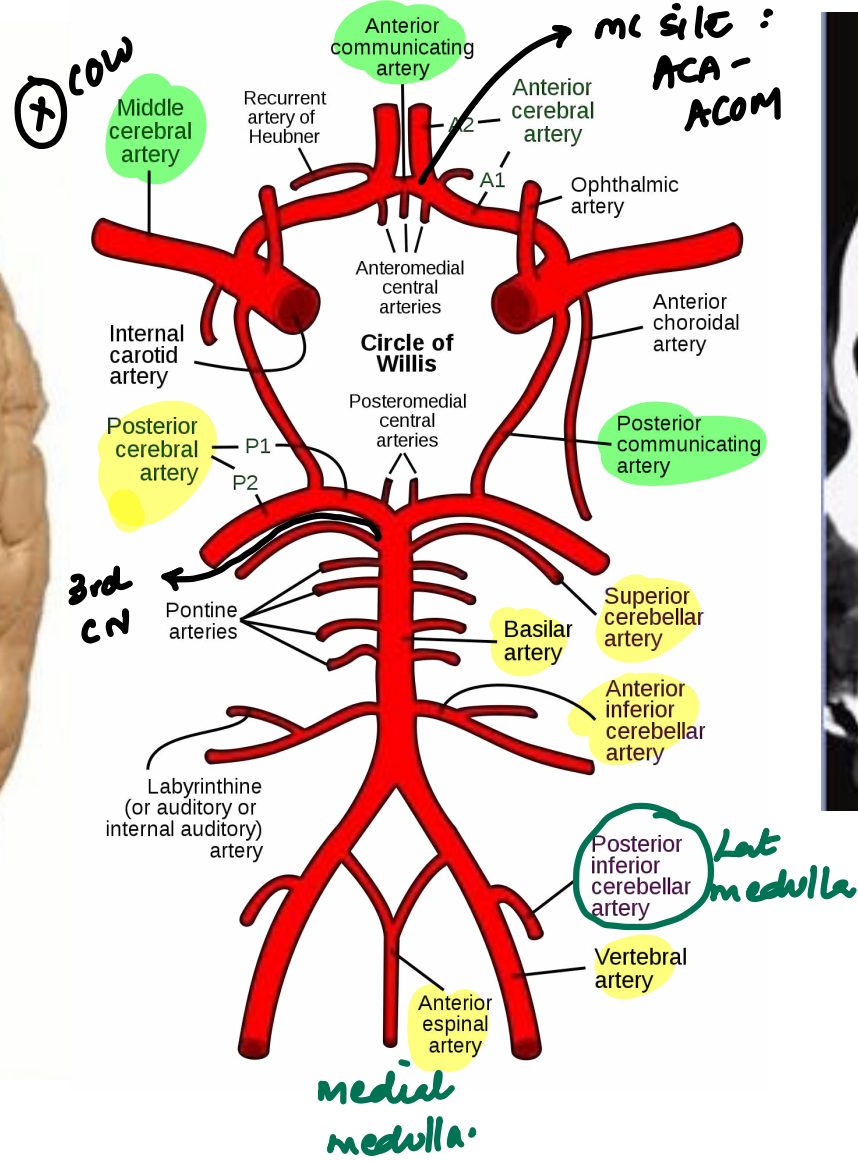
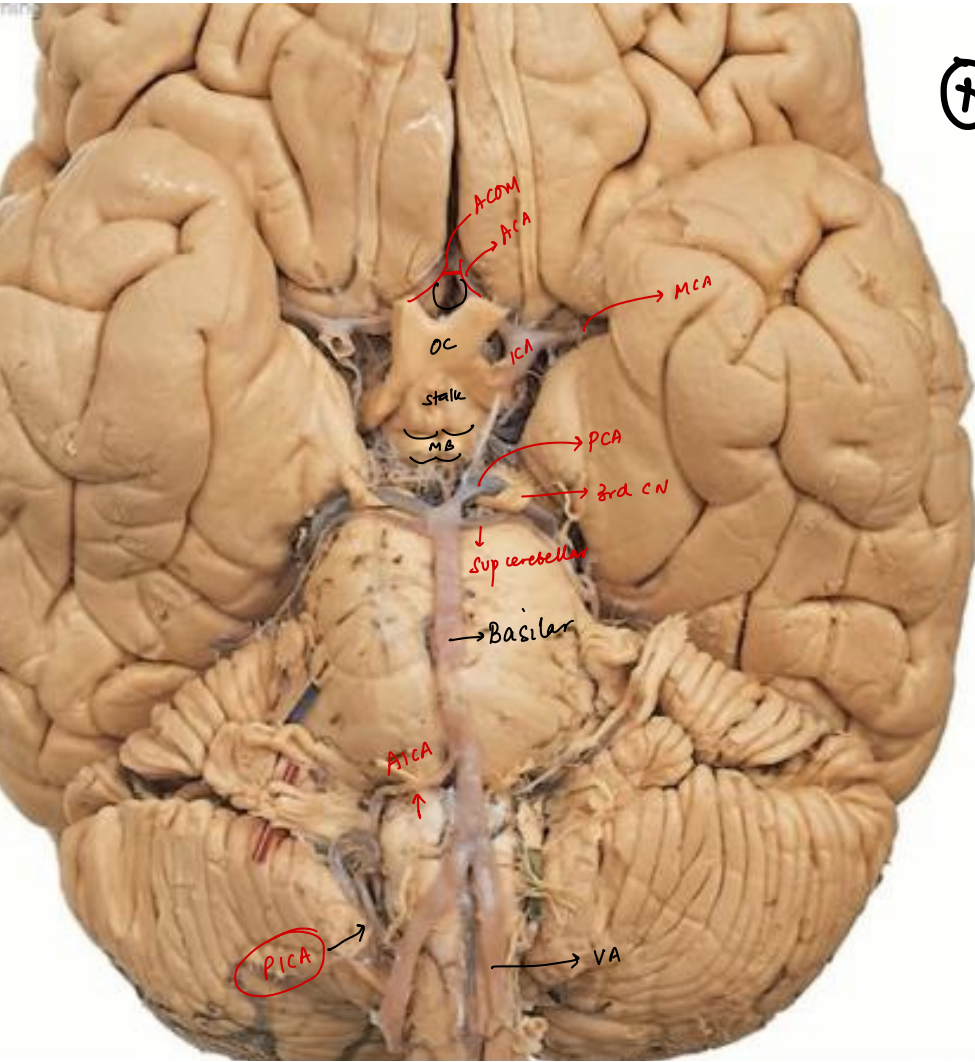
Lat medulla =

↑ Wallenberg Sx

VA / PICA

ASA

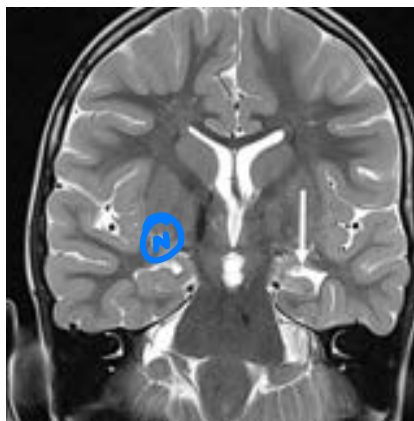
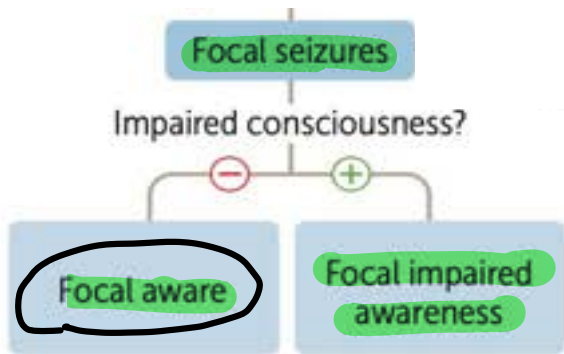
VASCULAR ANATOMY OF BRAIN



A → SSS
 B → Confluence → TSS
 C → Straight
 D → ICV
 E → ISS
 SSS Str

ICV → VO9 + ISS

Seizures



Status epilepticus—continuous (≥ 5 min) or recurring seizures without interictal return to baseline consciousness that may result in brain injury.

Jacksonian march distal \rightarrow proximal
Todd palsy transient post-ictal weakness
DOC focal seizure Carbamazepine
DOC focal seizure in elderly Lamotrigine
 Mesial temporal sclerosis
 Refractory temp lobe epilepsy

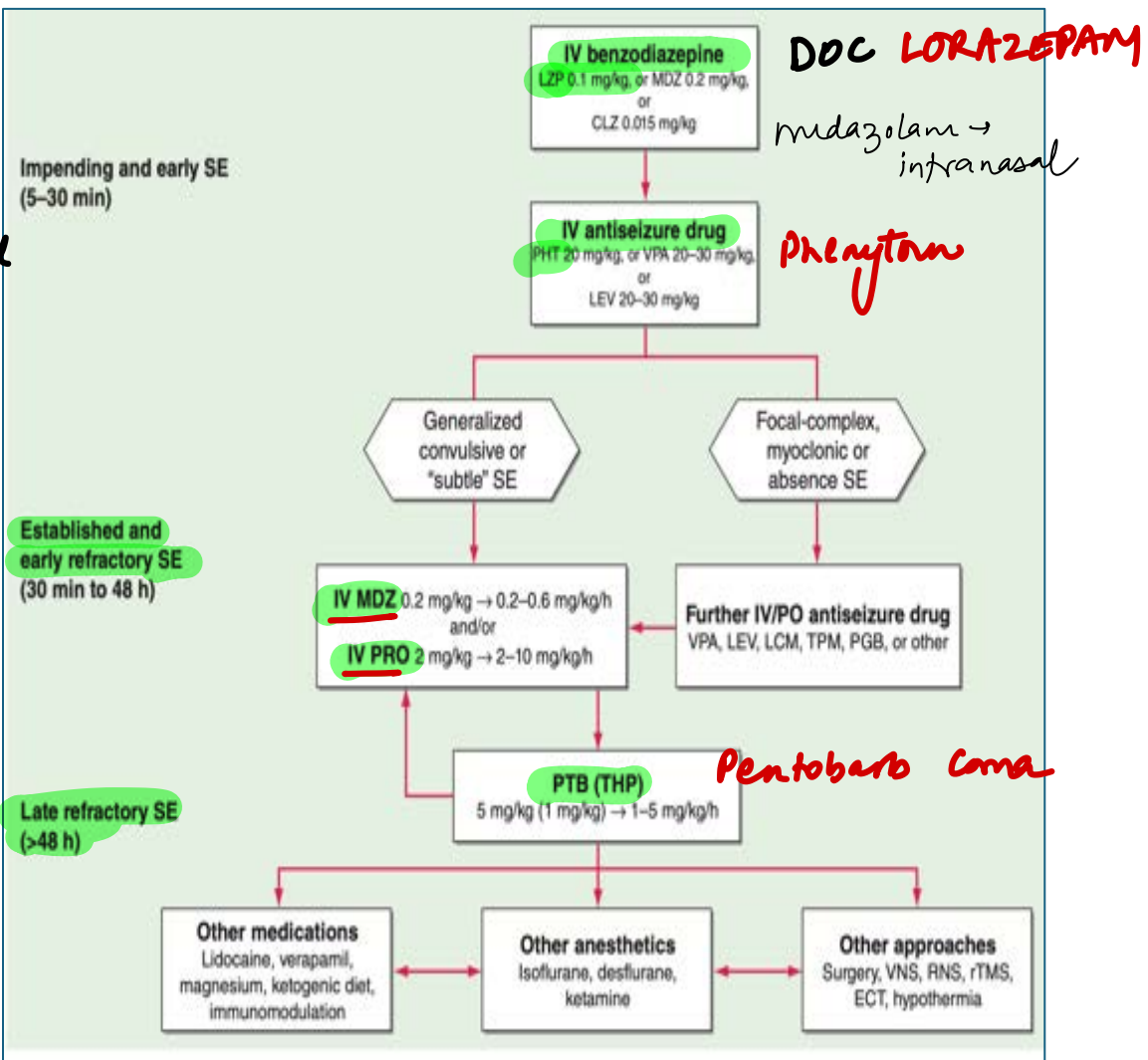


Table 6 Stopping antiepileptic drugs in patients in remission	
High-Risk Profile for Seizure Recurrence Off AEDs ⁶³	When May It Be Safe to Discontinue? ⁶⁴
<ul style="list-style-type: none"> Being 16 y or older Taking more than one AED Having seizures after starting AED therapy History of generalized tonic-clonic seizures History of myoclonic seizures Having an abnormal EEG in prior year 	<ul style="list-style-type: none"> Seizure freedom >2 y implies 60% chance of persistent remission in certain epilepsy syndromes Favorable factors: <ul style="list-style-type: none"> Control easily achieved on a low dose of one drug No previous unsuccessful attempts at withdrawal Normal neurologic examination and EEG Primary generalized epilepsy except juvenile myoclonic epilepsy Benign syndromes

EPILEPSY SYNDROMES

West Sx / Infantile spasm

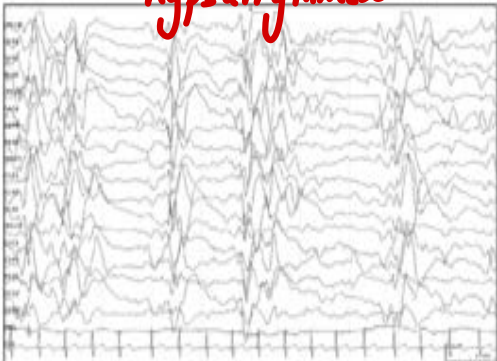
Infant + Global developmental delay

DOC: ACTH

DOC in TSC: Vigabatrine



Hypserrhythmia

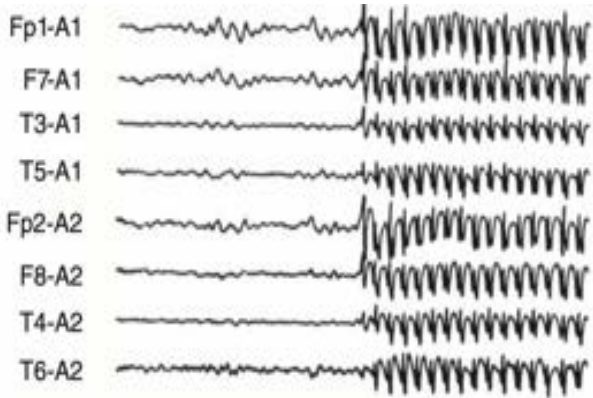


typical Absence S2

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

DOC Typical: Ethosuximide

DOC Atypical: Valproate



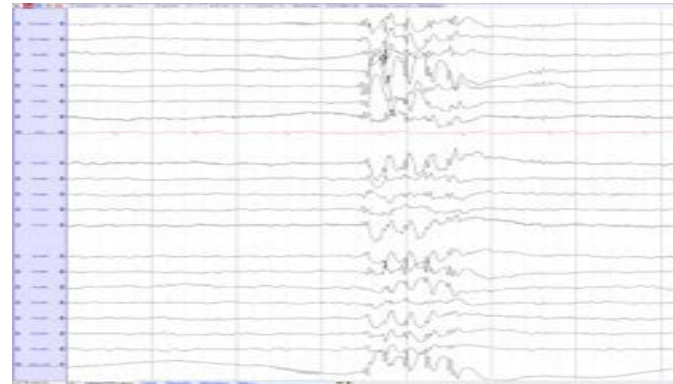
JME

MC in Adolescent

Early morning "clumsy"

3-6 Hz generalized polyspike and wave discharge

DOC: Valproate



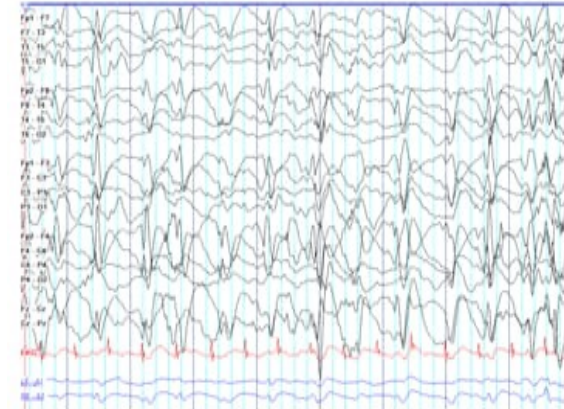
Lennox Gastaut Sx

Multifocal sz

<2.5Hz spike and wave pattern

DOC: Valproate

BZD approved: Clobazam



SLC2A1: GLUT1

Rp - pure ketogenic diet

SCN1A: Dravet syndrome

DOC - Valproate

ANTI-EPILEPTIC DRUGS

S/e stones / ACG: **topiramate**

Carbamazepine: SJS

Diplopia, ataxia, blood dyscrasias (agranulocytosis, aplastic anemia), liver toxicity, teratogenesis (cleft lip/palate, spina bifida), induction of cytochrome P-450, SJS

Oxcarb → SIADH

PPHENYTOIN: cytochrome P-450 induction, Pseudolymphoma, Hirsutism, Enlarged gums, Nystagmus, Yellow-brown skin, Teratogenicity (fetal hydantoin syndrome), Osteopenia, Inhibited folate absorption, Neuropathy. Rare: SJS, DRESS syndrome, drug-induced lupus. Toxicity leads to diplopia, ataxia, sedation.

Na⁺ channel blockers
Carbamazepine
Oxcarbamazepine
Phenytoin
Topiramate
Zonisamide
Lacosamide
Rufinamide

wt loss

SV2A Receptor blocker
Levetiracetam

best safety profile

Ca²⁺ Channel blockers
Ethosuximide
Gabapentin

EFGHLJ-Ethosuximide
Causes Fatigue, GI distress
Headache, Itching (and urticaria), SJS

K channel opener:
Retigabine
Ezogabine

All CYP inducers except: **Valproate CYP ⊖**

well controlled: Valpr
- min dose
+ folate 5mg

Pregn
Levetiracetam
Lamotrigine

DOC → Neonatal SS
Diabetic N / Herpeti neuralgia
RLS

INCREASE GABA RELEASE:
Pregabalin / Gabapentin

GABA agonists
Benzodiazepines → ↑ freq
Topiramates
Phenobarbital

Barbiturate → duration

INHIBITORY NEURON
GABA
GAD
Glutamate
GABA reuptake receptor
GABA transaminase

Succinic semi-aldehyde (SSA)

PERAMPANEL
AMPA receptor

FELBAMATE
NMDA receptor

GABA receptors
GABA receptor
Cl⁻

GABA reuptake inhibitor
Tiagabine

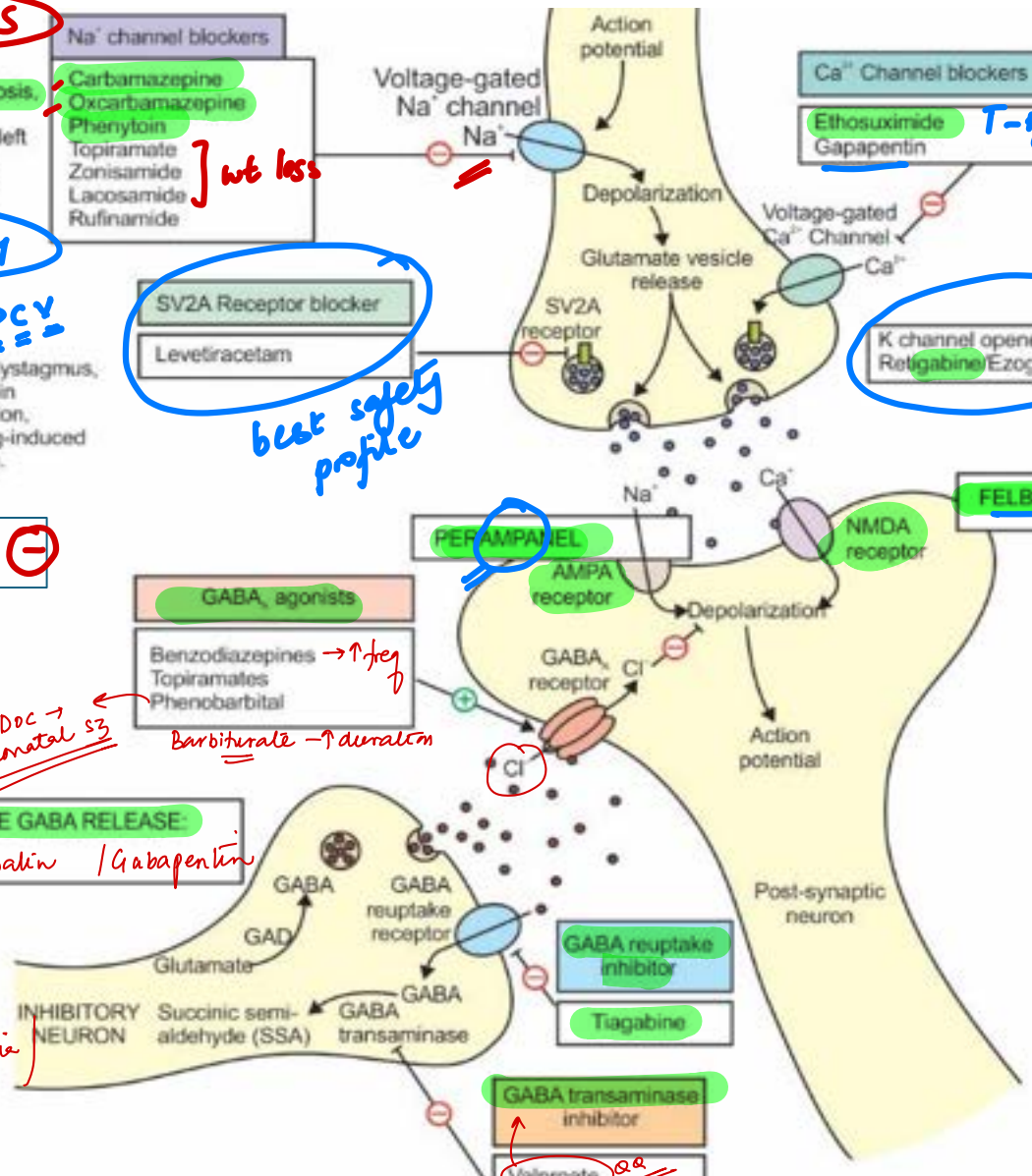
GABA transaminase inhibitor
Valproate
Vigabatrin

VALPROATE: Vomiting, Alopecia, Liver damage (hepatotoxic), Pancreatitis, P-450 inhibition, Rash, Obesity (weight gain), Tremor, Teratogenesis (neural tube defects), Epigastric pain (GI distress).

gender sp
↓
PCOD

Valproate antidote: **L-carnitine**

SJS (must be titrated slowly), hemophagocytic lymphohistiocytosis (black box warning)



Raised ICP

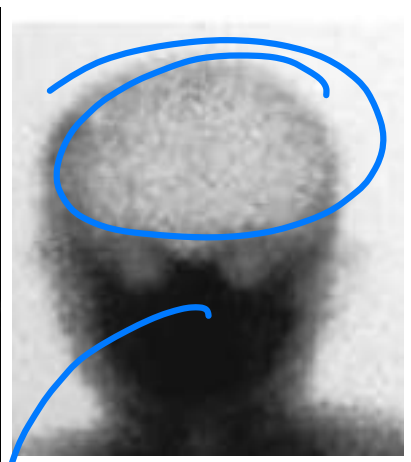
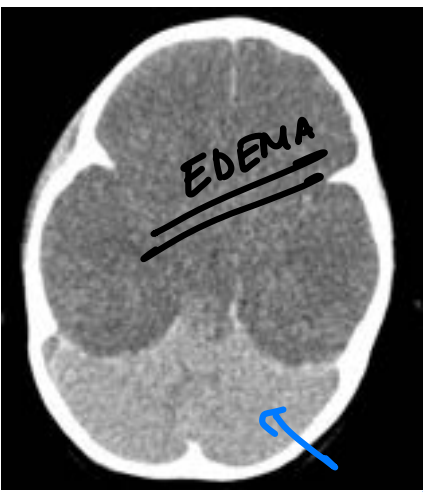
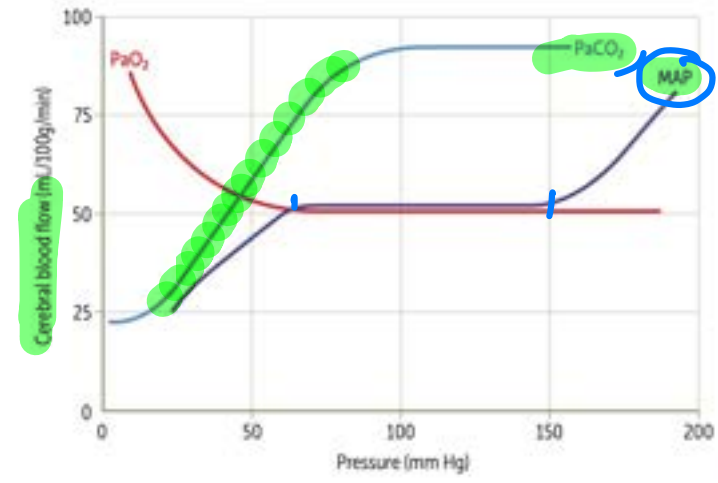
Cushing triad: *brady cardia / RR ↓ / BP ↑*

CPP = MAP - ICP

Target: ICP < 20mm and CPP > 60mm

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

cytotoxic edema *vasogenic edema*

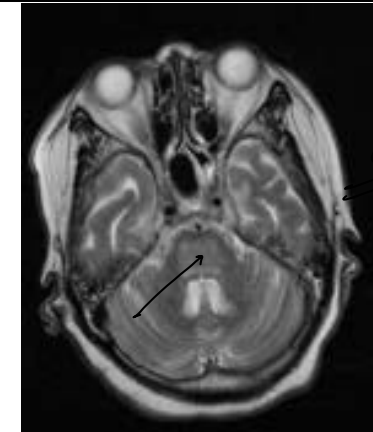
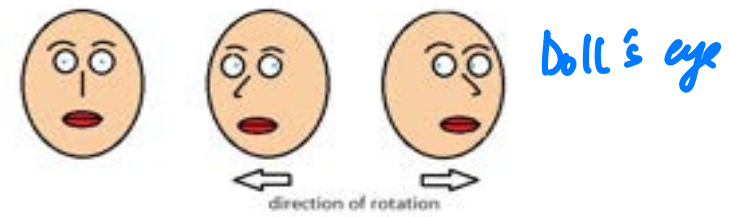


GCS 3/15 *Brain death*
 Apnea test
 (Preoxygenate -> pCo₂ > 60mm)
 Brainstem reflex: Absent
 Spinal reflex: *present @ R*
 No motor function or posturing
 EEG silent

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

White cerebellar signs

Rot nose sign



Locked-in S_x
ODS osmotic demyelⁿ S_x
↓ Na⁺ - RAPID overcorrecⁿ