Tract	Origin	Crossing	Synapse	Ends	Purpose
Motor Descending Pathways (Ventral Root)					
LCST	M1	pyramids (medulla)	lateral intermediate zone	full cord	limb movement
ACST	M1	bilateral	medial intermediate zone	cervical/thoracic	gait & posture
Rubrospinal	red nucleus	central tegmental decussation (midbrain)		cervical cord	unknown
Lateral Vestibulospinal	pons (superior ganglia)	extrapyramidal		full cord	balance
Medial Vestibulospinal	medulla (inferior ganglia)	bilateral		cervical/thoracic; medial longitudinal fasciculus	head & neck; ocular muscles
Reticulospinal	reticular formation	extrapyramidal		full cord	gait & posture
Tectospinal	superior colliculus	extrapyramidal		cervical	unknown
Autonomic Pathways (Dorsal Root)					
SANS			paravertebral ganglion (symp. chain)	thoracic/lumbar	
PANS			peripheral	brainstem/sacral	
Somatosensory Ascending Pathways (Dorsal Root)					
Dorsal Column	fasciculus gracilis (lower) & cuneatus (higher)	medial lemniscus (internal arcuate) in medulla	DRG	VPL → S1	vibration & position sense
Anterolateral/ Spinothalamic	full cord	anterior commissure (2 levels above)		VPL → S1	pain & temperature & crude touch
Dorsal & Cuneo Spinocerebellar	Golgi tendon organ & spindle fibers	does not cross	Clark's & cuneate nuclei	cerebellum	proprioreception
Mesencephalic	face	does not cross			proprioreception
Chief	face	trigeminal lemniscus in midbrain	trigeminal ganglion	VPM → S1	fine touch & dental pressure
Spinal	face	trigeminothalamic tract in midbrain	trigeminal ganglion	VPM → S1	pain & temperature & crude touch

tracts

M1 → internal capsule (posterior limb) → cerebral peduncles (midbrain) & basis pontis (pons) → pyramids
VPL/VPM (gets raw & processed copy) → internal capsule (posterior limb) → S1
cauda equina: below L1

reflex arcs

muscle spindle (stretch) & Golgi tendon (force) afferents
muscle stretch → Ia afferent firing rate increases → gamma efferents cause intrafusal fiber contraction & increase gain AND extensor contraction via alpha MN, flexor relaxation via interneurons on alpha MN (+ DC/SCT)

input to M1 → inhibition of inhibition → more input to gamma MN → intrafusal fibers of extensor contract → raise Ia gain

gamma: tension → Ia → SCT → cerebellum → excitatory → inhibitory → gamma (contract spindle)
withdrawal/crossed-extensor reflex:
thermo/nocio receptors → ALT → VPL
excitation of ipsilateral flexor & contralateral extensor
inhibition of ipsilateral extensor & contralateral flexor
UMN disease:
rest: increased gamma MN activity enhances muscle tone → shortens spindle, increasing Ia gain
stretch: Ia activity elevation is abnormally high → sudden movements leads to spasticity & clonus
Babinski's sign: extensor (toes fanned) plantar response

sensory neurons

touch: mechanoreceptors with different 2-point discrimination

Merkel (texture) & Meissner (motion) = small, superficial receptive fields
Pacinain (vibration) & Ruffini (stretch) = large, deep receptive fields

thermo/nocioreceptors: free nerve endings with chemical & heat-sensitive channels

Nerve Plexus

terms to know: transverse & spinous processes, intervertebral disc (usually herniates laterally), foramen (spinal column)
cervical nerves exit below disc → thoracic & lumbar nerves exit above disc → sacral nerves exit not next to discs
plexuses are susceptible to avulsion (tearing) injury → eg whiplash can damage nerves
cervical plexus – C1-C5, including phrenic nerve (C3-C5)

Brachial Plexus

radial (C5-T1):
- motor: arm extension, forearm and thumb movements
- sensory: medial (inner) surfaces of arm

median (C5-T1):
- motor: wrist and thumb movements
- sensory: first three fingers, palm

ulnar (C6,8 and T1):
- motor: wrist and finger movements
- sensory: outer two fingers and palm

axillary (C5,6; axilla = armpit):
- motor: abduction of shoulder
- sensory: sensation on shoulder

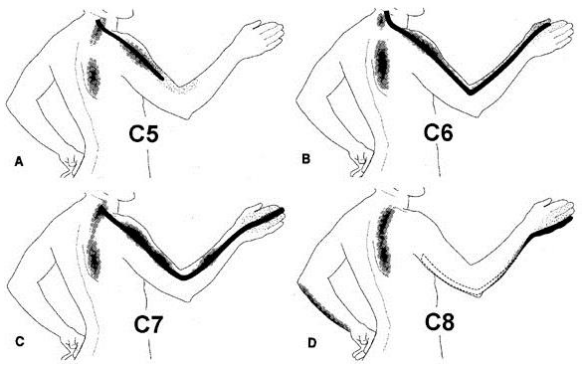
musculocutaneous (C5-7):
- motor: arm flexion and supination
- sensory: lower arm

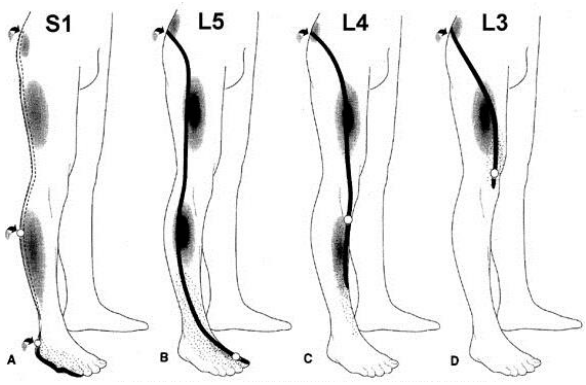
Lumbar Plexus

femoral (L2-L4):
- motor: raise femur (quads), extend shin
- sensory: upper thigh and medial shin

obiturator (L2-L4):
- motor: adduct femur
- sensory: inner thigh

sciatic (L4-S2):
- motor: flex knee (hamstrings)
- sensory: calf and top of foot
- gives rise to: tibial (plantar flexion, sensation on soles of feet) and peroneal (foot eversion, dorsiflexion, sensation on lateral shin and toes) nerves





Motor/Sensory Deficits

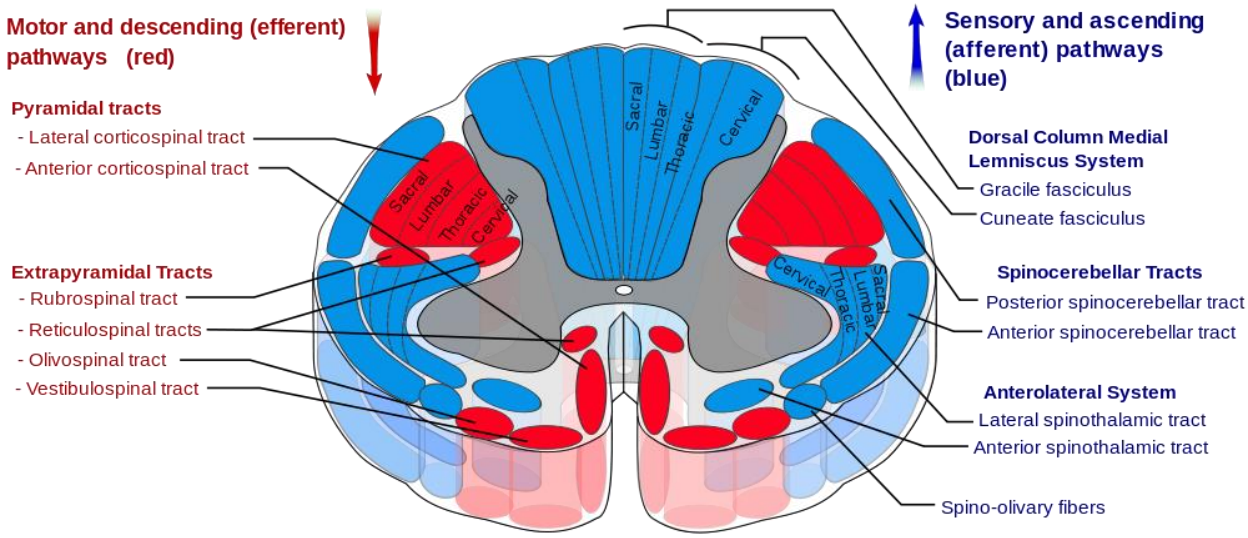
- ALS: primary (cortical UMNs), bulbar (brainstem LMNs), typical (spinal cord LMNs)
- MS: demyelinating neuropathy (disease of axon tracts)
- musculoskeletal (e.g., disc disease, trauma; myasthenia gravis (autoimmune NMJ) & muscular dystrophy)
- peripheral neuropathies (e.g., diabetes- and chemotherapy-induced; stocking and glove syndrome)
- diseases affecting LMNs (e.g., polio) and DRG neurons (e.g., syphilis)
- cortical lesions (bilateral loss in internal capsule & pyramids (below face); graphesthesia & sterognosis)
- UMN vs LMN: atrophy & fasciculations vs clonus; tone; power

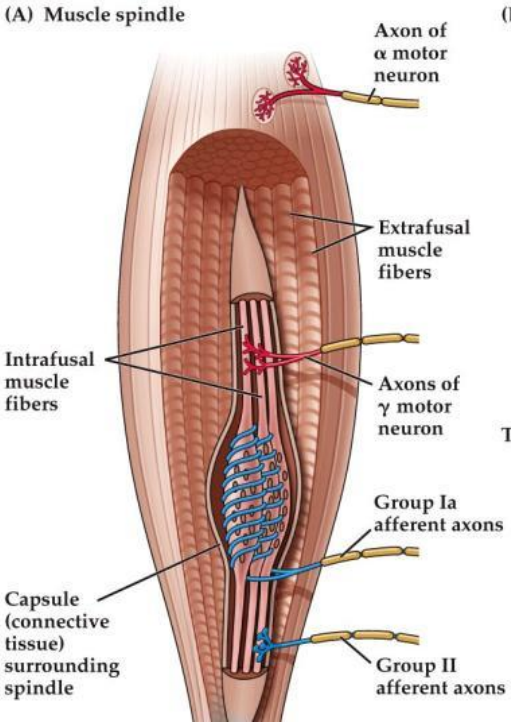
ALS

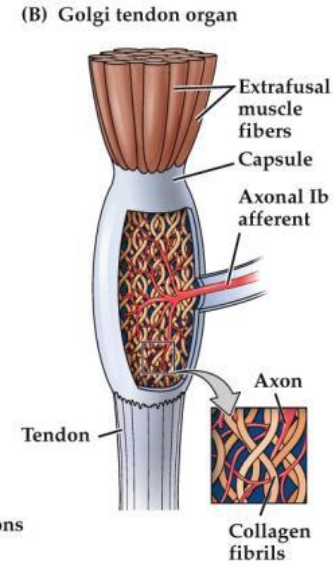
- amytrophic lateral sclerosis
- motor neurons die from oxidative stress: unique expression of transporters, glutamate receptors, and Ca2+ buffers
- treatment: Na channel inhibition to tamper exitotoxicity
- mitochondria failing → oxidative stress → not enough ATP → defective axonal transport → not interacting with postsynaptic partners → loss of trophic factors → presynaptic die back → stress → don't buffer calcium well → activate secondary messengers they shouldn't → more mitochondrial damage → reactive gliosis → AHHHHHHHHH
- Wallerian degeneration - damaged nerve retracts from target towards root
- familial ALS: mutated superoxide dismutase interferes with ETC, triggering apoptosis
- BCL2 family regulates apoptosis by modulating cytochrome c release
- excitotoxicity hypothesis: NMDA receptors letting in too much calcium, binding too often, too much extracellular glutamate, glial cells aren't reuptaking glutamate

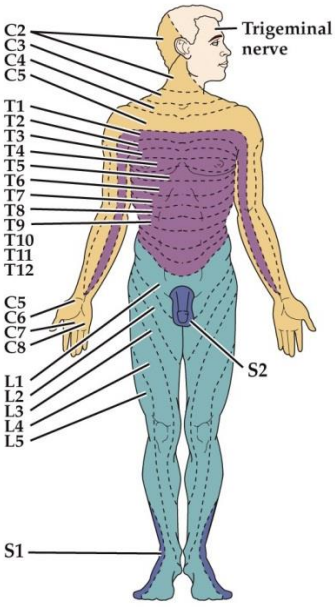
Multiple Sclerosis

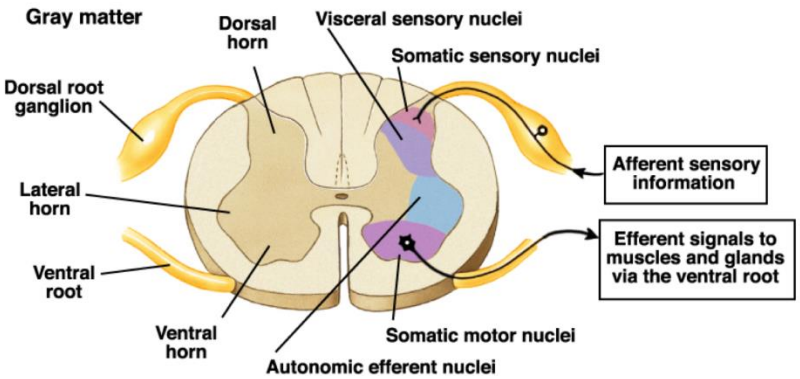
- autoimmune attack of myelin sheaths (interleukin receptor mutation; shown in oligoclonal CSF bands) → reactive gliosis (diffuse glial white matter lesions) → diffuse symptoms (mood, optic neuritis, dysarthria, etc)
- treatment: reduce permeability of BBB to immune cells; inhibit IL genes in T cells and IL receptor in B cells

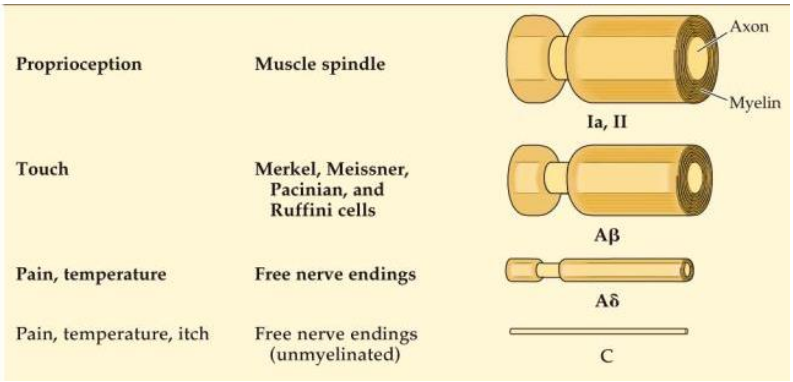

Motor and descending (efferent) pathways (red)
Pyramidal tracts
- Lateral corticospinal tract
- Anterior corticospinal tract
Extrapyramidal Tracts
- Rubrospinal tract
- Reticulospinal tracts
- Olivospinal tract
- Vestibulospinal tract
Sensory and ascending (afferent) pathways (blue)
Dorsal Column Medial Lemniscus System
Gracile fasciculus
Cuneate fasciculus
Spinocerebellar Tracts
Posterior spinocerebellar tract
Anterior spinocerebellar tract
Anterolateral System
Lateral spinothalamic tract
Anterior spinothalamic tract
Spino-olivary fibers
Sacral
Lumbar
Thoracic
Cervical

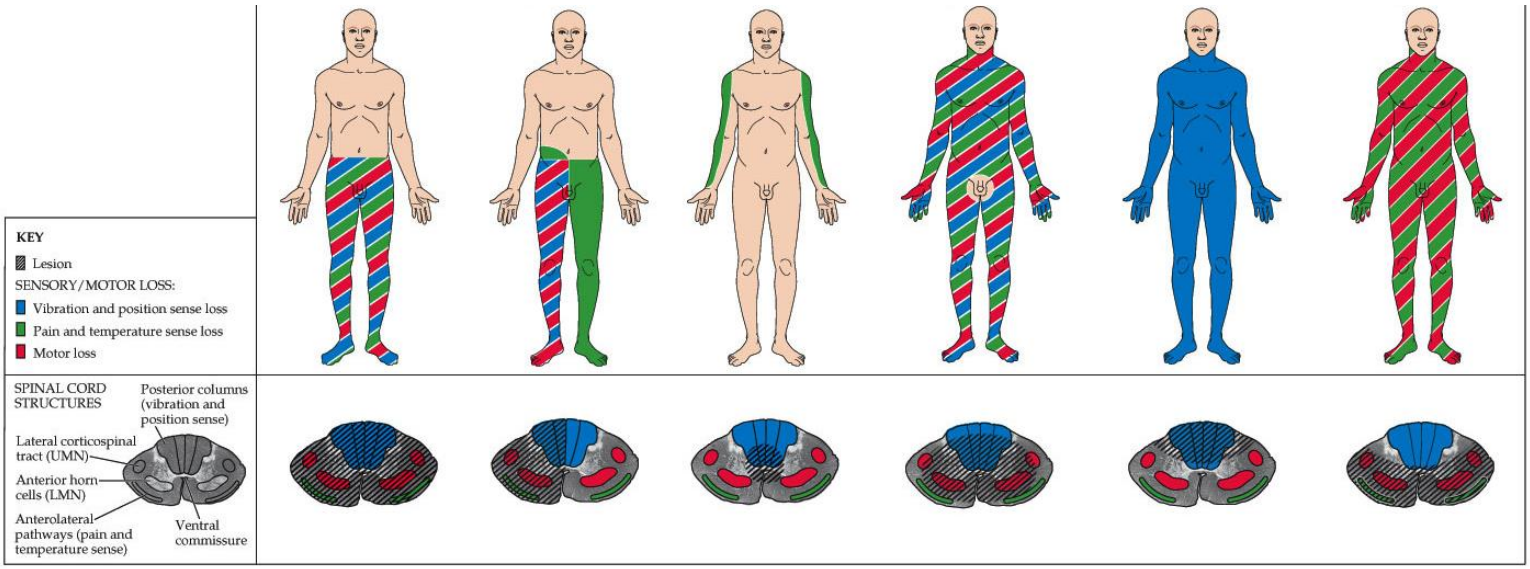

(A) Muscle spindle
Axon of α motor neuron
Extrafusal muscle fibers
Intrafusal muscle fibers
Axons of γ motor neuron
Group Ia afferent axons
Capsule (connective tissue) surrounding spindle
Group II afferent axons

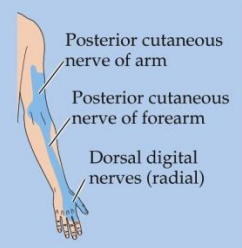
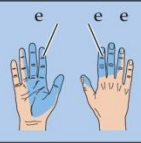
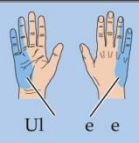
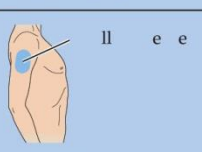
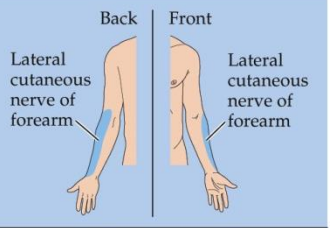

(B) Golgi tendon organ
Extrafusal muscle fibers
Capsule
Axonal Ib afferent
Axon
Tendon
Collagen fibrils


Trigeminal nerve
C2
C3
C4
C5
T1
T2
T3
T4
T5
T6
T7
T8
T9
T10
T11
T12
C5
C6
C7
C8
L1
L2
L3
L4
L5
S2
S1

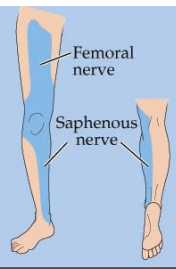
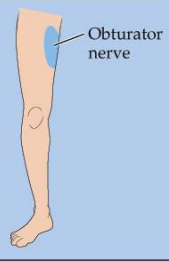
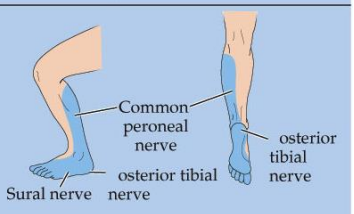
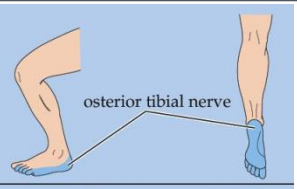
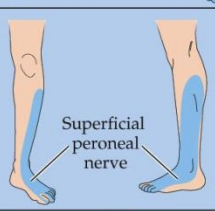
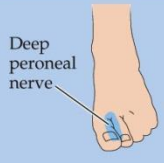

Gray matter
Dorsal horn
Visceral sensory nuclei
Somatic sensory nuclei
Dorsal root ganglion
Afferent sensory information
Lateral horn
Efferent signals to muscles and glands via the ventral root
Ventral root
Ventral horn
Somatic motor nuclei
Autonomic efferent nuclei


Proprioception
Muscle spindle
Axon
Myelin
Ia, II
Touch
Merkel, Meissner, Pacinian, and Ruffini cells
Aβ
Pain, temperature
Free nerve endings
Aδ
Pain, temperature, itch
Free nerve endings (unmyelinated)
C



Radial	Extension at all arm, wrist, and proximal finger joints below the shoulder; forearm supination; thumb abduction in plane of palm	
Median	Thumb flexion and opposition, flexion of digits 2 and 3, wrist flexion and abduction, forearm pronation	
Ulnar	Finger adduction and abduction other than thumb; thumb adduction; flexion of digits 4 and 5; wrist flexion and adduction	
Axillary	Abduction of arm at shoulder beyond first 15°	
Musculo-cutaneous	Flexion of arm at elbow, supination of forearm	

C5	Deltoid, infraspinatus, biceps	Biceps, pectoralis	Shoulder, upper lateral arm
C6	Wrist extensors, biceps	Biceps, brachioradialis	First and second fingers, lateral forearm
C7	Triceps	Triceps	Third finger
L4	Iliopsoas, quadriceps	Patellar tendon (knee jerk)	Knee, medial lower leg
L5	Foot dorsiflexion, big toe extension, foot eversion, inversion	None	Dorsum of foot, big toe
S1	Foot plantar flexion	Achilles tendon (ankle jerk)	Lateral foot, small toe, sole

Femoral	Leg flexion at the hip, leg extension at the knee	
Obturator	Adduction of the thigh	
Sciatic	Leg flexion at the knee (see also tibial and peroneal nerves, in column at left)	
Tibial	Foot plantar flexion and inversion, toe flexion	
Superficial peroneal	Foot eversion	
Deep peroneal	Foot dorsiflexion, toe extension	

Cranial Nerves

midbrain = 2-4; pons = 5-7; medulla = 8-11

CN2: retinal ganglion cells → *dorsal lateral geniculate nucleus of thalamus* (image-forming)
superior colliculus (eye movement → vestibular output)
superchiasmatic nucleus (light intensity → pupillary reflex & circadian regulation)

CN8: hearing: cochlea → cochlear nerve (soma in spiral ganglion) → cross extensively in trapezoid body fibers→ lateral lemniscus carries output to contralateral inferior colliculus
vestibular sense: semicircular canals = angular acceleration; utricle & saccule = linear acceleration

Eyes:
muscles: 3 (medial & upward), 4 (superior oblique – head tilt), 6 (lateral rectus)
PANS: 3 (pupils & lens), 7 (lacrimal glands), 9 (lacrimal glands)

Mouth:
motor: 12 (tongue), 5 (mastication)
salivary glands: 7
taste: 7 (front), 9 (back), 10 (epiglottis & pharynx)
sensory: 5 (front tongue & teeth), 9 (back tongue)

Ear:
motor: 5 (tensor tympani) & 7 (stapedius)
somatic sensory: 7 & 10 (outer), 9 (inner & outer)
hearing & vestibular senses: 8

Face:
motor: 7
sensory: 5

Throat:
motor: 9 & 10 (swallowing), 10 (voice box)
sensory: 9 & 10 (pharynx)

Parasympathetic:
carotid body chemo & carotid sinus baro-receptor: 9
aortic arch chemo & baro-receptor: 10
all organs of chest and abdomen (heart, lungs, & digestive tract via splenic flexure): 10

cranial nerve pathology

- CN III,IV,VI palsies
- Migraine (CN V): cerebrovascular (CAv2.1 channel antagonists, triptans to block transmission from spinal nocioreceptors, tricyclics to lower cortical excitability, steroids treat CBF & CSD)
- Wallenberg syndrome (CN V): medullary stroke above ALT crossing & below trigeminal crossing: pain/temperature loss contralateral, trigeminal loss ipsilateral
- UMN (CN VII): spares forehead; can also cause arm/hand weakness
- Bell's palsy (CN VII): entire face; simultaneous PANS & motor output; treat with steroids
- Hearing/vestibular deficits (CN VIII)

Brainstem

label: 5 structures, 4 junctions, inferior olive, pyramid, pyramidal decussation, superior & inferior colliculus, cerebral peduncle, cerebellar peduncles, nuclei cuneatus & gracilis
cranial nuclei – sensory & motor pathways carry information from multiple nuclei, but are spatially segregated (motor is medial & sensory is lateral)
inferior olive – inputs: contralateral SCT & CST + ipsilateral M1 & red nucleus
output: contralateral cerebellum
midbrain: tectum: *superior colliculus* (visual nuclei) & *inferior colliculus* (auditory nuclei) → tecto & vestibulo spinal tracts
tegmentum: *substantia nigra, red nucleus, periaqueductal grey*, & *reticular formation* + medial lemniscus
pain: ALT & limbic system → periaqueductal grey → modulates dorsal columns
basis: long tracts of corticospinal & corticobulbar fibers
pons: pontomesencephalic reticular formation (PRF) receives inputs from somatosensory (cord), limbic/cingulate cortex, frontoparietal association cortex, & thalamic reticular nucleus
thalamic reticular nucleus: cortical input → modulate other thalamic structures → project to PRF
locked-in syndrome: bilateral damage to corticospinal & corticobulbar tracts in ventral pons

neurotransmitters

up = cortex, thalamus, & basal ganglia
down = cerebellum, medulla, & spinal cord
NE: increase MN excitability, sleep, deficits in attention & mood disorders
down from *lateral tegmental area* & up from *locus ceruleus*
5-HT: increases MN excitability, psychiatric disorders (transporter mutations)
down from *caudal raphe nuclei* (caudal pons & medulla) & up from *rostal raphe nuclei* (rostral pons & midbrain)
Histamine: *tuberomammilary nucleus* → alertness
Ach: *pontine nuclei* → motor function via thalamus, cerebellum, basal ganglia, tectum, medulla/cord
basal forebrain → attention & memory via Alzheimer's, theta rhythm (arousal, memory formation)

internal capsule

anterior limb: frontopontine (corticofugal) & thalamocortical fibers (between lenticular nucleus & head caudate)
genu ("knee"): corticobulbar (cortex to brainstem) fibers
posterior limb: corticospinal & sensory fibers (medial lemniscus and the anterolateral system) (between lenticular nucleus & thalamus)
other: retrolenticular fibers from LGN, branch to optic radiation
sublenticular fibers including auditory radiations and temporopontine fibers

The Cerebellum

gross anatomy

cerebellar peduncles: fiber tracts that run through brainstem (trace these)

superior: primary output of the cerebellum to red nucleus & thalamus

middle: input from the contralateral cerebral cortex via the pons

inferior: fibers from ipsilateral spinocerebellar tract (proprioceptive), inferior olives, vestibular nuclei

somatotopic input: repeats & layering provide multiple modes of coordination & interactions

inner → outer::head → legs in posterior & anterior lobes

audio/visual input in medial vermis

motor planning: direction, force, speed, & amplitude of movements

circuitry

all ascending fibers are excitatory & descending fibers are inhibitory

output: *Purkinje* (spontaneously active/tonic) → deep cerebellar & vestibular nuclei

input: *climbing fibers* (inferior olive)

mossy fibers (pontine nuclei & vestibular ganglia) → granule cells → parallel fibers

structures providing input to Purkinje also provide input to structure that receives inhibitory output of Purkinje cells (raw & processed nuclei)

big proprioreceptive-motor loop modulated by input from locus coeuruleus (NE), raphe nuclei (5-HT)

output circuitry

all output paths are double-crossed: once in decussation of superior cerebellar peduncle & once in spinal cord (or bilateral)

all deep cerebellary nuclei project to VLN → motor & associate cortices → down LCST

ventral SCT: cross in ventral commissure → synapse in intermediate zone → affect ACST/LCST

lateral: dentate nucleus → parvo red nucleus → inferior olivary nucleus → down rubrospinal tract

extremity ataxia: finger tapping test

intermediate/paravermis: interposed nuclei (emboliform & globose) → same as above, except through magno red nucleus

appendicular ataxia: dysrhythmia (abnormal timing) or dysmetria (abnormal trajectories in space) (excessive check/finger to nose test)

medial: vermis: fastigial nucleus → contralateral tectospinal; bilaterally to VLN → cortex → ACST

flocculonodular lobe: reticular formation & vestibular nuclei

truncal ataxia, disequilibrium, eye movement abnormalities (Romberg's test)

cerebral pathology

infarcts & hemorrhages:

- small in SCA: unilateral ataxia
- PICA and SCA: vertigo, nausea, horizontal nystagmus, limb ataxia, unsteady gait, headache (from swelling, hydrocephalus, usually occipital)
- SCA has brainstem involvement while PICA does not

ataxia:

- peduncle/pontine lesions; hydrocephalus; prefrontal cortex; spinal cord disorder; contralateral ataxia-hemiparesis

- sensory ataxia: loss of joint-position sense; overshooting movements
- vestibular ataxia is gravity dependent: goes away when patient lies down
- cerebellar ataxia: irregularities in rate, rhythm, amplitude, & force of movements
- inherited ataxia: polyglutamine expansion (CAG) which affects channels or other proteins (like PKC) → these are in all neurons/cells → kills Purkinje cells

disorders of equilibium

parapontine reticular formation: input from VN + superior colliculus & output to motor nuclei where vestibulo & tecto tracts interact

front eye fields: activated prior to planned eye movements; also integrate these inputs

control the excitability of medial motor neurons based on head position

Basal Ganglia

striatum (caudate + putamen), globus pallidus (lenticular nucleus when combined with putamen), subthalamic nucleus, substantia nigra, nucleus accumbens, ventral pallidum
basal ganglia evaluate voluntary motor program based on cortical & thalamic inputs → signal to thalamus to initiate or terminate
inhibition of thalamus → reduction of drive back to motor system

circuitry

input: from striatum (98% GABAergic, 2% cholinergic)
cortical & thalamic + domainergic modulation from SNc
output: GABAergic via GP and SNr (pars reticulata)
GPi inhibits thalamus, which projects to frontal lobe
SNr inhibits superior colliculus (visual & vestibular inputs influence locomotion in Parkinson's)
both output to reticular formation → influence over lateral & medial motor systems
distinct pathways for: motor control, eye movements, cognitive & emotional functions
direct pathway: excite thalamus via disinhibition
cortex → striatum → inhibits GPi/SNr → reduces inhibition of thalamus
indirect pathway: inhibit thalamus via STN
cortex → striatum → inhibits GPe → reduces inhibition of STN → excites GPi/SNr → inhibit thalamus
dopamine enhances striatum output depending on DA receptor expression in medium spiny neurons: D1Rs excite direct & D2Rs inhibit indirect → disinhibition of thalamus
input modulates spontaneous firing activity: low activity: striatum (putamen) & SNc; moderate activity: STN; high activity: GPi & SNr; irregular (low & high): GPe

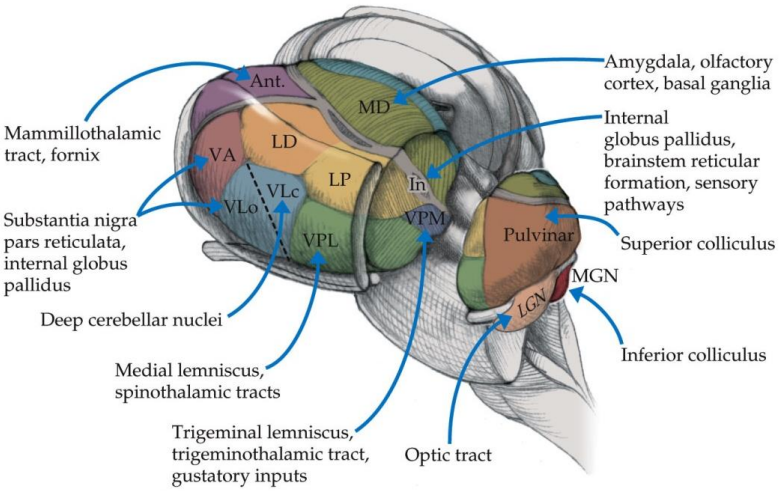
pathology

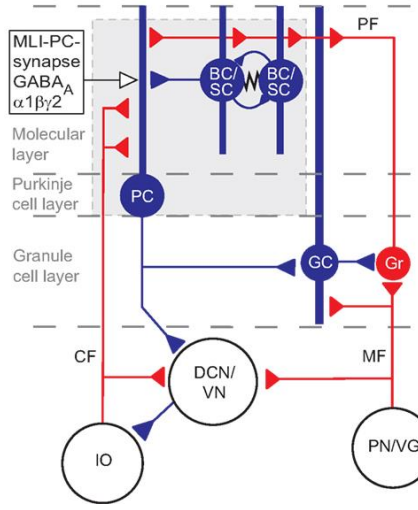
movement disorders distinct from cerebellar ataxia: all have cognitive/emotional components
hypokinetic (e.g., Parkinson's): rigidity, difficulty initiating movement, direct pathways

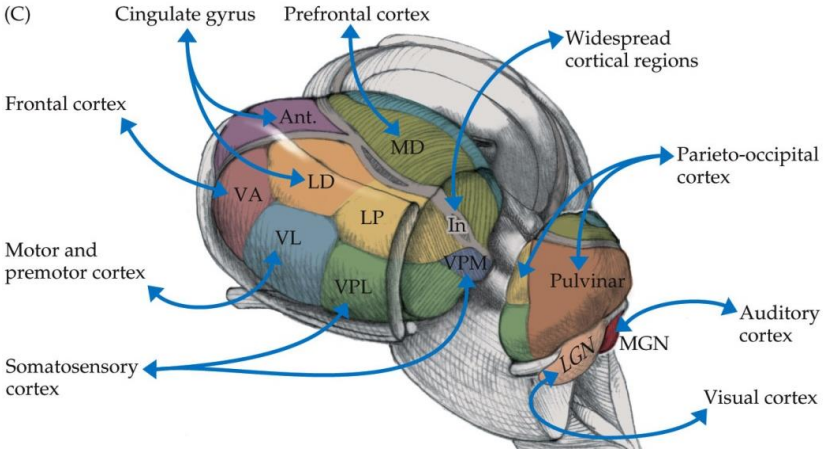
- motor symptoms: tremor, bradykinesia, cog-wheel rigidity, postural and gait instability (antero- or retro-pulsion)
- DA in SNc die → direct pathway loses strength → more inhibition of thalamus
- treatment: levodopa (BBB-permeant DA precursor) increases DA "tone" in striatum; deep brain stimulation stimulate thalamus via depolarizing block of GPi & STN; isradipine
- continuous Ca2+ influx in these pacemaking cells may lead to mitochondrial dysfunction by disrupting ATP production (same genes tied to PD, patients have reduce mitochondrial complexin 1, blocking influx causes reversion of juvenile pacemakers)

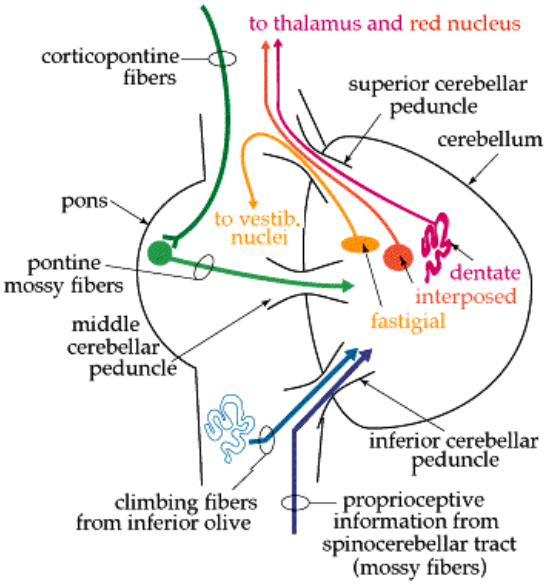
hyperkinetic (e.g., Huntington's): uncontrolled involuntary movements, indirect pathways

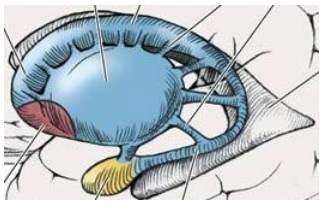
- degeneration of projections from striatum to GPe → STN more inhibited → SNr less inhibited → less inhibition of thalamus
- increased polyglutamine repeats in Huntington gene (autosomal dominant and fully penetrant)
- initial symptom is chorea (jerky, random movements); cognitive/emotional component arises later

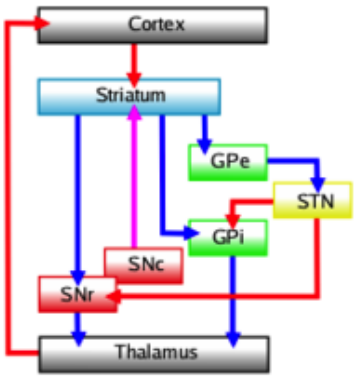












SOURCES OF CORTICAL INPUT	BASAL GANGLIA INPUT NUCLEI	BASAL GANGLIA OUTPUT NUCLEI[a]	THALAMIC RELAY NUCLEI[b]	CORTICAL TARGETS OF OUTPUT
MOTOR CHANNEL				
Somatosensory cortex; primary motor cortex; premotor cortex	Putamen	GPi, SNr	VL, VA	Supplementary motor area; premotor cortex; primary motor cortex
OCULOMOTOR CHANNEL				
Posterior parietal cortex; prefrontal cortex	Caudate, body	GPi, SNr	VA, MD	Frontal eye fields; supplementary eye fields
PREFRONTAL CHANNEL				
Posterior parietal cortex; premotor cortex	Caudate, head	GPi, SNr	VA, MD	Prefrontal cortex
LIMBIC CHANNEL				
Temporal cortex; hippocampus; amygdala	Nucleus accumbens; ventral caudate; ventral putamen	Ventral pallidum; GPi; SNr	MD, VA	Anterior cingulate; orbital frontal cortex