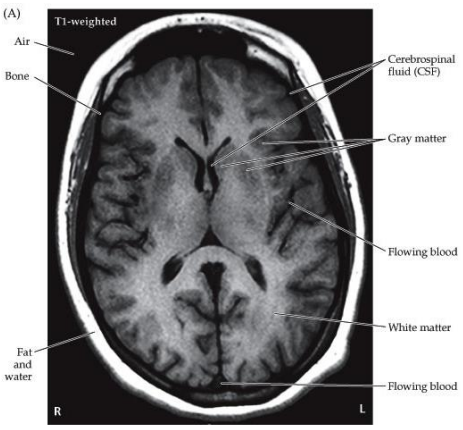
http://www.dartmouth.edu/~dons/index.html
www.neuroanatomy.wisc.edu

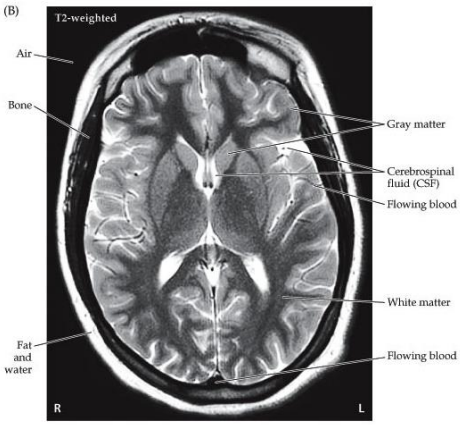
TABLE 4.3 MRI Appearance of Commonly Scanned Tissues

TISSUE	T1-WEIGHTED	T2-WEIGHTED	FLAIR
Gray matter	Gray	Light gray	Light gray
White matter	White	Dark gray	Gray
CSF or water	Black	White	Dark gray
Fat	White	White[a]	White[a]
Air	Black	Black	Black
Bone or calcification	Black	Black	Black
Edema	Gray	White	White
Demyelination or gliosis	Gray	White	White
Ferritin deposits (e.g., in basal ganglia)	Dark gray	Black	Black
Ca^{2+} bound to protein	White	Dark gray	Dark gray
Proteinaceous fluid	White	Variable	Variable

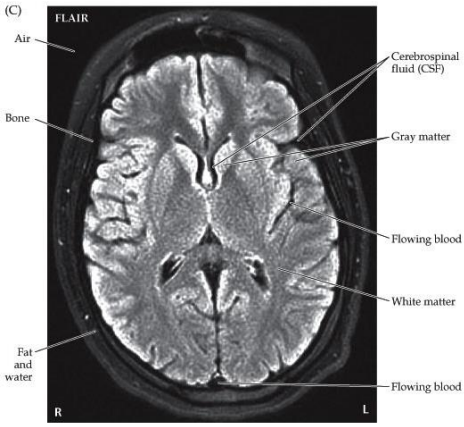
Chapter 4: Clinical Neuroradiology
2D slices called imaging planes along **horizontal** (axial; most CT scans), **coronal** (face), and **sagittal** (side) planes
CAT – computer-assisted (detector reconstructs image) tomography (rotated)
x-ray source moves around CT gantry aperture, which is absorbed by detector array
absorption varies with density: water/brain is isodense (grey), bone is hyperdense (white), & fat is hypodense (black)
fresh hemorrhages (Fe) are slightly hypodense
can highlight blood vessels with IV contrast
MRI – nuclear magnetic resonance imaging
protons have spin & precession relative to an external static magnetic field
intensity of MRI signal determined by proton density & proton relaxation time

Relaxation
T1 relaxation along z axis parallel to magnetic field
T2 relaxation along x,y axis perpendicular to magnetic field
in spin echo (SE) pulse sequence, T1-weighted images from shorter repetition time (TR) & echo time (TE); reverse for T2-weighted images
all: air/bone is black; fat is white
T1: water is dark, lipids (white matter/myelinated axons) bright → vice versa for T2
FLAIR: like T2 except CSF is dark so subtle abnormalities are enhanced





CAT vs



MRI:
- CAT is better for bone/blood/restrictions: head trauma, calcified lesions, fresh hemorrhage, pacemaker, obesity, claustrophobia, lower cost & higher speed
- MRI is better for anatomical detail, old hemorrhages, lesion near base of skull, or subtle structures like tumors, infarcts, or demyelination

Unit 1: Spinal Cord
Aim
- afferent sensory pathways bring information from periphery to brain
- efferent motor pathways carry motor commands from brain to muscles
- efferent autonomic pathways control visceral functions

Brain surface

gyri (ridge), **sulci** (trough; wrinkles), & **fissue** (deep gap dividing lobes :)

primary motor cortex *is on the precentral gyrus, anterior to central sulcus, in front lobe*

primary somatosensory cortex *is on the post-central gyrus, posterior to central sulcus, in parietal lobe*

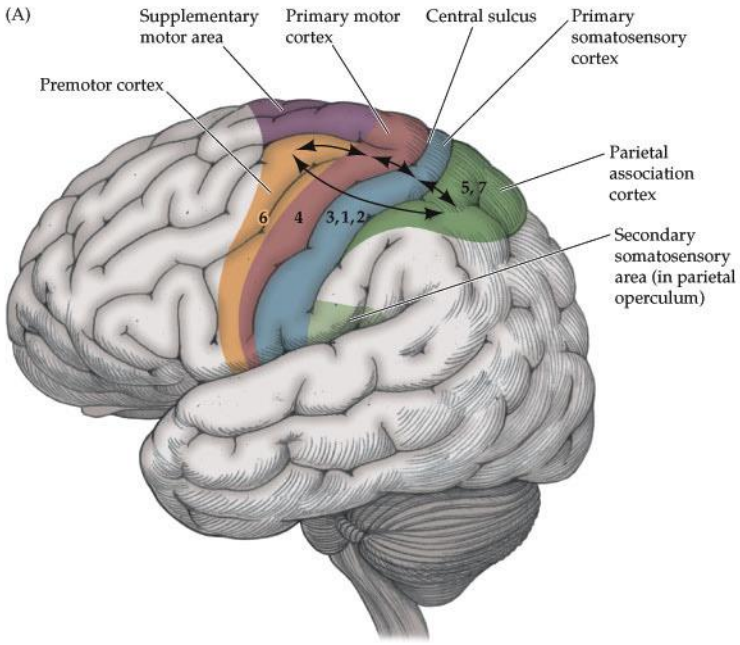
both are superior to Sylvan fissue that separates temporal lobe from frontal/parietal lobes

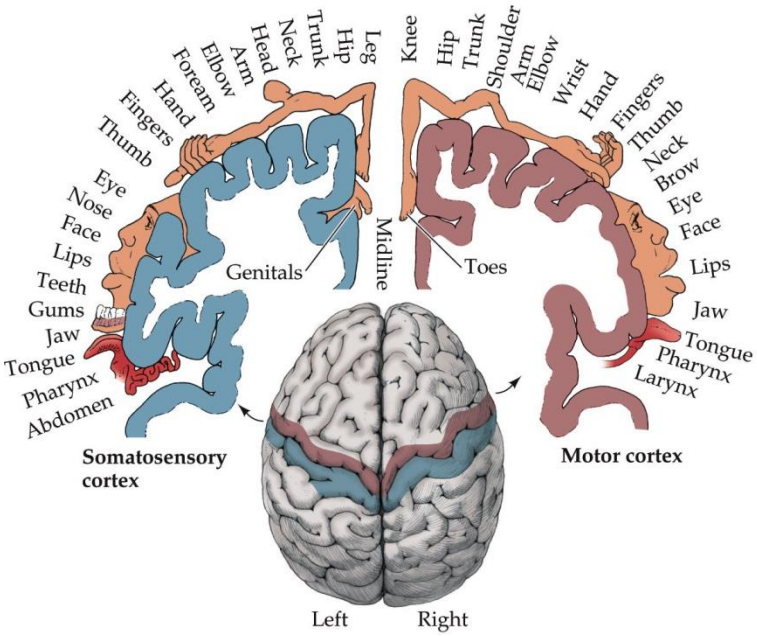
brain stem: pons, midbrain, & medulla

somatotopic organization: specific parts of brain control different parts of body & vice versa

maintained throughout spinal cord

coronal plane homunculus





Spinal Cord

axon tracts: **white matter**, descend through **internal capsule**

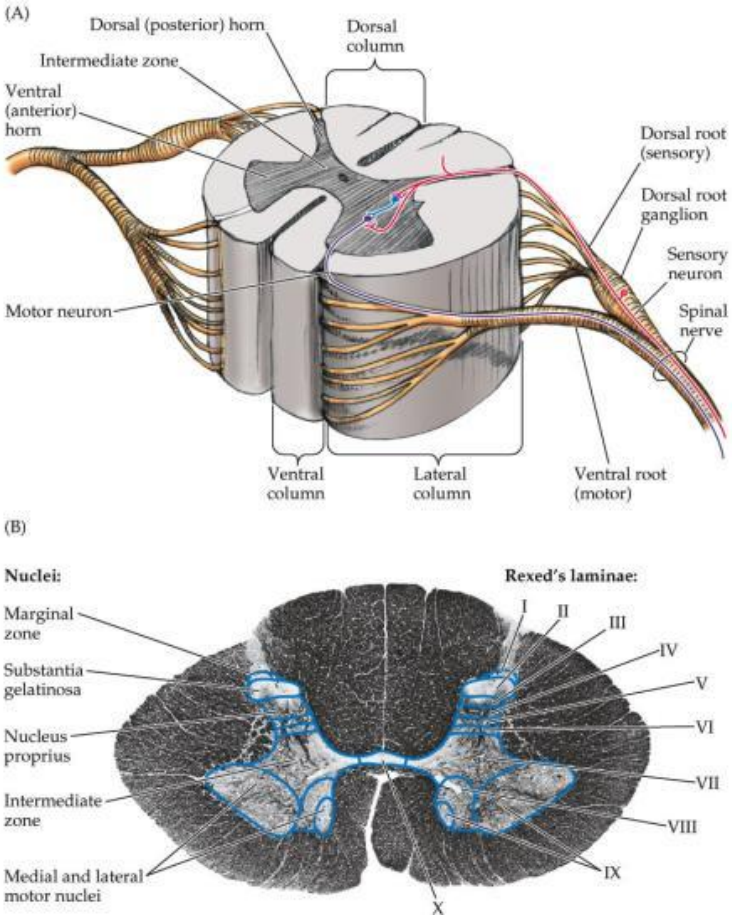
cell bodies in the spinal cord: **grey matter**

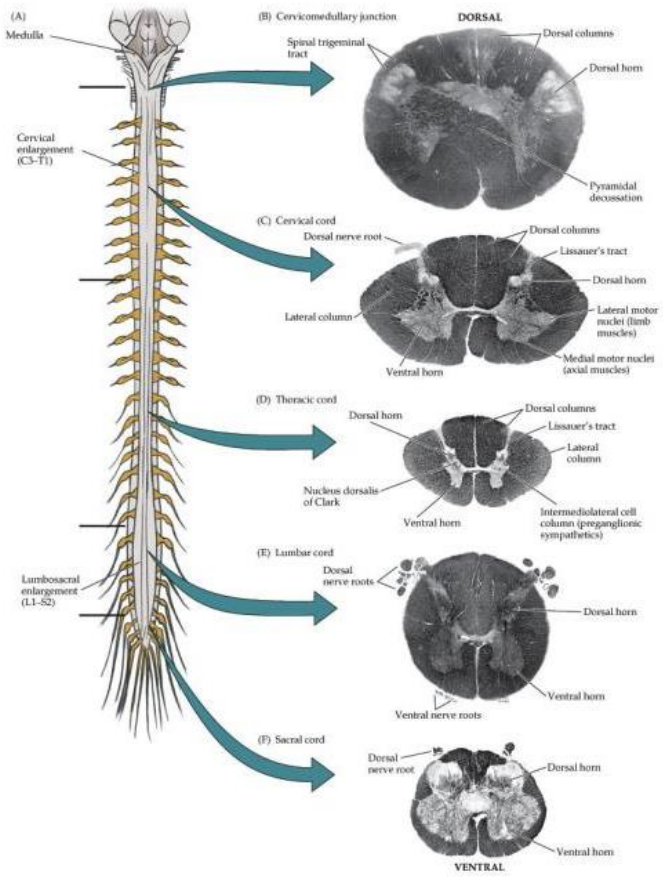
sensory in dorsal horn; motor in ventral horn (larger Rexed's numbers); interneurons in intermediate zone

spinal cord: cervical (head & neck), thoracic (torso), lumbar & sacral (legs)

ventral root expansion in cervical & lumbar-sacral regions due to greater fine motor control

pyramidal decussation in medulla: crossing right brain to left half of body & vice versa





Descending Motor Pathways

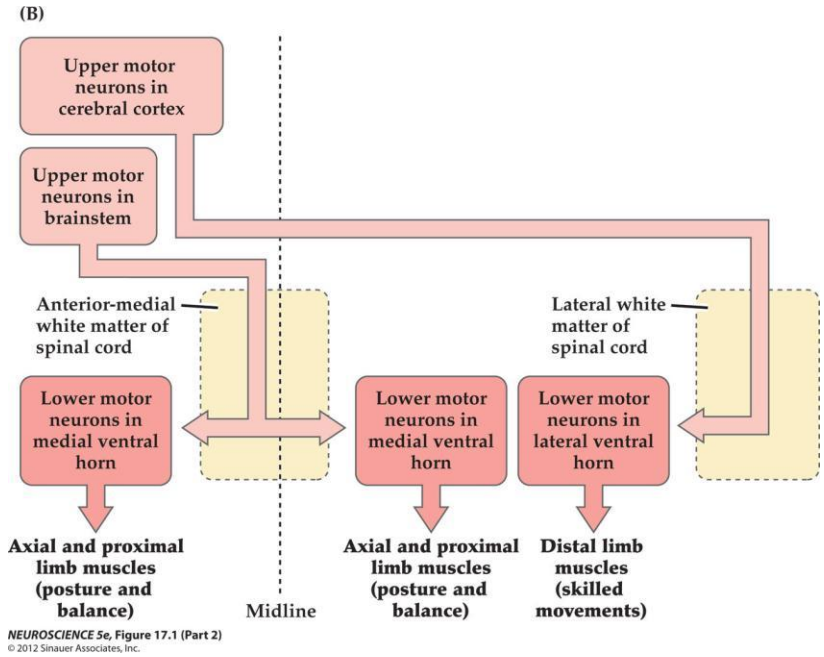
<u>Lamina</u>

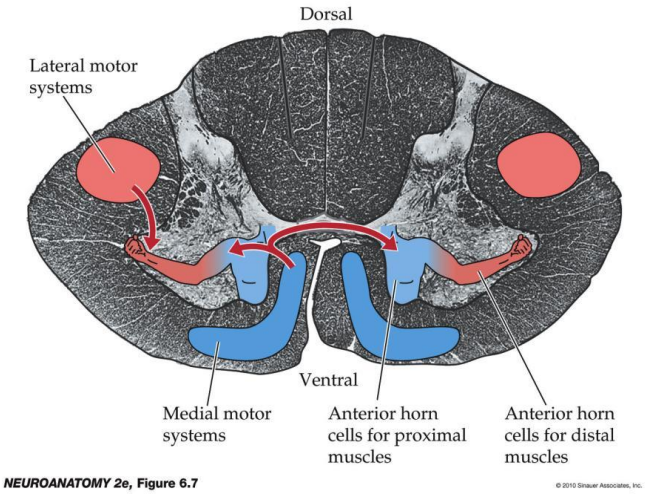
layer 6: interface with deep thalamus neurons
layer 5: output neurons (pyramidal cells → special type is Betz cell, huge soma, fine control of muscles)
layer 4: thalamus input
layer 2 & 3: cortical neurons synapse w/ interneurons
layer 1: lateral connections

<u>Upper Motor Neuron Pathway</u>

1. **corticospinal tracts**: primary motor cortex layer 5 → corticospinal & corticobulbar tracts → posterior limb of internal capsule → basis pedunculi (midbrain) → basis pontis (pons) → ventral column in medulla for crossing in pyramidal decussation (lateral CT) or in ventral column (anterior CT)
    LCT: dorsal column & lateral intermediate zone/lateral motor nuclei (LIZ/LMN) (dorsal grey matter) → full cord, movement of contralateral limbs
    ACT: ventral column & medial intermediate zone/medial motor nuclei (MIZ/MMN) (ventral grey matter) → cervical/upper thoracic, bilateral axial & girdle muscles
2. **rubrospinal tract**: red nucleus & central tegmental decussation (midbrain) → lateral column
    RST: cervical cord, function not well known in primates
3. **vestibulospinal tracts**: lateral vestibular nucleus (pons) or medial vestibular nucleus (medulla)
    MVT: MIZ/MMN → cervical/thoracic, head & neck positioning
    LVT: MIZ/MMN → full cord, balance
4. **reticulospinal tracts**: pontine/medullary reticular formation → meduallary reticulospinal tract
    RCT: MIZ/MMN → full cord, gait & posture
5. **tectospinal tract**: superior colliculus (midbrain) → tectospinal tract

TST: MIZ/MMN → cervical, function not well known in primates





<u>Neuromuscular Synapse</u>

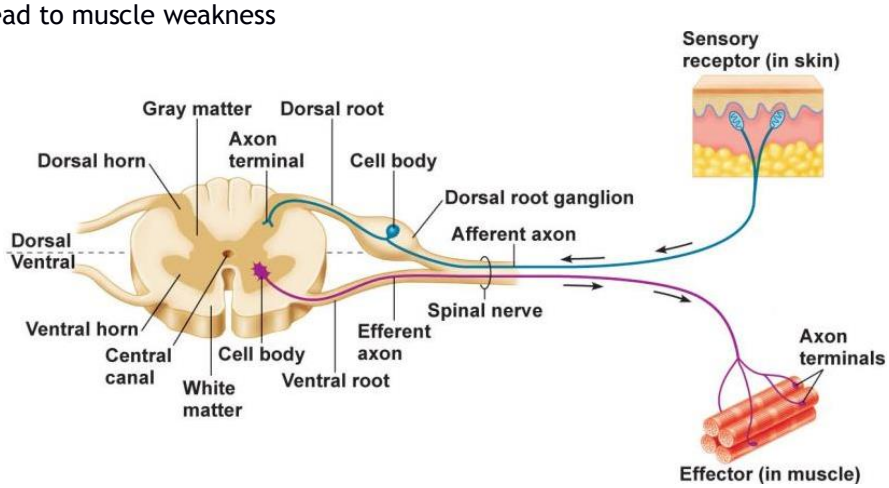
motor unit = motor neuron + fiber(s) it innovates (smaller unit = less force, more fine control)

primary motor neuron → glutamate (major excitatory NT in CNS) → motor interneuron → Ach → muscle

UMN lesions: enhanced muscle tone & reflexes

LMN lesions: muscular atrophy/fasciculations & reduced reflexes/tone

both lead to muscle weakness



Reflex Arcs

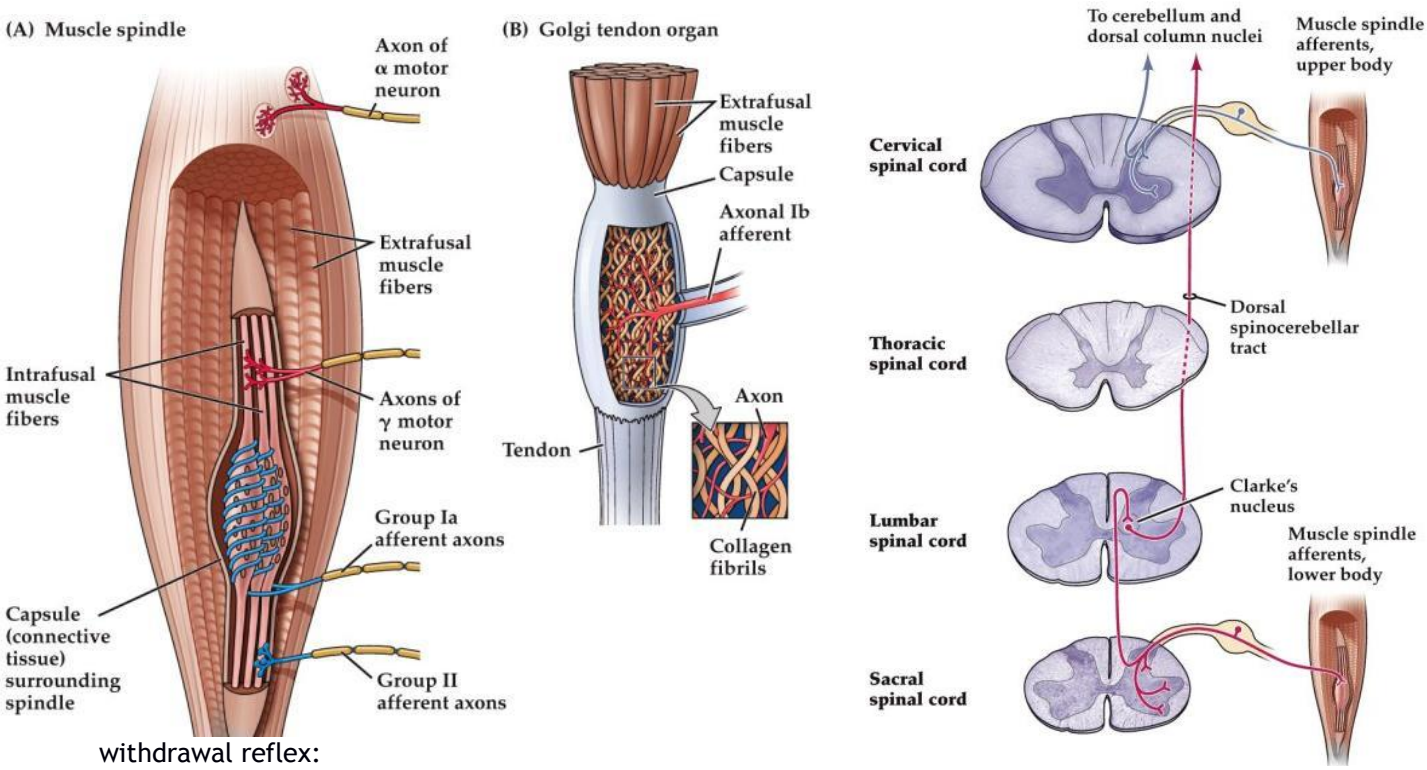
proprioceptors → stretch & withdrawal reflexes

reflex grades: 0 = absent, 1-3 = normal, 4-5 = clonus

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

input to primary motor cortex → inhibition of inhibition → more input to gamma MN → intrafusal fibers of extensor contract → raise Ia gain



withdrawal reflex:

polysynaptic crossed-extensor reflex

excitation of ipsilateral flexor & contralateral extensor

inhibition of ipsilateral extensor & contralateral flexor

mechanoreceptors → touch

nerve ending has encapsulated afferent fiber (amplified transducer) which expands sensory SA

different receptor types have different field sizes on different skin surfaces to detect textures, skin motion, vibration, or skin stretch

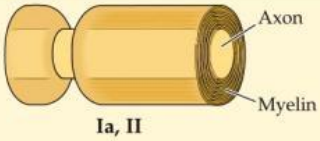
two-point discrimination: calipers test integrity of somatosensory input

deficit indicates peripheral neuropathy

receptive fields are more discriminatory in fingers, face, & toes

thermo/nocioreceptors → free nerve endings with chemical & heat-sensitive channels (pain, temperature, itch :)

TABLE 9.1 Somatic Sensory Afferents that Link Receptors to the Central Nervous System

SENSORY FUNCTION	RECEPTOR TYPE	AFFERENT AXON TYPE[a]	AXON DIAMETER	CONDUCTION VELOCITY
Proprioception	Muscle spindle	 Ia, II	13–20 μm	80–120 m/s
Touch	Merkel, Meissner, Pacinian, and Ruffini cells	 Aβ	6–12 μm	35–75 m/s
Pain, temperature	Free nerve endings	 Aδ	1–5 μm	5–30 m/s
Pain, temperature, itch	Free nerve endings (unmyelinated)	C	0.2–1.5 μm	0.5–2 m/s

current flow resistance is proportional to fiber diameter
different processes have axons with different properties
myelin: reduce membrane capacitance → less charge moved for same voltage change → saltatory conduction between nodes of Ranvier

---

Motor Pathology
UMN Disease
loss of cortical control of spinal reflex arcs
LST synapses on interneurons to inhibit gamma MNs
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

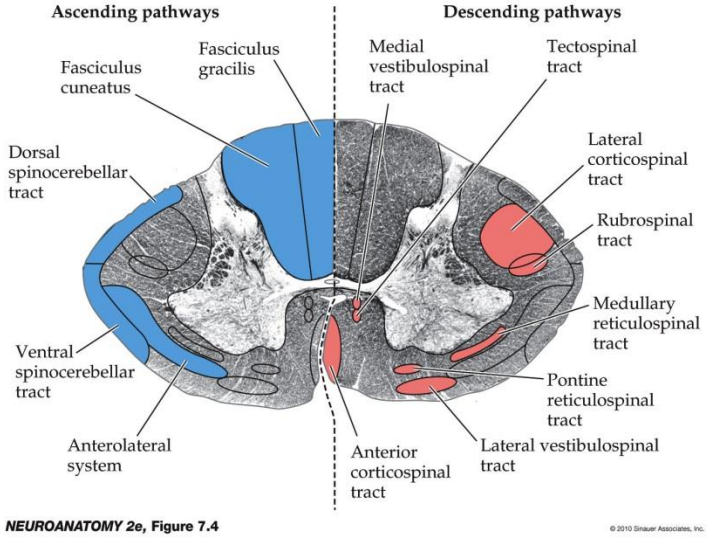
Autonomic Control
from hypothalamus, pons, & medulla → cell bodies in medial portions
nAchR → NE or Ach (synpase effector organ via varicosities en passant)
SANS: thoracic/lumbar → intermediolateral nucleus (Rexed's lamina #5) → ventral nerve root → paravertebral ganglion via white ramus → synapse → to effector organ via grey ramus
preganglioinc neuron sends axon collaterals up and down sympathetic chain → generalized response
PANS: brainstem/sacral → sacral parasympathetic nuclei → ventral nerve root → peripheral synapse near effector organ
damage to sacral spinal cord will lead to urination/defecation/sexual function deficits

Descending Motor Control Pathology
Cortical insult/lesion (stroke)
UMN disease (primary lateral sclerosis)
UMN axonal damage (MS)
spinal cord injury (trauma)
LMN disease (ALS)

Stroke
ischemic: blood clot from plaque in artery (thromolitic), break off from elsewhere (embolitic), or atherosclerotic plaque
hemorrhagic: burst blood vessel
lacunar infarct: silent stroke, block from deep artery from Circle of Willis

Lesions

cortex → unilateral weakness according to somatotopic mapping
internal capsule → pure hemiparesis (including lower face)
pyramidal decussation → hemiparesis sparing face
spinal cord → weakness below lesion site
qaudriparesis: could be medullary lesion (bilateral lesions are unlikely in cortex & efferents), but more likely generalized motor neuron disease



Ascending Sensory Pathways

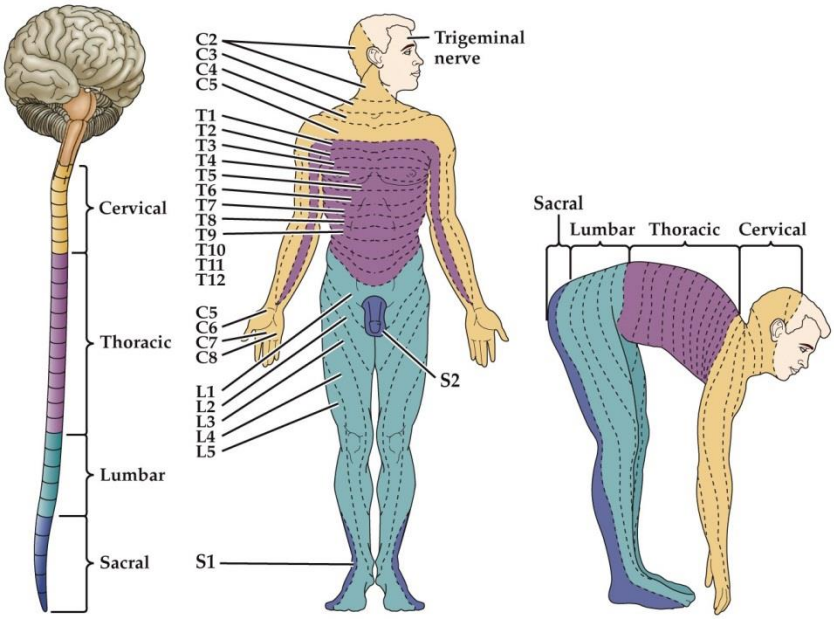
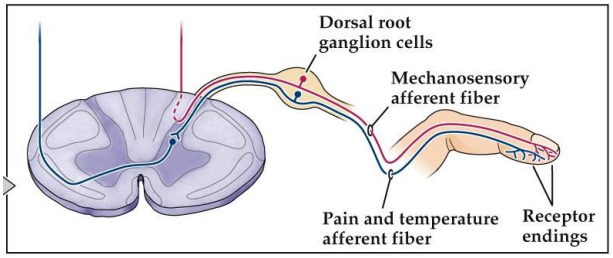


TABLE 7.1 Main Long Tracts of the Nervous System

PATHWAY(S)	FUNCTION	NAME (AND LEVEL) OF DECUSSATION
Lateral corticospinal tract	Motor	Pyramidal decussation (cervicomedullary junction)
Posterior column–medial lemniscal pathway	Sensory (vibration, joint position, fine touch)	Internal arcuate fibers (lower medulla)
Anterolateral pathways	Sensory (pain, temperature, crude touch)	Anterior commissure (spinal cord)

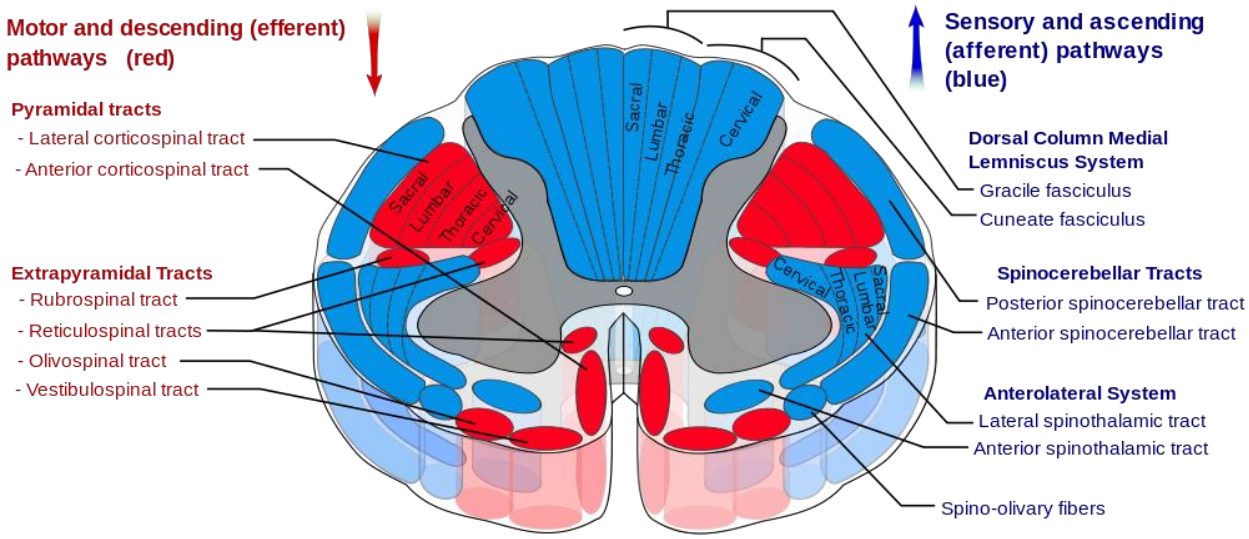


sensory & motor input layout is pretty much the same (except that muscles can run across two dermatomes)

Sensory Pathways
1. posterior column: VPL → cross in medulla via medial lemniscus → descend through dorsal columns (fasciculus gracilis for lower body and cuneatus for upper body) → dorsal root ganglion (DRG) → vibration & position sense
2. anterolateral pathways: VPL → secondary sensory neuron → anterolateral pathway → cross via anterior commissure → DRG → pain & temperature

3. spinocerebellar tracts: Golgi apparatus & spindle fibers also send synapses to dorsal & ventral spinocerebral tracts to convey point position via collaterals to cerebellum (also cross in medulla) → via posterior column collaterals?

4. **trigeminal nerve**: emerges from brainstem rather than spinal cord, sensory input for face
   crosses in trigeminal limnesces
   eg Tick de la Rue – facial pain tics



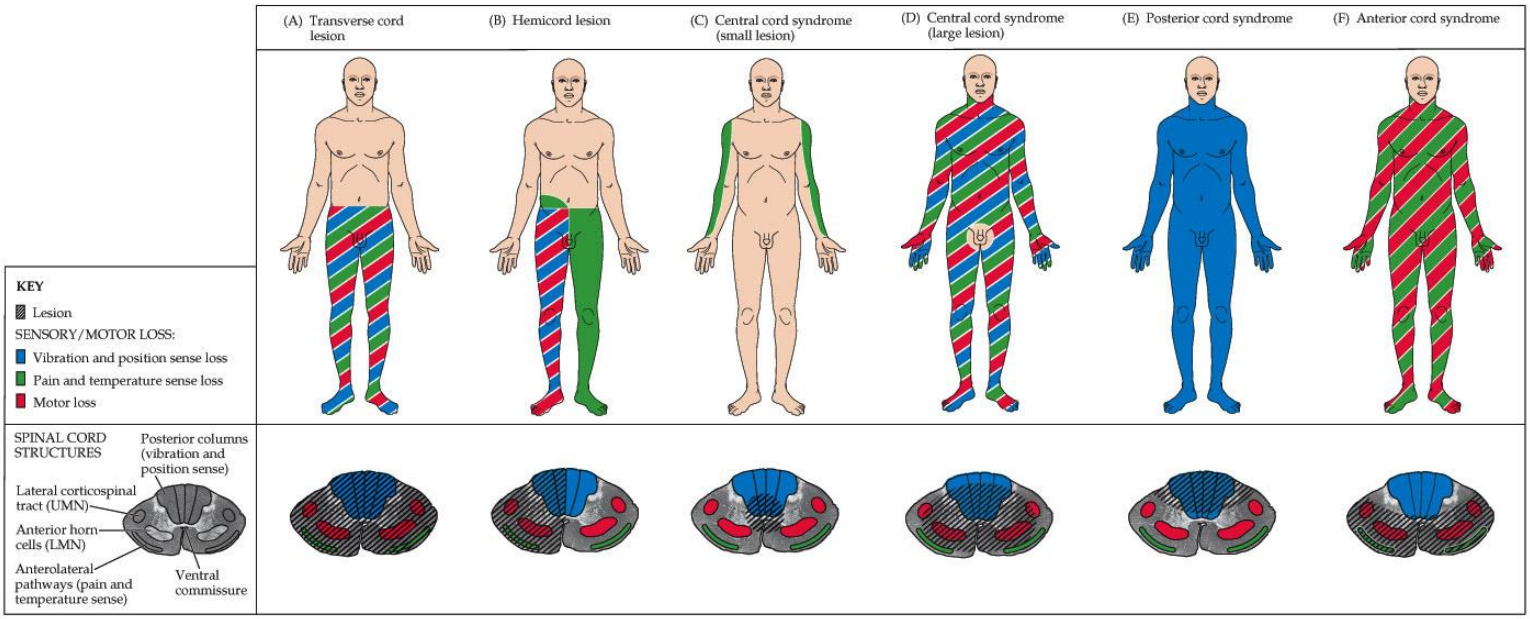
Primary Somatosensory Cortex

sensory cortex: anterior part of parietal lobe, behind central gyrus (has 3 sections)
gets input from ventral posterior lateral (VPL) or medial (for facial) nuclei of thalamus
layer 2 & 3: projections from layer 4; local integration
layer 4: thalamic input
layer 5: output to body
layer 6: output to thalamus
feedback loop: somatosensory projections go to VPL and other brain areas AND output of primary sensory cortex goes to other brain areas → give more weight to raw/reference or processed signal → hormones, pain perception, etc
   eg thalamus gets a raw copy from ascending tracts & a processed copy from cortex which affects how it relays & modulates sensory input to cortex
pain modulation in periaqueductal gray matter: input from anterolateral system & hypothalamus/amydala/cortex modulates output to dorsal horn

Patterns of Sensory Loss

differentiate primary input vs processing problem
stereognosis – determination of tactile stimulation, mediated by posterior column pathways
graphesthesia – recognition of letters traced on skin, mediated by posterior column pathways & cortical circuits
lesions: pons – contralateral anterolateral/posterior columns tract & ipsilateral trigeminal (already crossed)
peripheral neuropathy – bilateral distal sensory loss (stocking and glove syndrome)

pathways to know: pinprick, temperature, vibration, joint position sense, two-point discrimination, graphesthesia, stereognosis, tactile extinction

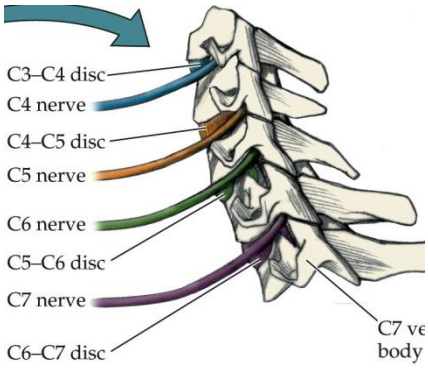


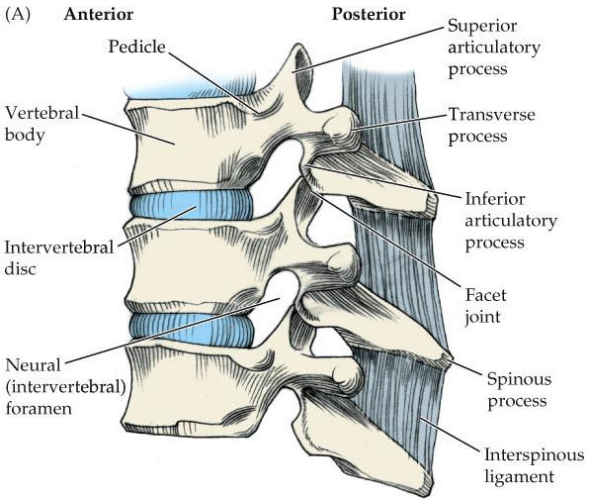
Nerve Plexus

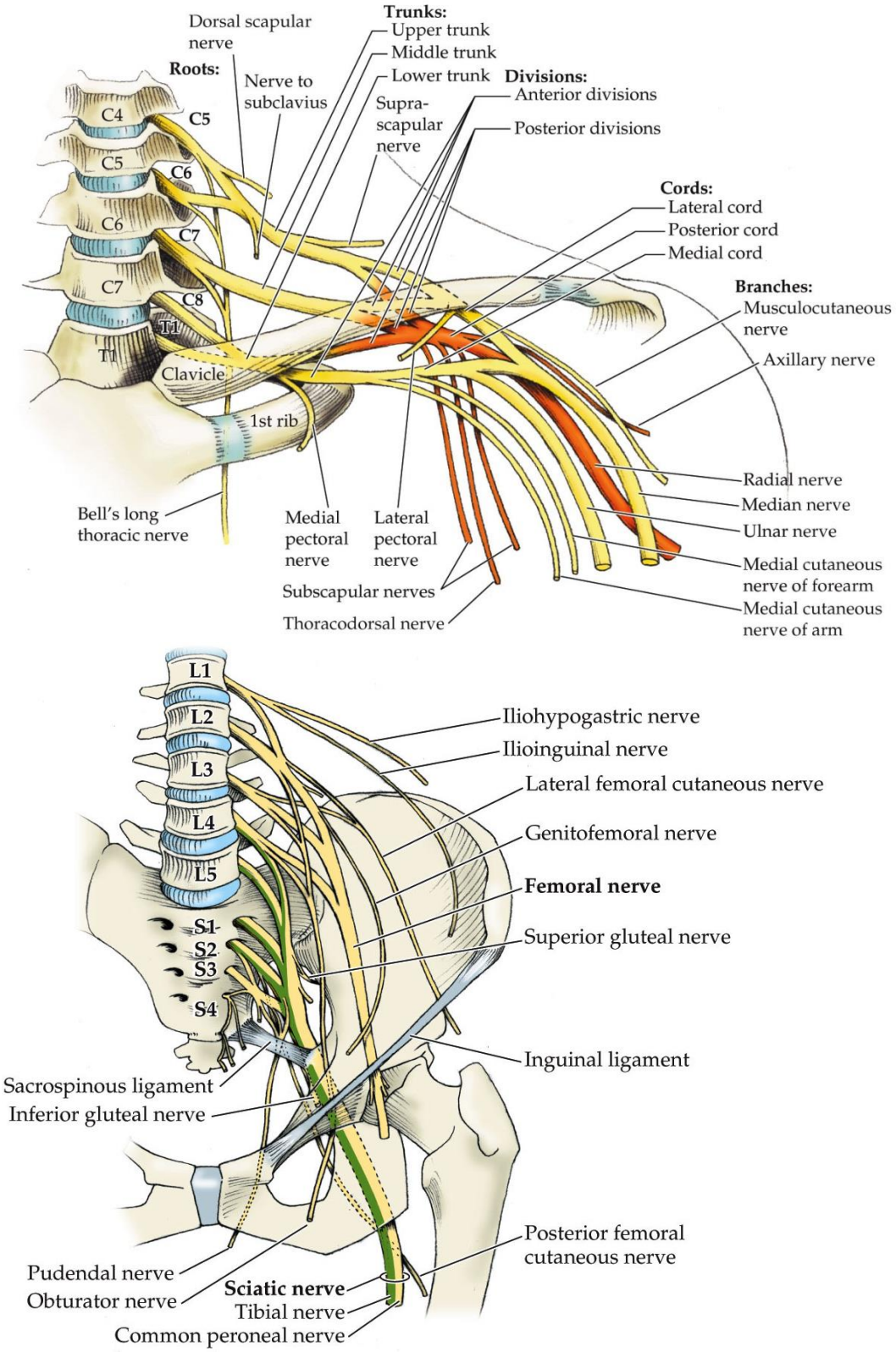
terms to know: transverse & spinous processes, intervertebral disc (usually herniates laterally), foramen (spinal column)

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

TABLE 8.5 Three Important Nerve Roots in the Arm

NERVE ROOT	MAIN WEAKNESS[a]	REFLEX DECREASED[a]	REGION OF SENSORY ABNORMALITY[b]	USUAL DISC INVOLVED	APPROXIMATE PERCENTAGE OF CERVICAL RADICULOPATHIES
C5	Deltoid, infraspinatus, biceps	Biceps, pectoralis	Shoulder, upper lateral arm	C4–C5	7%
C6	Wrist extensors, biceps	Biceps, brachioradialis	First and second fingers, lateral forearm	C5–C6	18%
C7	Triceps	Triceps	Third finger	C6–C7	46%

TABLE 8.6 Three Important Nerve Roots in the Leg

NERVE ROOT	MAIN WEAKNESS[a]	REFLEX DECREASED[a]	REGION OF SENSORY ABNORMALITY[b]	USUAL DISC INVOLVED	APPROXIMATE PERCENTAGE OF LUMBOSACRAL RADICULOPATHIES
L4	Iliopsoas, quadriceps	Patellar tendon (knee jerk)	Knee, medial lower leg	L3–L4	3%–10%
L5	Foot dorsiflexion, big toe extension, foot eversion, inversion	None	Dorsum of foot, big toe	L4–L5	40%–45%
S1	Foot plantar flexion	Achilles tendon (ankle jerk)	Lateral foot, small toe, sole	L5–S1	45%–50%

Muscle Movements

Flexion: joint angle decreases
Extention: joint angle increases
Adduction: away from median plane
Abduction: toward median plane
Supination:

- arm: palm up
- leg: weight on lateral edge of foot

Pronation:

- arm: palm down
- leg: heels in

TABLE 9.1 Five Important Nerves in the Arm *(Part 1)*

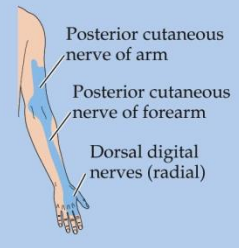
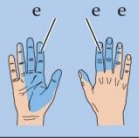
NERVE	MOTOR FUNCTIONS	REGION OF SENSORY LOSS WITH NEUROPATHY
Radial	Extension at all arm, wrist, and proximal finger joints below the shoulder; forearm supination; thumb abduction in plane of palm	
Median	Thumb flexion and opposition, flexion of digits 2 and 3, wrist flexion and abduction, forearm pronation	

TABLE 9.1 Five Important Nerves in the Arm *(Part 2)*

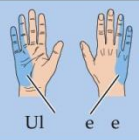
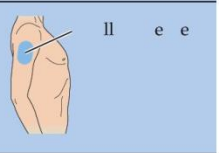
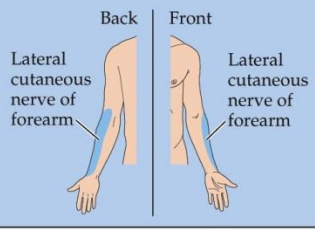
NERVE	MOTOR FUNCTIONS	REGION OF SENSORY LOSS WITH NEUROPATHY
Ulnar	Finger adduction and abduction other than thumb; thumb adduction; flexion of digits 4 and 5; wrist flexion and adduction	
Axillary	Abduction of arm at shoulder beyond first 15°	
Musculo-cutaneous	Flexion of arm at elbow, supination of forearm	

TABLE 9.3 Important Nerves in the Leg *(Part 1)*

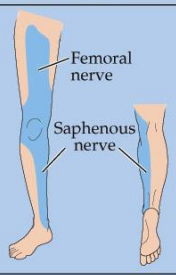
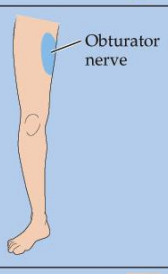
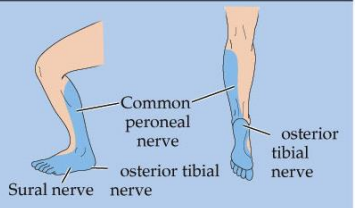
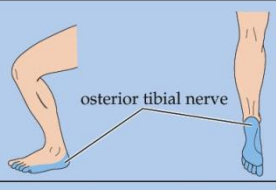
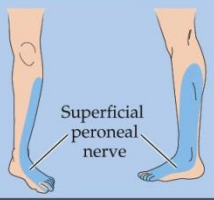
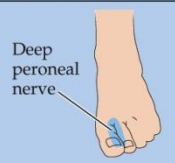
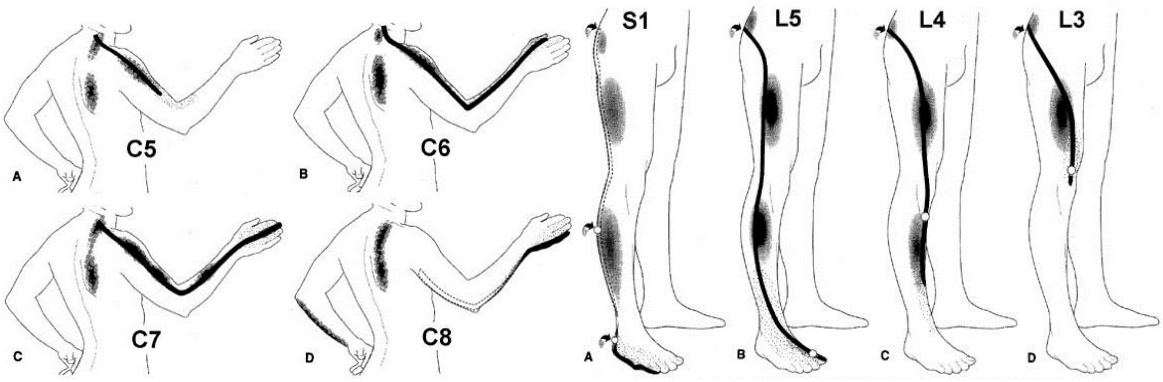
NERVE	MOTOR FUNCTIONS	REGION OF SENSORY NERVE LOSS WITH NEUROPATHY
Femoral	Leg flexion at the hip, leg extension at the knee	
Obturator	Adduction of the thigh	
Sciatic	Leg flexion at the knee (see also tibial and peroneal nerves, in column at left)	

TABLE 9.3 Important Nerves in the Leg *(Part 2)*

NERVE	MOTOR FUNCTIONS	REGION OF SENSORY NERVE LOSS WITH NEUROPATHY
Tibial	Foot plantar flexion and inversion, toe flexion	
Superficial peroneal	Foot eversion	
Deep peroneal	Foot dorsiflexion, toe extension	



Terms review
ventral & dorsal roots merge into a nerve root which exits at spinal canal
nerve – bundle of axons: sensory afferents & motor efferents
nerves move towards dorsal and distal portions of limbs
lower sacral: innervation medial pelvis + descending sympathetic (eg sphincters)
piriformis (hip abductor) muscle can entrap sciatic nerve

Every Pathway Ever
Three major pathways: somatotopic
LCST:
M1 (UMNs)->posterior limb of internal capsule->cerebral peduncles->pyramids->LCST->LMNs
Distinguish UMN and LMN dysfunction with reflexes, tone
Dorsal columns:
gracile (legs, medial) and cuneate (arms and neck, lateral)
DRG->nuclei in medulla->internal arcuate fibers->VPL->S1 posterior limb of internal capsule
Anterolateral system:
DRG->dornal horn->anterior commisure->VPL->S1 (spinothalamic pathway; discriminative)
cord->elsewhere (emotional, modulatory aspects of sensation)

Autonomic efferents
control bladder, rectal, and sexual function
Preganglionic in intermediate zone->postganglionic->target
Sympathetic:
preganglionic cholinergic neurons in thoracic cord
postganglionic noradrenergic neurons in thoracic chain ganglia
Parasympathetic:
preganglionic cholinergic neurons in brainstem and sacral cord
postganglionic cholinergic neurons in ganglia at target tissue

Major Tracts
Dorsal (sensory) and ventral (motor and autonomic) roots
cervical (8), thoracic (12), lumbar (5), and sacral (5) levels
cord ends at L1 vertebra (approximate); cauda equina continue below
most clinically relevant: C5-7 (arms) and L4-S1 (legs)
Cervical plexus arises from C1-5
phrenic (C3-5): diaphragm
Brachial plexus arises from C5-T1
radial (C5-T1): all arm extension, forearm and thumb, sensation on medial surface of arm
median (C5-T1): wrist and thumb, sensation on first three fingers
ulnar (C6,8 and T1): wrist and finger, sensation on lateral hand

axillary (C5-C6): abduction of shoulder, sensation on shoulder
musculocutaneous (C5-7): arm flexion, supination, sensation on lower arm
Lumbar plexus arises from L1-S4
femoral (L2-L4): raise femur (quads), extend shin, sensation on upper thigh and medial shin
obiturator (L2-L4): adduct femur, sensation on inner thigh
sciatic (L4-S2): flex knee (hamstrings), sensation on calf and top of foot
tibial: plantar flexion, sensation on soles of feet; from sciatic
peroneal: foot eversion, dorsiflexion, sensation on lateral shin and toes; from sciatic

---

Motor/Sensory Deficits
ALS & MS
how to diagnose motor deficits:

1. localize level of neuromuscular system by associated symptoms (eg a pure motor problem is probably not a spinal cord lesion)
2. heriditary? family history?
3. distribution: radiculopathy, plexopathy, or peripheral neuropathy? neurogenic or myogenic?

radiculopathy – nerve (eg compression) damage radiating out from cord
neuropathy – pathological process originating from within the nerve

TABLE 7.4 Differential Diagnosis[a] of Spinal Cord Dysfunction

- Trauma or mechanical
  - Contusion
  - Compression
  - Disc herniation
  - Degenerative disorders of vertebral bones
  - Disc embolus
- Vascular (see Figure 6.5)
  - Anterior spinal artery infarct
  - Watershed infarct
  - Spinal dural AVM (arteriovenous malformation)
  - Epidural hematoma
- Nutritional deficiency
  - Vitamin B_{12}
  - Vitamin E
- Epidural abscess
- Infectious myelitis
  - Viral, including HIV
  - Lyme disease
  - Tertiary syphilis
  - Tropical spastic paraparesis
  - Schistosomiasis
- Inflammatory myelitis
  - Multiple sclerosis
  - Lupus
  - Postinfectious myelitis
- Neoplasms
  - Epidural metastasis
  - Meningioma
  - Schwannoma
  - Carcinomatous meningitis
  - Astrocytoma
  - Ependymoma
  - Hemangioblastoma
- Degenerative/developmental
  - Spina bifida
  - Chiari malformation
  - Syringomyelia

Symptoms:
Aphasia/visual defect: higher cortex
Face: cranial nerves above brain stem
Arms & legs: anything below C5

Sensory:
same side: cortical lesion, especially if basic sensation intact but complex processing is impaired
below a level on trunk: spinal cord/brain stem
none: MN disease, myopathy

Muscles:
appearance: atrophy or fasciculations, aka spontaneous contractions (lower MN) vs flexor/extensor spasms/clonus, aka hyperreflexia (upper MN)
LCST & all decending pathways are excitatory/glutaminergic & provide input to interneurons (mostly inhibitory/glycinergic)
excitatory: step on a tack → must retract leg & stiffen opposite leg
interneurons synapse with gamma motor neurons, which innervate muscle spindle, increasing gain of stretch reflex
tone: :) flaccid (lower) vs rigid (upper)
upper: too much innervation from spindle, leading neurons to believe muscle is always flexed
lower: less input
power: distinguish between tone & strength
upper: arm extensors & abductors affected most; leg flexors more than extensors
lower: symptoms vary based on MN affected

Gait:

impaired sensation (proprioreception) → high-stepping gait
    eg tabes dorsalis (syphiliss) → degeneration of DRG neurons in dorsal columns → loss of vibration and position sense
    sensory neuropathies (chemotherapy, diabetes)
    worsened by removing visual input
LMN & muscle disorders → foot drop (lower leg weakness) & waddling (hip/core weakness)

Motor deficits: acute vs chronic
acute: vascular, toxins, spinal cord injury
chronic: days/weeks: neoplastic (tumor), infection, inflammation
    months/years: degenerative, endocrine

Pathology: nerve root & plexus lesions
disc prolapse
spondylolisthesis - movement of vertebrae relative to each other → stenosis of canal or nerve compression
spondylosis – fractures between facet joints
spinal stenosis – narrowing of spinal foramen
osteophytes – bony spurs between adjacent vertebrae
avulsion – tearing underlying faschia/muscle
    Erb-Duschenne: dislocation of shoulder/hip in birth canal

Pathology: spinal cord disorders
traumatic myelopathy: whiplash, fracture/vertebral dislocation
cord transection:
    acute: spinal shock (swelling; flaccid paralysis; loss of reflexes, sensory, & autonomic capabilities)
    chronic: hyperreflexia & clonus except flaccid where ventral roots/LMNs are damaged, intermittent autonomic function, loss of UMN control
treatment: immediate cold to prevent swelling (corticosteroids don't promote healing)
sacrolitis – inflammation of sacrum-illeum joint connection (eg reactive gliosis)
sciatica – disk compression
L4-L5 disc is frequently herniated which compresses L5 root (narrowest form in lumbar spine)
    can fix with formenautomy (make a bigger window)

Pathology: NMJ & muscle disorders
myasthenia gravis – antibodies target nAchR (autoimmune)
    ptosis (eyelid droop)
    treated with Ach-esterase inhibitors & immunosuppression
    break down of the cytoskeletal structure that defines neuromuscular junction
muscular dystrophy – dystrophyn complex (anchors actin to cell membrane) is mutated
    Ducchene's is worst (no protein), Becker's is milder

ALS
Amytrophic (no muscle nourishment) Lateral (position in spinal cord) Sclerosis (scarring)
motor neurons die from oxidative stress
    unique expression of transporters, glutamate receptors, Ca buffers?
other spinal-muscular atrophies: can be UMN or LMN only; can affect brain stem or spinal MNs
infections that target MNs: polio, West Nile (variant that targets MN specifically)
post-polio syndrome: surviving neurons innervate more fibers → stressors → activate apoptotic processes

presentation:
20% bulbar onset
40% upper extremity weakness

clinical & pathological overlap with fronto-temporal dementia → MN stressors may be the same as frontal lobe stressors

treatment:
riluzole – Na channel inhibition; presynaptic inhibition to tamper excitotoxicity
    doesn't work well, but cheap & no side effects
    feeding tubes & ventilator
progressive, fatal 3-5 years after onset, death from pulmonary infections

diagnosis:
problems are bilateral, upper & lower, in multiple regions
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 (<10% cases) have mutated superoxide dismutase 1
binds copper & zinc, neutralizes free radicals
several mutations, which vary disease intensity (eg mutation in beta-sheet enzymatic pocket leads to worst prognosis)
this interferes with mitochondrial ETC, triggering apoptotic pathway
BCL2 family members regulate apoptosis by modulating cytochrome c release from mitochondria into cytosol
classic morphology of neuron death can be seen in all degenerative diseases
    cytohistology: p53, tunel labeling

excitotoxicity hypothesis:
NMDA receptors letting in too much calcium, binding too often, too much extracellular glutamate, glial cells aren't reuptaking glutamate
oxidative stress is a hypothesized cause of many MN degenerative disorders

<u>Multiple Sclerosis</u>
histology: demyelinating neuropathy → sensory and motor
myelin – oligodendrocytes (CNS) & Schwann cells (PNS) wrap around axons
must recognize axon, then have PM proteins on one side that recognize proteins on other side of PM
scattered demyelination followed by reactive gliosis (astrocytes in CNS are activated, clear debris, and can leave glial scar)

risk factors:
presents at age 20-40, more common in women, increases with distance from equator & positively correlated with hygiene
genetic predisposition (interleukin receptor mutations)
is there an initial metabolic insult (mitochondria)?

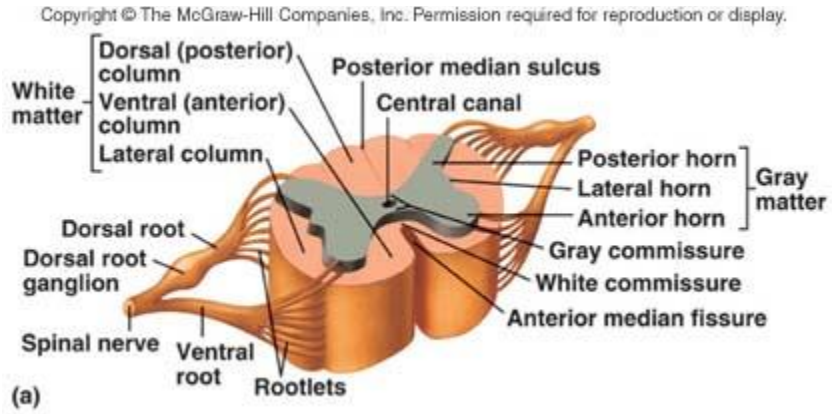
symptoms:
episodes of focal motor & sensory deficits
MRI: diffuse glial white matter lesions
diffuse symptoms: dysarthria, dysphagia, unstable mood, optic neuritis, pain, incontinence
oligoclonal bands within CSF (autoimmune problem)

treatment:
remission can be spontaneous or drug-assisted
drugs target immune system
- steroids: inhibit transcription of IL genes in T cells & IL receptors in B cells

- interferons: anti-inflammatory, reduce permeability of BBB to immune cells
- natalizumab: monoclonal antibody against ECM protein which reduces permeability of BBB to immune cells

---

Anatomy & Physiology Quiz
cervical & lumbar enlargements supply upper & lower limbs
dorsal horn = sensory; ventral horn = motor; lateral horn = autonomic
stretch reflex: excitatory, no interneuron (eg knee-jerk)
withdrawal reflex: excitatory, interneuron
Golgi reflex: inhibitory, interneuron
crossed extensor reflex: excitatory & inhibitory, interneurons



Radiology
<u>Introduction</u>
1895 – X-ray machine invented, first brain scan by Cushing at JHU
"He did a scan of a bullet in the brain, and their doing a lot of those down in Baltimore still today" - I. Weinberg
role of radiologist:
disease detection by symptoms → confirmation by imaging
differential diagnosis (could be this, rara avis)
assist in management decisions (anticoagulants, surgery) & monitor therapy
research

sources of signal:
CT/electron density: calcifications, hemorrhage, edema, contrast enhancement, mass effect
MRI/water density: same as CT except diffusion, flow, no calcifications
PET/radiotracer density: glucose utilization, receptor density
different pulse sequences & contrast → examine different structures :)

<u>Normal Brain Catechism</u>
ventricles & sulci have normal size, shape, & position
no mass effect or midline shift
no abnormal attenuation/signal to suggest hemorrhage or cerebrovascular accident
no abnormal contrast enhancement

<u>Differential Diagnosis</u>
infectious
neoplastic
developmental/congenital

vascular
inflammatory/autoimmune
environmental
trauma
degenerative

Case Studies
toxoplasmosis – abnormal attenuation from ring-enhancing lesion & inflammation
cysticercosis – same as above
meningitis – abnormal contrast enhancement
abcess
pilocytic astrocytoma – juvenile tumor, 90% survival
"If the issue is tissue, the answer is cancer."
mestastasis
glioblastoma multiforme – midline shift & mass effect
meningioma – nothing in the brain is benign (neoplasm, but not cancer because it can't metastasize)
heterotopia – developmental migration error
chiari – herniated cerebellar tonsils, smaller cerebellum
stroke – CT scan, bright white clot & dark hemorrhage with swelling
internal coratid aneurysm
crescental epidural hematoma
subarachnoid hemorrhage
subdural hematoma
sarcoid – inflammatory disease, meningeal thickening
global edema - asphyxiation
radiation – low attenuation in radiated areas
drug toxicity – white matter lesions
grey/white junction hemorrhages – diffuse axonal/shear injury
frontal lobotomy
hydrocephalus – enlarged ventricles

New Stuff
super-fast imaging
magnetic drug delivery
small PET/MRI

BSCI338N Midterm Two: Study Guide

Cranial Nerves

Names: On old Olympus' towering tops, a Finn and German vend snowy hops.
Functions: Some say make merry but my brother says bad business making merry.

CN1: olfactory nerve [frontal lobe] special sensory
olfactory epithelium → olfactory bulb → periform cortex (only sensory with no thalamic relay)
anosmia & frontal lobe lesions

CN2: optic nerve [midbrain] special sensory
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)
optic neuritis: common symptom of MS

CN3: oculomotor nerve [midbrain] somatic motor parasympathetic
top eyelid, medial & upward eye movement (roll & cross your eyes)
PANS for pupillary constriction & lens focusing

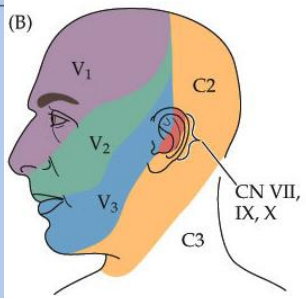
CN4: trochlear nerve [midbrain] somatic motor
rotate eyes when head tilts (superior oblique muscles)

CN6: abducens nerve [pons] somatic motor
move eyes laterally (lateral rectus muscles)

CN5: trigeminal nerve [pons] branchial motor somatic sensory
somatosensory for face, dental pressure, anterior 2/3 of tongue, sinus meninges
branchial motor: mastication & tensor tympani (middle ear gain of transduction)
trigeminal ganglia above jaw → TMJ
three branches are analogs of spinal pathways
mesencephalic: only case in which primary neurons are in CNS; sensory loss ipsilateral to nuclei lesion
chief: trigeminal ganglion analog of DRG
Wallenberg syndrome – medullary stroke above anterolateral crossing & below trigeminal crossing → loss of pain/temperature sensation contralateral, trigeminal loss ipsilateral

TABLE 12.6 Analagous Trigeminal and Spinal Somatosensory Systems

NUCLEUS	SENSORY MODALITIES	MAIN PATHWAY TO THALAMUS	MAIN THALAMIC NUCLEUS[a]
TRIGEMINAL SENSORY SYSTEMS			
Mesencephalic trigeminal nucleus	Proprioception	—	—
Chief trigeminal sensory nucleus	Fine touch; dental pressure	Trigeminal lemniscus	VPM
Spinal trigeminal nucleus	Crude touch; pain; temperature	Trigeminothalamic tract	VPM
SPINAL SENSORY SYSTEMS			
Posterior column nuclei	Fine touch; proprioception	Medial lemniscus	VPL
Dorsal horn	Crude touch; pain; temperature	Spinothalamic tract	VPL



CN7: facial nerve [pons] branchial motor parasympathetic visceral sensory somatic sensory
branchial motor: stapedius muscle & facial expressions (including eyelid)
PANS: lacrimal & salivary glands
visceral sensory: anterior 2/3 of tongue (distributed bilaterally)
somatic sensory: external auditory meatus (EAM)

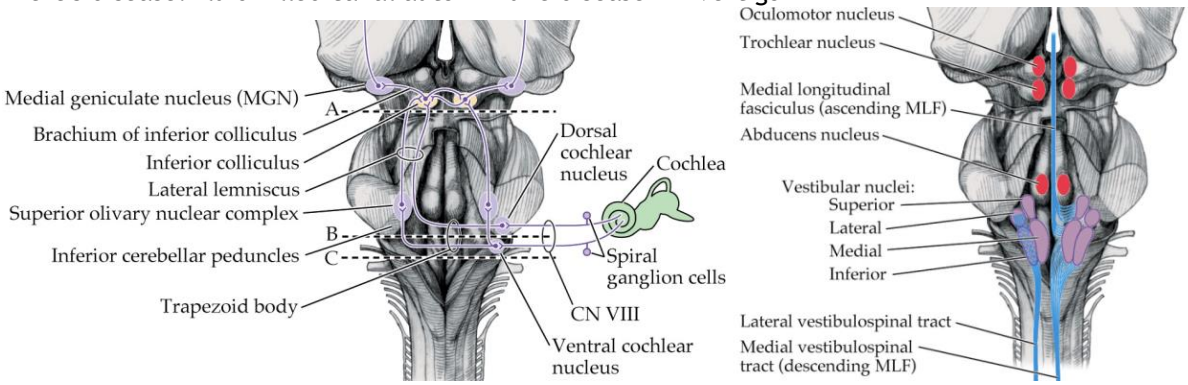
CN8: vestibulocochlear nerve [medulla] special sensory
hearing: sound waves enter EAM → transmitted mechanically to middle ear via cochlea → transduced by hair cells to neural signals (excite cochlear nerve, somata in spiral ganglion) → fibers cross extensively in brainstem (trapezoid body fibers) → lateral lemniscus carries output to contralateral inferior colliculus (via superior olive and other brainstem nuclei)

- tonotopy: high frequencies nearer oval window
- mechanical dampening by stapedius & tensor tympani muscles
- unilateral hearing loss must arise from a problem in the cochlea or CN VIII itself
- need auditory input from both ears to compare timing & intensity

vestibular sense:
vestibular hair cells: stereocilia deflected by medium movement → transmit to vestibular nerves (cell bodies in superior/inferior vestibular ganglia)

- semicircular canals: hair bundles in cupula → activate ampulla → detect angular acceleration
- utricle & saccule: maculae (otoliths in gelatinous layer) → detect linear acceleration & head tilt
- input & output: posture/muscle tone (cerebellum → brainstem motor) & eye position (cortical inputs of eye/head position → extra-ocular systems)
- symptoms: vertigo & nystagmus (eye tracking)
- vestibular nuclei: medial motor system (extrapyramidal, essentially uncrossed)
- lateral tract: extends length of spinal cord for balance and muscle tone
- medial tract: descending: neck, head position; ascending: extra-ocular muscles

Muniere's disease: fluid-filled canal autoimmune disease → vertigo



CN9: glossopharyngeal nerve [medulla] branchial motor parasympathetic visceral sensory somatic sensory
taste from posterior 1/3 of tongue
somatosensory from middle ear, EAM, pharynx, & posterior 1/3 of tongue
branchial motor to swallowing muscles in throat (sounds that contract the soft palette (G & K))
chemoreceptors (oxygen/carbon monoxide balance and acid/base balance of blood) located in the carotid body and baroreceptors of carotid sinus
PANS to parotid salivary gland

CN10: vagus nerve [medulla] branchial motor parasympathetic visceral sensory somatic sensory
taste receptors in throat (epiglottis & pharynx)
somatosensory from pharynx, meninges, & EAM
branchial motor: pharyngeal (swallowing) & laryngeal (voice box) muscles
chemo & baroreceptors in aortic arch
PANS to all organs of chest and abdomen (heart, lungs, & digestive tract via splenic flexure)

CN11: spinal accessory nerve [medulla] branchial motor
branchial motor to sternomastoid & upper trapezius → weakness of ipsilateral shoulder shrug & turning head away from lesion

CN12: hypoglossal nerve [entire brainstem] **somatic motor**
somatic motor to tongue

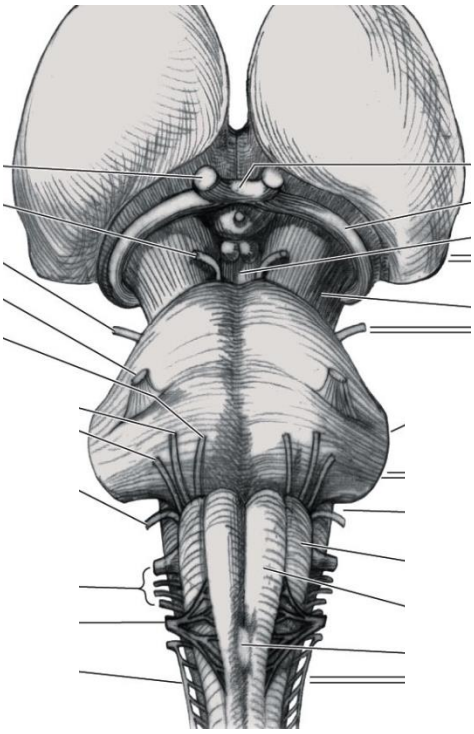
Cranial Nerve Pathways
Eyes:
muscles: 3 (medial & upward), 4 (superior oblique), 6 (lateral rectus)
pupils & lens: 3
lacrimal glands: 7, 9

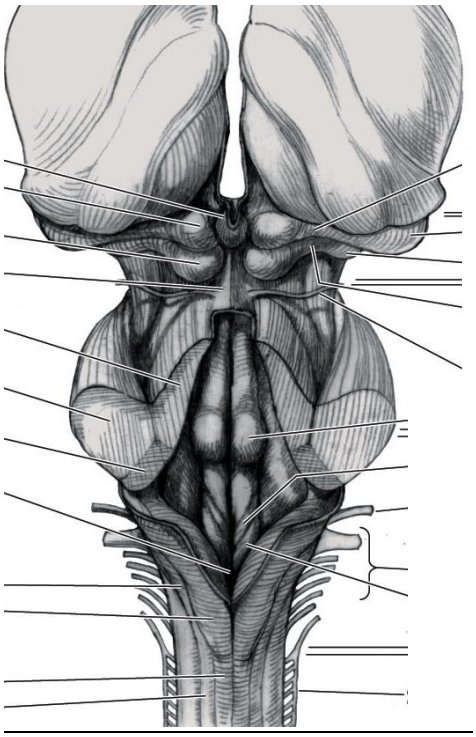
Mouth:
salivary glands: 7
taste: 7 (front), 9 (back), 10 (epiglottis & pharynx)
sensory: 5 (front tongue & teeth), 9 (back tongue)

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

Face:
motor: 5 (mastication), 7
sensory: 5
UMN: spares forehead (both hemispheres contribute), mild orbicularis oculi weakness (can control eye lashes), lower facial weakness, can also cause arm or hand weakness
LMN (Bell's Palsy): entire face, dry eye, ipsilateral taste loss, no hand weakness or aphasia
    herpes zoster (shingles) or autoimmune origin
    simultaneous tearing & salivation; blinking and platysma muscle contraction
    steroids & nerve stimulation → slow recovery, nerves may regenerate incorrectly

Parasympathetic:
carotid body chemo & carotid sinus baro-receptor: 9
aortic arch chemo & baro-receptor: 10
Brainstem
label: 5 structures, 4 junctions, inferior olive, pyramid, pyramidal decussation, superior & inferior colliculus, cerebral peduncle, cerebellar peduncles, nuclei cuneatus & gracilis





cerebral peduncles – (direct & indirect motor pathways) → pyramidal tract (flows through pons behind cerebellar peduncles) → pyramidal decussation (indirect motor crossing in medulla)

crus cerebi (pes pedunculi) = ventral efferent fibers

middle 1/3rd is corticospinal & corticobulbar tracts; remaining is corticopontine tracts

dorsal columns → nucleus gracilis/cuneatus → internal arcuate fibers → medial lemniscus

cranial nuclei – sensory & motor pathways carry information from multiple nuclei, but are spatially segregated (motor is medial & sensory is lateral)

inferior olive – major integrative center, function unknown

projects to contralateral cerebellum

input from collaterals from contralateral spinocerebellar tract, corticospinal tracts, red nucleus; direct input from ipsilateral M1 & red nucleus

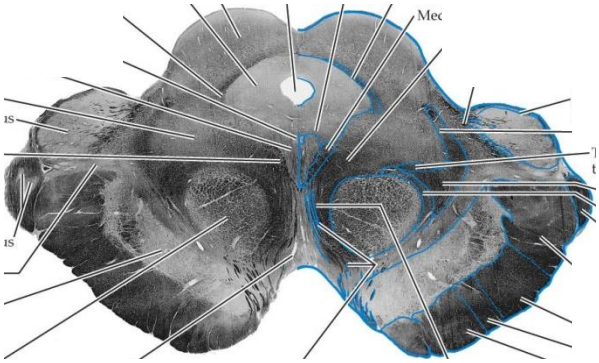
Midbrain

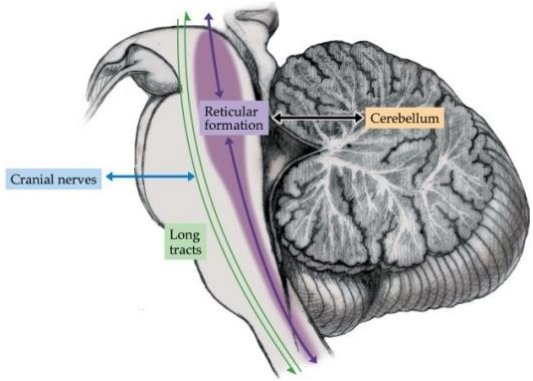
tectum: *superior colliculus* (visual nuclei) & *inferior colliculus* (auditory nuclei)

feed into tecto & vestibulo spinal tracts

tegmentum: *substantia nigra* (motor dopamine), *red nucleus* (rubrospinal tract), *periaqueductal grey* (pain modulatory), & *reticular formation* + medial lemniscus (spinothalamic tract)

basis: long tracts of corticospinal & corticobulbar fibers





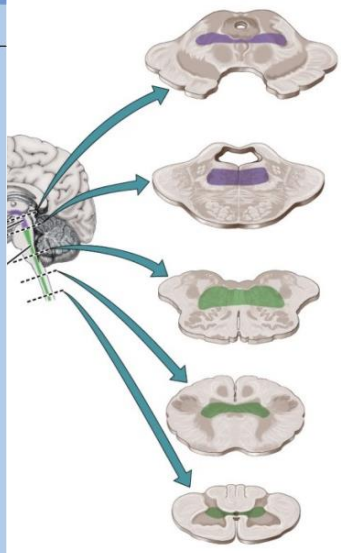
Pons

pontine nuclei: ipsilateral input from motor cortex → project via middle cerebellar peduncle to contralateral cerebellum as mossy fibers → preparation, initiation, & execution of movement
where sensory (dorsal) & motor (ventral) tracts split → these have different blood supplies

Reticular Formation
collection of "mesh-like" regulatory nuclei that project to nearly every area
rostral regulates forebrain (alertness)
caudal works with cranial nerve nuclei to modulate cord, reflexes, ANS

TABLE 14.1 Summary of Brainstem Structures *(Part 2)*

MAIN FUNCTIONAL GROUPINGS	SUBCOMPONENTS
2. Long tracts (see Chapters 6, 7)	Motor pathways Corticospinal and corticobulbar tracts; other descending somatomotor pathways; descending autonomic pathways
	Somatosensory pathways Posterior column–medial lemniscal system; anterolateral system
3. Cerebellar circuitry (see Chapter 15)	Superior, middle, and inferior cerebellar peduncles
	Pontine nuclei; red nucleus; (parvocellular portion); central tegmental tract; inferior olivary nucleus
4. Reticular formation and related structures	Systems with widespread projections Reticular formation; cholinergic nuclei; noradrenergic nuclei; serotonergic nuclei; dopaminergic nuclei; other projecting systems
	Nuclei involved in sleep regulation
	Pain modulatory systems Periaqueductal gray; rostral ventral medulla
	Brainstem motor control systems: somatic, branchial, and autonomic Posture and locomotion (reticular formation; vestibular nuclei; superior colliculi; red nucleus [magnocellular portion]; substantia nigra; pedunculopontine tegmental nucleus); respiration, cough, hiccup, sneeze, shiver, swallow; nausea and vomiting (chemotactic trigger zone); autonomic control, including heart rate and blood pressure; sphincter control, including pontine micturition center



Neurotransmitters
neuromodulation:
- bulk release of neurotransmitter (e.g., DA, 5-HT)
- action through metabotropic receptors (7-TM domains, G-proteins)
- control of gain/state of circuits (e.g.: 5-HT makes spinal MNs more responsive to input)

functions:
- alertness: all but DA
- mood elevation: NE, 5-HT
- others: breathing control (5-HT); memory (Ach); movements, initiative, & working memory (DA)

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*
DA: *substantia nigra* → motor output to straitum, causes gain (tremor) & loss (rigidity) in Parkinson's
ventral tegmental area → motivation/reward (mesolimbic); attention (mesocortical); Schizophrenia
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)

Consciousness
Reticular activating system:
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

Consciousness: alertness (PRF, thalamus, & cortex); attention (alertness & association cortex); and awareness (abstract cognitive process)
loss of cortex, thalamus, or pontine RAS (not caudal RAS) → coma
brain dead (EEG is flat line) → *coma* (some basic reflexes/EEG, severely depressed function throughout) → *vegetative state* (variably depressed diencephalon/PRF) → *minimally conscious* (variably depressed cortex) → *akinetic mutism* (variably depressed frontal lobe)
Locked-in syndrome: damage to ventral pons, usually from infarct
bilateral damage to corticospinal and corticobulbar tracts
sensory pathways spared: patient is aware, able to feel, unable to move (save for some eye movements)
severely depressed function in brainstem reflex & motor

Headaches
cranial nerve disorders: headache & facial pain; equilibrium problems; vision problems
nocioreceptors on meninges, BV, nerves, & muscles
headache types:
new (acute onset): subarachnoid hemorrhage, meningitis or encephalitis
subacute onset: temporal arteritis (autoimmune disease, hardening of temporal arteries that feed trigeminal nerve → steroids), trigeminal neuralgia (Tic de la Rue → tricyclic antidepressants), postherpetic neuralgia (shingles of the face)
chronic (ongoing): migraine, cluster headaches
steroids reduce vascular permeability

migraine: trigeminal neuralgia, cerebrovascular headache
cortical spreading depression or PAG activation → activation of the trigeminal vascular system → rCBF increases, then decreases (including in red nucleus & substantia nigra)
heightened cortical excitability hypothesis – lack of habituation in migraine patients
Ca^{2+} channels: only in neurons, heritable mutation causes migraines
familial hemipalegic migraine: motor aura, $CAv2.1$ channel in cerebellum & nocioreception brainstem nuclei → increase glutamate release in cortex → more CSD
triptans also block transmission from spinal trigeminal nucleus (pain nucleus)
prophylaxis with tricyclics, beta-blockers, $CAv2.1$ antagonists OR avoid triggers (foods with tyramine, nitrates, stress)

cluster: always unilateral, usually behind eye at night
patients have recurrent headaches followed by remission
treated with triptans, Ca channel blockers, steroids OR avoid alcohol/vasodilators

tension: bilateral squeezing over forehead, often accompanied by neck spasm and pain
Other: TMJ, dental disease, sinusitis, cervical spine disease

The Cerebellum

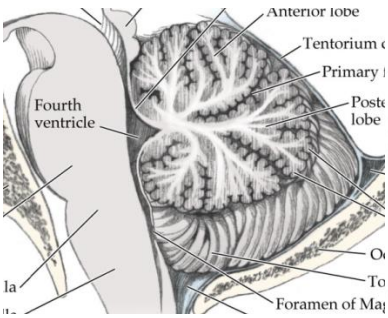
Gross Anatomy

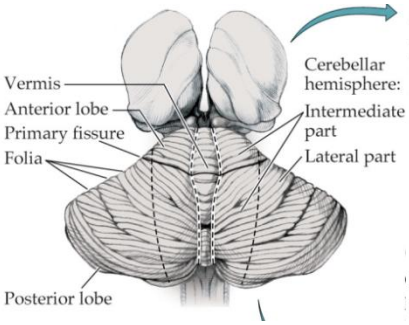
purpose: integrates sensory inputs & motor outputs to modify ongoing movement
ataxia – inability to coordinate smooth limb movement based on sensory feedback
bounded by midbrain tectum, tentorium cerebelli, posterior fossa, & 4th ventricle
blood supply: offshoots of basilar artery
cerebellar peduncles: fiber tracts that run through brainstem (trace these)

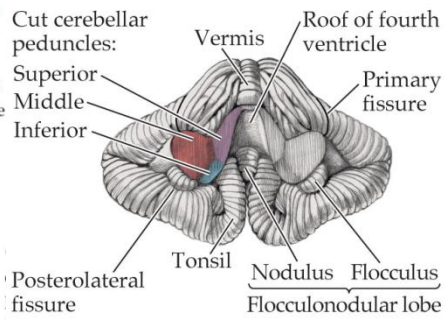
- **superior:** primary output of the cerebellum to red nucleus & thalamus
- **middle:** input from the contralateral cerebral cortex via the pons
- **inferior:** fibers from ipsilateral spinocerebellar tract (proprioceptive), inferior olives, vestibular nuclei

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

- inner → outer::head → legs in posterior & anterior lobes
- audio/visual input in medial vermis

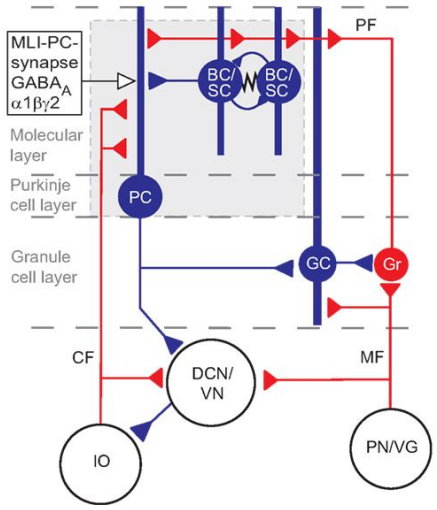


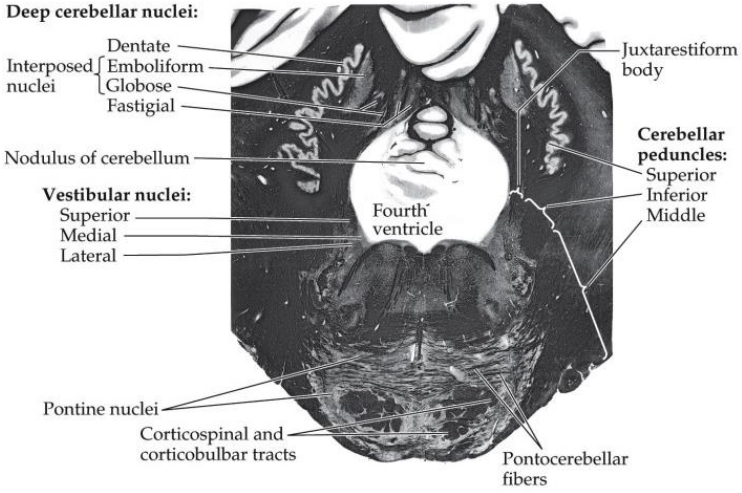




Circuitry

each area has the same circuitry, but different inputs & outputs
all ascending fibers are excitatory & descending fibers are inhibitory
output: *Purkinje* (spontaneously active/tonic) → deep cerebellar 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)
deep cerebellar nuclei/vestibular nuclei
other descending fibers, excited by parallel fibers: *Basket cells* (strongly inhibit Purkinje), *Stellate cells* (weakly inhibit Purkinje) & *Golgi cells* (inhibit granule cells)
eg guided arm movement: compare motor command (move hand) to proprioreceptive feedback
big sensory-motor loop modulated by input from locus coeuruleus (NE), raphe nuclei (5-HT)





deep cerebellar nuclei: each pair of nuclei is associated with a region of the surface anatomy

- dentate nuclei: lateral hemispheres
- interposed nuclei (emboliform & globose): paravermis (intermediate zone)
- fastigial nuclei: vermis

*from lateral to medial: **D**on't **e**at **g**reasy **f**oods*
vestibular nuclei receive direct PC input (from flocculonodular lobe)

Cerebellar Function
output:
lateral: extremity motor planning via LCST
intermediate: distal limb coordination via LCST & rubrospinal tract
vermis & flucculonodular lobe: proximal limb & trunk coordination via ACST & reticulo/vestibule/tecto-spinal tracts
balance & vestibulo-ocular reflexes via medial longitudinal fasciculus
all these paths are double-crossed: once in decussation of superior cerebellar peduncle & once in spinal cord (pyramidal decussation for cortico or ventral tegmental decussation for rubro)
medial: control over gamma motor system → hypotonia

lateral cerebellum circuitry:
from dentate nucleus, crosses through superior cerebellar peduncle, to…
1. ventral lateral nucleus of thalamus → motor & associate cortices (motor planning)
2. parvo red nucleus → (central tegmental tract, descends with pyramidal tracts) → inferior olivary nucleus → (olivocerebellar fibers, second crossing) (distal limb feedback)

lateral zone & dentate lesions lead to decomposition of movements: errors of direction, force, speed, & amplitude of movements

intermediate cerebellum circuitry:
(extra)pyramidal systems; from interposed nuclei, crosses through superior cerebellar peduncle, to…
1. VLN → cortex → down lateral corticospinal tract (crosses in pyramids)
2. magno red nucleus (rubrospinal tract & large muscles in upper limbs) → ventral tegmental decussation → down rubrospinal tract
these circuits update movement plan (fire after movement has been initiated)

medial cerebellum circuitry:
gait, balance, etc; from fastigial nucleus to…
1. contralateral to tectospinal; bilaterally to VLN → cortex → medial corticospinal
2. reticular formation & vestibular nuclei → cord
    loss of excitatory drive to one VN allows others to dominate

input: spinocerebellar tract
dorsal (gracile fascicle) & cuneo (cuneate fascicle) tracts (uncrossed): limb position
    DRG neurons synapse in Clark's nucleus & ascend ispilaterally
    external cuneate nucleus is extremity version of Clark's nucleus → gives rise to inferior peduncle (mossy fibers)
ventral & rostral tracts (double crossed): spinal interneuron activity
    nucleus dorsalis → interneurons in ventral horn → cross in anterior commissure → rise in ACST to cerebellum

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
large infarct causes swelling in posterior fossa → needs immediate treatment
fatal gastroenteritis: nausea/vomiting from infarct

midline (vermis/flocculonodular) lesions: truncal ataxia, disequilibrium, eye movement abnormalities
    tend to sway towards side of lesion
    Romberg's test: if patient sways with eyes closed, vestibular system cannot correct cerebellar deficit (also characteristic of LCST damage)
adult onset Tay-Sachs disease can be mistaken for spinocerebellar disorders (truncal ataxia)

intermediate lesions: appendicular ataxia (can be lesions in other areas)
    dysrhythmia (abnormal timing) or dysmetria (abnormal trajectories in space)
    tests: apply pressure to outstretched arms & release (excessive check); finger to nose

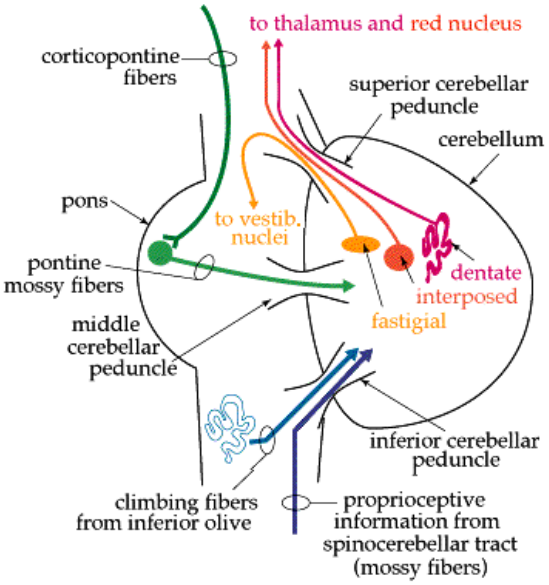
non-cerebellar ataxias:
peduncle/pontine lesions; hydrocephalus; prefrontal cortex; spinal cord disorder; contralateral ataxia-hemiparesis
sensory ataxia: loss of joint-position sense
    wide-based gait or overshooting movements (reduced by visual input)
    look for other cerebellar signs (lack of speech issues, nystagmus, etc)
vestibular ataxia is gravity dependent: goes away when patient lies down
cerebellar ataxia: irregularities in rate, rhythm, amplitude, & force of movements
    little muscle weakness and observable tremors during movement

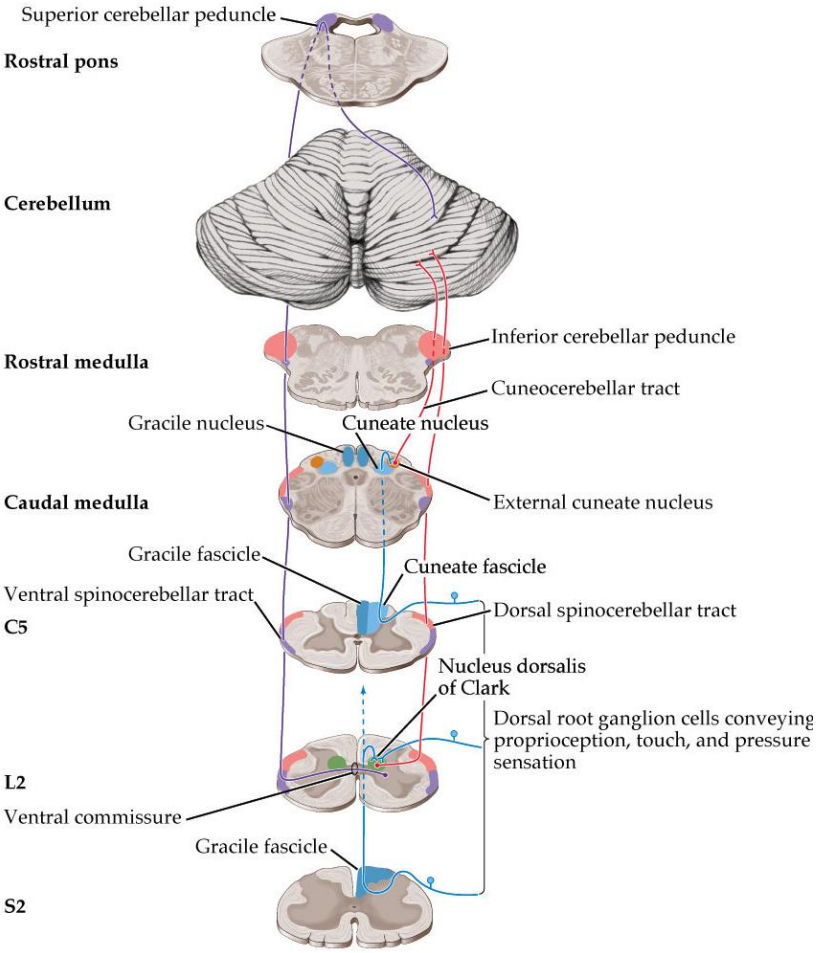
Disorders of Equilibium
pathways to know:
central & peripheral pathways
pathways controlling eye movements

pathways mediating proprioreceptive sensation

vertigo – illusion of movement of body or environment
impulsion – sensation of being pulled into space
oscillopsia – visual illusion of movement
    must be distinguished from dizziness (impaired oxygen or glucose delivery to brain :)
semicircular canal → vestibular nuclei → medial longitudinal fasciculus ascends → 3 cranial oculomotor nerves
    vestibulospinal tract descends → lateral (uncrossed) vs medial (bilateral)
parapontine reticular formation: input from VN & output to motor nuclei
    also receives input from superior colliculus (non-image forming vision)
    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
    tectospinal does the same thing, except with eye movement

infarct in left superior peduncle: motor symptoms, nausea, aphasia
    nausea → must be cerebellar, pressing on brainstem
optokinetic response: eyes move and reset to moving spatial grading (without head movement)
cerebellar atrophy: inherited spinocerebellar ataxia
    usually polyglutamine expansion (CAG) which affects channels or other proteins (like PKC) → these are in all neurons/cells → kills Purkinje cells





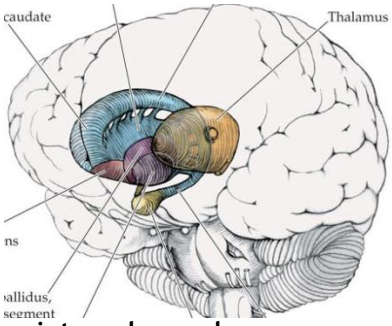
Basal Ganglia

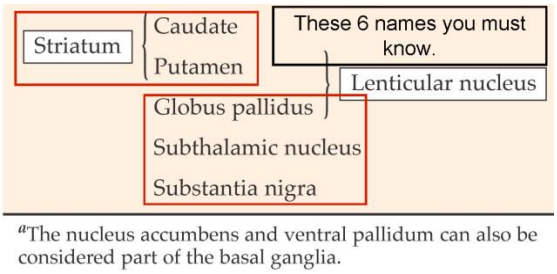
Gross Anatomy

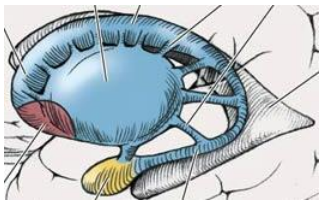
Nuclei: striatum (caudate + putamen + cellular bridges), globus pallidus (GP), subthalamic nucleus (STN), substantia nigra (SN)

putamen + nucleus accumbens + amydala = limbic system

limb caudate & thalamus are medial to internal capsule, while lenticular nucleus is lateral







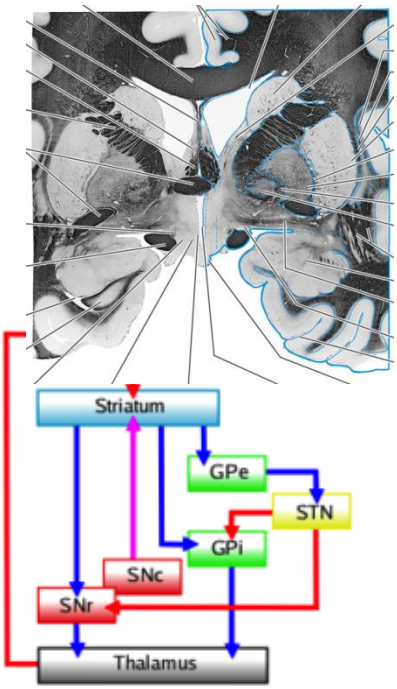
internal capsule

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



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: 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

somatotopy preserved in loops through basal ganglia

TABLE 16.2 Four Parallel Channels through the Basal Ganglia

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

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

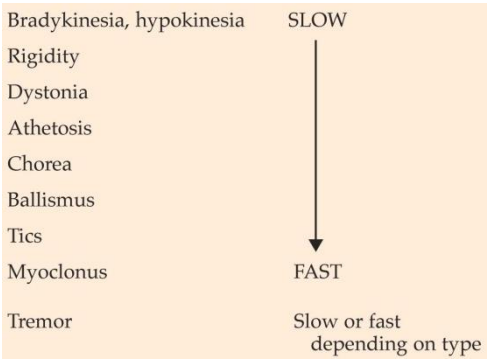
Parkinson's: symptoms
idiopathic (no known cause), onset 40-70 years, slow (5-15year) progression
degeneration of DA neurons in SNc → initial treatment with L-DOPA
motor symptoms: tremor, bradykinesia, cog-wheel rigidity, postural and gait instability (antero- or retro-pulsion)
other symptoms: decrease in facial expression and in blinking; cognitive/emotional

Parkinson's: neural circuitry
DA has opposite effect on direct & indirect pathways → net effect is disinhibition
DA in SNc die & DA input from striatum reduced → direct pathway loses strength → inhibition of thalamus & Lewy bodies

Parkinson's: treatment
initial: levodopa (BBB-permeant DA precursor), increases DA "tone" in striatum, but effects attenuate (circuitry changes)
    can cause dyskinesias/freezing as levels change: similar to "on-off" syndrome
    supplement with anti-cholinergics (2% of striatal neurons are cholinergic)
deep brain stimulation: stimulate thalamus directly

Huntington's disease: symptoms
degeneration of striatum, particularly of projections to GPe (indirect pathway)
    STN more excitable → more 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

Other Movement Disorders
differential diagnosis based on basal ganglia involvement:
    signs of UMN/LMN disease?
    sensory loss?



"extrapyramidal" – not cortical or cerebellar in origin, but instead basal ganglia influence on pyramidal tract
dyskinesia: MPP+ poisoning outbreaks, boxer's dementia, copper accumulation, or antipsychotic drugs (DA agonists → tardive dyskinesia)
rigidity: increased resistance to passive movement, continuous throughout movement
    Parkinson's is not velocity dependent, but corticospinal lesions are
dystonia (distorted positions): small basal ganglia lesions → treated with botulism toxin
athetosis & chorea: involuntary twisting, fluid, or jerky movements
ballismus: large amplitude movements of limbs
    hemiballismus: contralateral to lesion in STN, decreased indirect pathway
tics: urge for action → brief action → relief afterwards
tremors: rhythmic oscillations of agonist/antagonist muscles

Key Points
basal ganglia evaluate voluntary motor program & signal to thalamus to continue
basal ganglia loop is more initiation & termination than continuation & positioning
operate on cortical & thalamic inputs
normally results in disinhibition via direct & indirect pathways, which operate on different types of information & are affected differently by dopamine
dopamine is an important neuromodulator: loss of tone leads to underactive thalamus
Parkinson's: key's in the ignition, but the car has trouble starting
    inhibition of thalamus → reduction of drive back to motor system

Limbic System

cortex surrounding corpus callosum & basal ganglia

functions: olfaction (olfactory cortex), memory (hippocampal formation), emotion & drives (amygdala), and homeostasis: autonomic & neuroendocrine (hypothalamus)

main focus: hippocampal formation

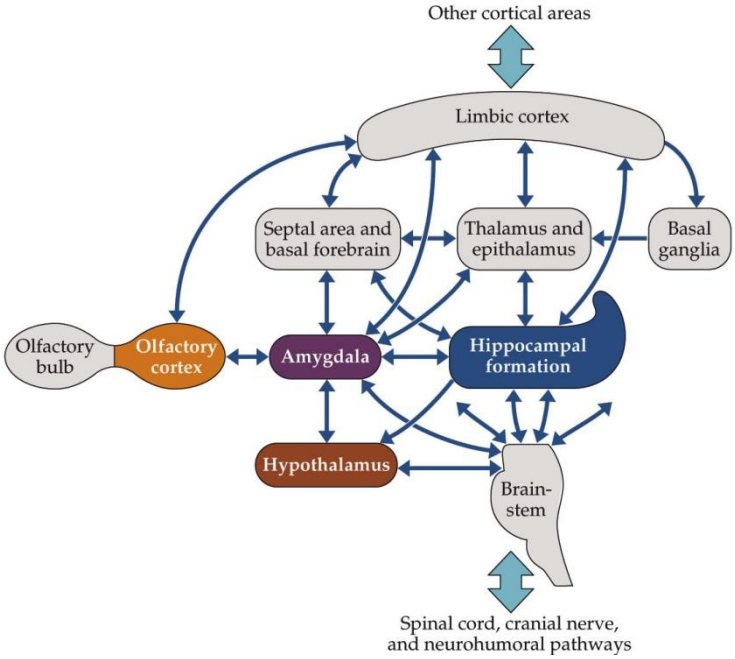
basal ganglia channel: [temporal cortex; hippocampus; amygdala] → [NA, ventral striatum] → [GPi/SNr, ventral pallidum] → [MD, VA] → [AC, OFC]

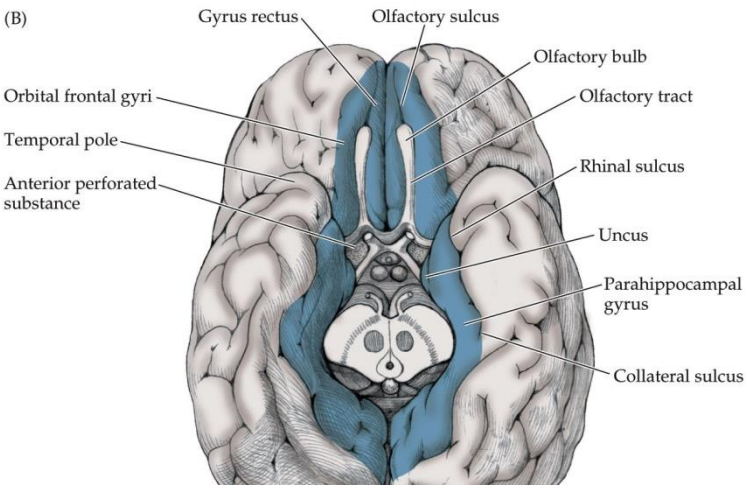
olfactory epithelium runs through cribiform plate

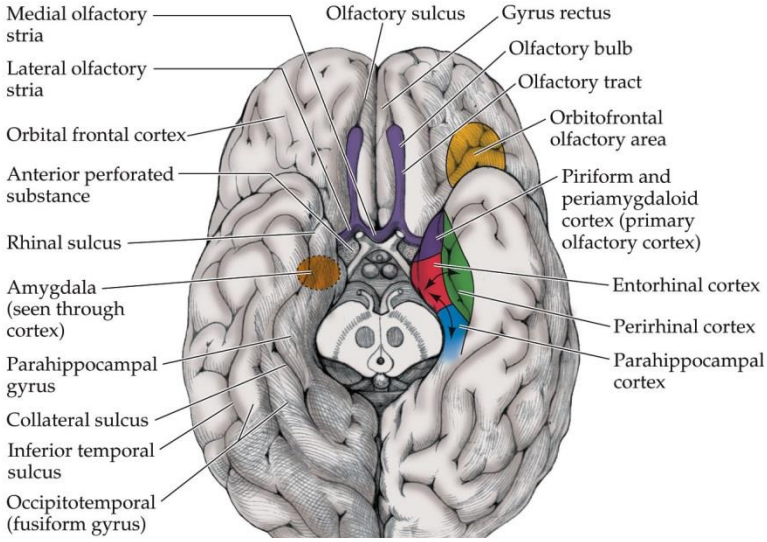
ACC – error & conflict monitoring (eg Stroop task)

TABLE 18.1 Main Components of the Limbic System

- Limbic cortex
  - Parahippocampal gyrus
  - Cingulate gyrus
  - Medial orbitofrontal cortex
  - Temporal pole
  - Anterior insula
- Hippocampal formation
  - Dentate gyrus
  - Hippocampus
  - Subiculum
- Amygdala
- Olfactory cortex
- Diencephalon
  - Hypothalamus
  - Thalamus
    - Anterior nucleus
    - Mediodorsal nucleus
  - Habenula
- Basal ganglia
  - Ventral striatum
    - Nucleus accumbens
    - Ventral caudate and putamen
  - Ventral pallidum
- Basal forebrain
- Septal nuclei
- Brainstem







hippocampus

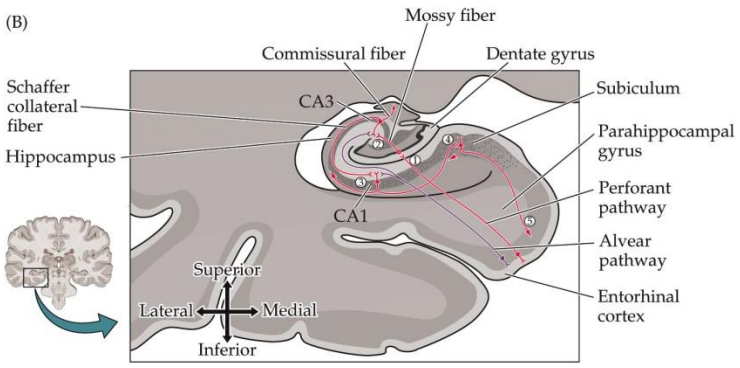
areas for memory:

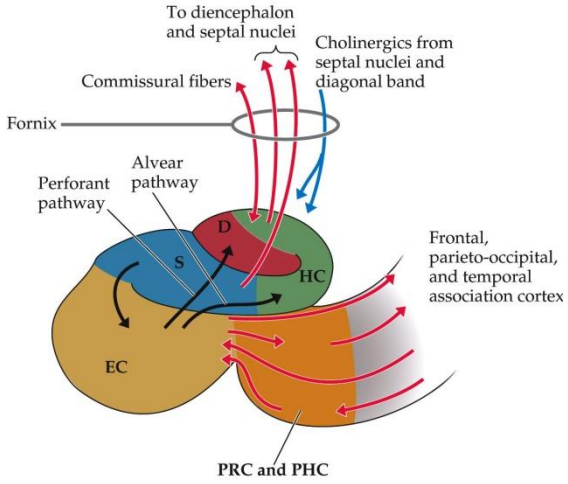
medial temporal lobe (including hippocampus): communicates with association cortex via bidirectional pathways via entorhinal cortex

medial diencephalic nuclei (around 3rd ventricle, including thalamic & mammillary nuclei): communicates with medial temporal lobe via several pathways

basal forebrain also has projections to cerebral cortex involved in memory

hippocampus: storage & retrieval of short-term memory
input from parahippocampal gyrus: piriform, periamygdaloid, presubmicular, parasubicular, entorhinal, prorhinal, prerhinal, and parahippocampal cortices
interconnected by several tracts
strong modulation by cholinergic projections from basal forebrain
hippocampal formation: dentate gyrus (granule cells), hippocampus (pyramidal cells/cornu ammonis), & subiculum (pyramidal cells)
older cortex because has only three layers
mossy fibers: large terminal which dendrites poke post-synaptic membrane into
hypocampus pyramidal sectors: CA4 (near dentate gyrus) through CA1 (near subiculum)
perforant pathway: layers 2 & 3 of entorhinal cortex → dentate gyrus → CA3 via mossy fibers → fornix (CA3 pyramidal cell axons) or CA1 via Schaeffer collaterals → fornix or subiculum
alveolar pathway: entorhinal cortex → CA1 & CA3
both pathways primarily output to subiculum → monosynaptic connections to amygdala, OFC, & ventral striatum
example of processed & unprocessed copy to CA3
medial temporal lobe: long-term memory
input: association cortex → perirhinal & parahippocampal cortices → entorhinal cortex → hippocampus
perforant output pathway → subiculum → entorhinal cortex → association cortex
fornix: fiber tracts that start in alveus & project counterclockwise around hippocampal formation
fornix output pathways: subiculum → mammillary nuclei & lateral septal nuclei
hippocampus → lateral septal nuclei & anterior thalamic nucleus
medial septal nucleus & mammillary nuclei → hippocampal formation





memory
mechanisms of storage (consolidation) & retrieval of memories are different
long-term memories relies of short-term memory relies on working memory
patient HM has medial temporal lobes resected bilaterally to control epilepsy → declarative memory loss: long-term retrograde amnesia & short-term anterograde amnesia
causes of memory loss: lesions in bilateral medial temporal lobe, bilateral medial diencephalon, basal forebrain, or diffuse (eg MS)
eg Wernicke-Korsakoff: alcoholic encephalopathy caused by B1 deficiency → diencephalon
eg Whipple's disease: bacterial infection → diencephalon
not lesions: seizures, concussions, anoxia, psychogenic, toxins, Alzheimer's
normal: infantile, sleep, passage of time
unilateral lesions do not normally produce severe memory loss, although left temporal./diencephalon lesion = verbal memory loss & right lesion = visual-spatial memory loss

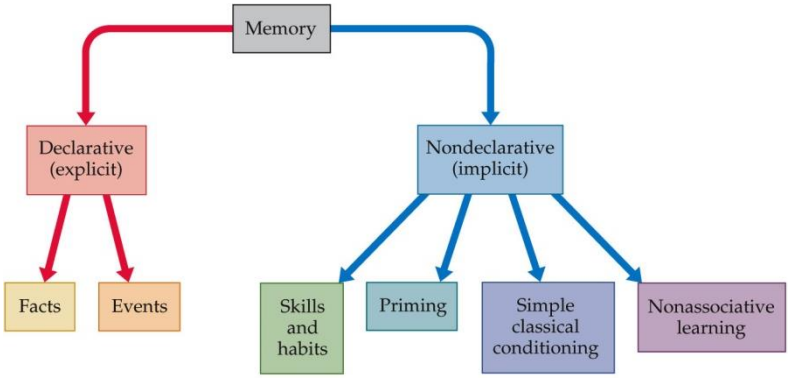


TABLE 18.6 Memory Mechanisms in the Time Domain and in the Spatial Domain

A. CELLULAR MECHANISMS INVOLVED AT DIFFERENT TIMES IN MEMORY STORAGE

SECONDS TO MINUTES	MINUTES TO HOURS	HOURS TO YEARS
Ongoing electrical activity of neurons; changes in intracellular Ca^{2+} and other ions; changes in second messenger systems	Protein phosphorylation and other covalent modifications; expression of immediate early genes	Additional changes in gene transcription and translation resulting in structural changes of proteins and neurons

B. ANATOMICAL STRUCTURES INVOLVED AT DIFFERENT TIMES IN STORAGE OF EXPLICIT MEMORIES

LESS THAN 1 SECOND ("ATTENTION" OR "REGISTRATION")	SECONDS TO MINUTES ("WORKING MEMORY")	MINUTES TO YEARS ("CONSOLIDATION")	YEARS
Brainstem–diencephalic activating systems; frontoparietal association networks; specific unimodal and heteromodal cortices	Frontal association cortex; specific unimodal and heteromodal cortices	Medial temporal structures; medial diencephalic structures; specific unimodal and heteromodal cortices	Specific unimodal and heteromodal cortices

amygdala

coordinate behavior, autonomic, & endocrine
nuclei (corticomedial, basolateral, central) plus bed nucleus of stria terminalis
    stria terminalis: fiber tracts to hypothalamus & septal area (fornix of amygdala)
output: association cortex & subcortical structures like hippocampus, plus olfactory structures
    cortical connections: hippocampal formation, OFC, cingulate cortex
    subcortical connections: thalamus, septal area, basal forebrain, ventral striatum, hypothalamus
    olfactory connections: piriform cortex & olfactory bulb
emotion & drive are interactions between amygdala and other areas
    not involved in encoding emotions into memories
lesions: failure to recognize emotion & social cues; placid
septal area associated with pleasure (monkey studies, sham rage)
neuroendocrine function: why depressed patients contract infections more often

seizures

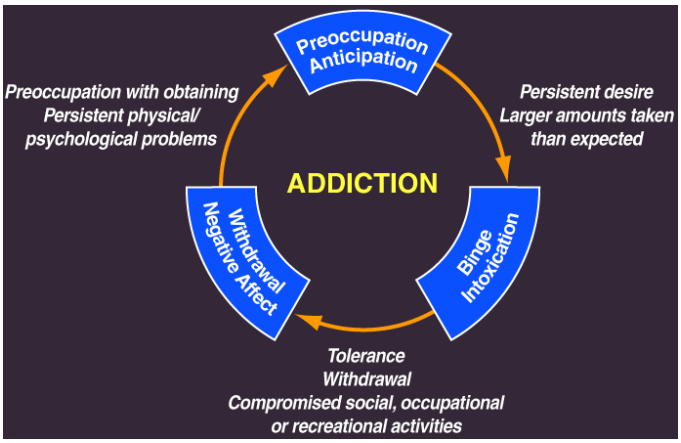
common seizures: simple partial, complex partial, absence (petit mal), tonic-clonic (grand mal)
types: partial (particular brain structure) vs generalized (cut corpus collosum)
    partial: simple (retain consciousness) vs complex; normally no post-ictal deficits
    generalized: tonic phase (loss of consciousness, muscle rigidity) & clonic phase (rhythmic bilateral jerking, autonomic output) & recovery (deep breathing to accommodate for acidosis, confusion, amnesia, lethargy, etc)
auras similar to those in migraines in that they are symptomatic of abnormal brain activity
drugs: anticonvulsants & sedatives to reduce neural activity
    stabilize inactive Na channels, potentiate GABA transmission, or affect Na/Ca channels

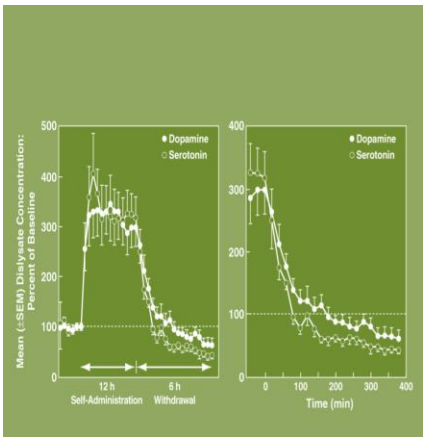
Addiction

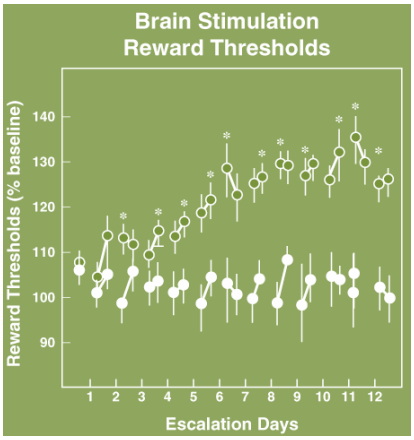
addiction - a chronic, relapsing brain disease characterized by compulsive drug seeking and use, despite harmful consequences. It is a disease because it causes brain changes, which are long lasting and cause self-destructive behaviors

key areas: ventral tegmental area (VTA) & ventral striatum in binge stage, amygdala in withdrawal stage, & OFC (+ dorsal striatum, PFC, amygdala, hippocampus, cingulate gyrus, etc) in preoccupation stage

addiction causes changes in the mesolimbic DA pathway leading to plasticity in the striatum, OFC, PFC, cingulate cortex, & amygdala







dopamine

all rewards increase dopamine in the brain, not just drugs of addiction

dopamine: neuromodulator from midbrain

- mesocortical pathway: VTA to prefrontal cortex (attention, anticipation)
- mesolimbic pathway: VTA to NA (reinforcement learning, motivation/reward)
- nigrostriatal pathway: SNc to dorsal striatum (habits, gain & loss of motor output)

DA neurons signal errors in reward prediction (better or worse than expected)

- Schultz in 1997: introduce reward after stimulus → originally fire in response to reward, then fire in response to stimulus & ceases firing in response to no reward at expected time

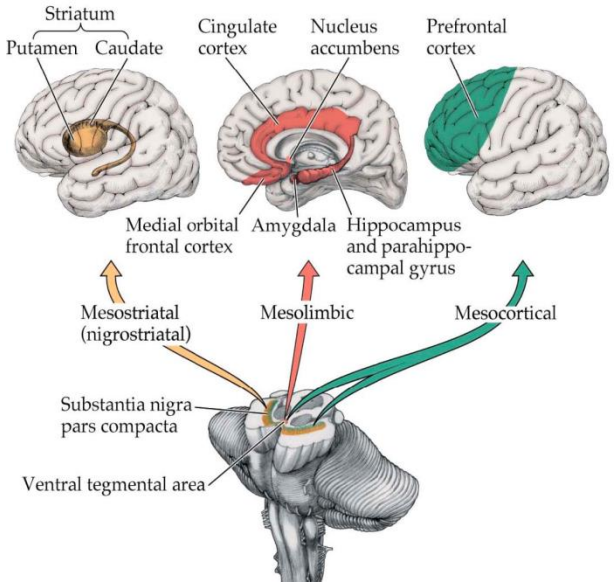
natural rewards are correlated with dopamine release, as measured by microdialysis

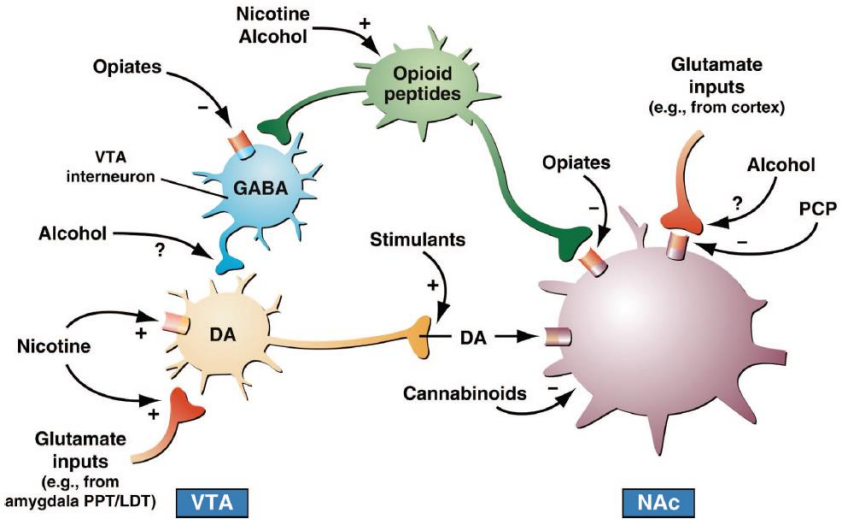
artificial rewards also elevate DA (intracranial self-stimulation)

- stimulate (threshold) → turn wheel → learn that turning a wheel produces more stimulus

when DA is blocked, rats will no longer work for reward

tonic-phasic theory of DA: phasic = reinforcement learning, tonic = pleasure threshold



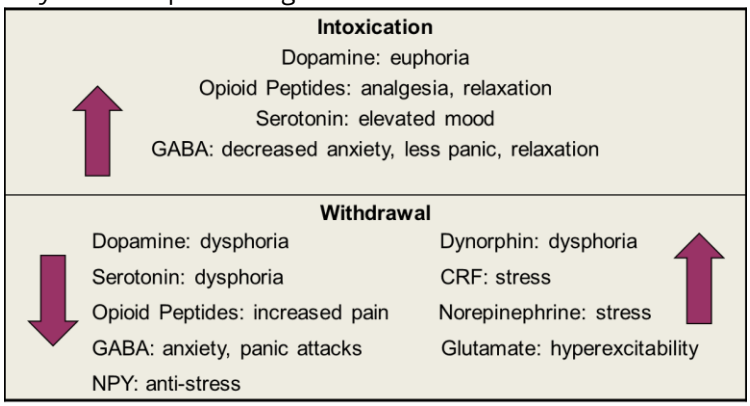


drug action on downstream areas

direct: impact DA receptor
indirect: modulate DA via other receptor systems & NT that modulate DA system
cocaine: direct, binds to and inhibits DAT
alcohol: inhibits GABAergic neurons that project to DA neurons in the VTA
nicotine: activates Ach neurons that project to DA neurons of the VTA
heroin: binds opioid receptors that inhibits GABAergic neurons that project to DA neurons of the VTA
drugs of addiction can work on other NT reward systems, but all of them work on DA

problems with long-term use

tolerance: long-access rats will press the lever more during a single session than short-access rats
    self-administration frequency & reward threshold both increase
withdrawal: disturbance of ANS, activation of locus coeruleus, & release of corticotrophin releasing factor
    NT drop below baseline → brain is compensating for overload
stress reliably reinstates drug seeking in rats
    CRF facilitates & enhances freezing, startling, burying, conditioned fear, place aversion, & lack of exploration
    can give them a single injection or foot shock them → will press lever even though saline is administered
    incubation of craving: this frequency never decreases → stress becomes a conditioned stimulus
    this is attenuated by CRF receptor antagonists



models of addiction

tolerance: reinforcing properties of drugs are gradually decreased
withdrawal: use is increased to maintain auphoria & avoid withdrawal
dependence: need to maintain this new homeostasis is increased
drug abuse results in structure & functional brain changes with changes in behavior: decreased DAT & decreased DA-D2 receptor binding
dependent in pre-existing receptors (eg different D2 receptors or decrease in DAT make rats more impulsive & subordinate monkeys more likely to self-administer)
model of addiction: percentage of rats who will take a footshock to get the drug is about the same as drug users who become addicted
    these rats have the hardest mPFC DA neurons to drive (frequency of firing given stimulation)
    top-down control of inhibiting things you don't want to do
optogenetics: use selective virus with pond scum activated by light → channel protein transcribed and inserted into PM → blue laser excites only these neurons, green light inhibits only these neurons
    excite mPFC → addiction cured!; inhibit mPFC → addiction worsened!
cocaine abuse decreases metabolism in OFC → inhibits reversal learning (discriminate between two stimuli, then reverse this association)

strong OFC phasic responses to odor that means sucrose
    this reward firing was decreased in rats given cocaine
substance abusers all demonstrate executive control deficits (fail to switch to good decks from bad decks in Iowa gambling task)
delay discounting – determine when low reward = high reward + delay
    substance abusers have steeper discounting functions
review: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2805560/pdf/npp2009110a.pdf

summary
DA pathways:
    nigra: regulation of motor output; produces both gain (tremor) & loss (rigidity) in Parkinson's
    VTA: motivation/reward (mesolimbic); attention (mesocortical); implicated in Schizophrenia
basal ganglia "decide" between competing cortical programs
    modulated by SNc (motor programs) or VTA (limbic programs)

Epilepsy
epilepsy – a chronic disorder characterized by recurrent (at least 2) *unprovoked* seizures
seizures – manifestations of excessive & hypersynchronous (usually self-limited) activity of networks of neurons in the brain
seizures transiently interfere with normal brain function
partial seizure: symptoms & signs reflect the part of the brain involved
    motor, sensory, autonomic (limbic), psychic (limbic)
    hippocampus is very commonly involved
seizures are spontaneous, but some stimuli can trigger a seizure (eg photosensitive epilepsy)
patients can have seizures without being epileptic (eg withdrawal from CNS depressants such as Xanax or alcohol, hypoglycemia)

types & symptoms
seizure onset: modeled by interictal discharges (brief high amplitude network-driven bursts of high frequency firing)
seizure spread: serial (Jacksonian march), parallel, feedback loop, commissural, distributed (grand mal, usually through thalamus)
aura: fear/anxiety, euphoria, deja vu, autonomic (epigastric, piloerection), indescribable
complex partial seizure: aura → unilateral nonpurposeful repetitive movements → unresponsive → postictal confusion & amnesia
juvenile myoclonic epilepsy: small myoclonic seizures precede tonic-clonic seizure
    loss of breathing (only 1-2 minutes, so not dangerous)
patients with grand mal seizures are more likely to respond to medication (genetic disposition), but are also more likely to die from epilepsy
provoked seizures: usually generalized convulsive types
    causes: fever (in young children), head trauma, stroke, infection (eg meningitis), drug withdrawal, medications, electrolyte abnomalities, hypoglycemia

differential diagnosis
incidence (first clinical presentation): 1 in 1000 in infants, 0.5 in 1000 at age 40, 1.5 in 1000 at age 80
age-specific etiologies: genetic/metabolic/congenital defects in infants; infections in children; trauma in young adults; tumors & vascular disease in adults

vast majority are idiopathic
after severe traumatic brain injury, 17% occurrence of developing epilepsy over the next 20 years
epileptogenesis – as neurons recover, become the source of seizures
other diagnosis: syncope, migraine, pseudoseizure

imaging
used to supplement family/clinical history, can help classify type of epilepsy & identify abnormal brain area
EEG: alpha rhythm: resting awake with eyes closed, thalamic-cortical relay
MRI: detect abnormalities correctable by surgery
PET: brain metabolism

treatments & side effects
40% risk of recurrence after first seizure → 70% after second
comorbidities more common in patients who do not respond to medication
traumatic accidents, underemployment, cognitive dysfunction, depression/anxiety, endocrine disorders, drug side effects, mortality rate
50% become seizure-free on first prescription → 67% eventually become seizure free
non-medication treatments: vagal nerve stimulation
ketogenic diet (atkins)
surgery: tissue removed is scarred, displastic, has wrong connections & morphology, etc
corpus collosotomy: prevent seizures from generalizing (makes them less severe)
surgery: for tumor, vascular problem, sclerosis in hippocampus

---

Schizophrenia
schizophrenia – severe chronic disorder characterized by hallucinations, delusions, & cognitive deficits
"to split" + "mind" = splitting of mental functions
disorder of thought & function
1% of adult population (childhood onset is rare; usually age 18-25)
most expensive illness to treat (need custodial treatment for full life span)
affects men 1.5x as often as women (also presents earlier)
ascertainment bias: men tend to be more aggressive when acting out, tend to recognize emotional disorders in men more than in women
50% of psychiatric hospital patients are schizophrenic
neurodevelopmental stages:
presymptomatic (age <15): risk factors
prodrome (age 15-18): cognitive/social deficits emerge, unusual thought content, minor functional deficits
psychosis (age 18-25): acute disability, withdrawal, lack of hygeine
chronic illness (age 25+): medical complications, long-term disability
episodic psychosis or delusions (associated with change in mood) is not enough to qualify for the diagnosis
depression with psychotic features & bipolar disorder can look like schizophrenia, but course of onset differentiates
severe interactive pervasive delusions are more characteristic of schizophrenia
psychosis: disorder of thought characterized by hallucinations, delusions, & eccentric beliefs
neurosis: habits, not a thought disorder

symptoms
positive, negative, & cognitive deficits; all must present for diagnosis

positive (added on): hallucinations, delusions, thought disorder, abnomal movements
    hallucination: unusual sensory perceptions of things that are not present
    auditory: most common, can be command, are very real to unmedicated patients, may be inability to differentiate own mental dialogue from voice of demon
    visual: more common to other disorders
    delusion: false beliefs that are persistent & organized, do not go away after receiving logical rationalization, normally based on subconscious fears of the individual, misinterpret common experiences as a conspiracy against them
negative (taken away): flat affect (even with treatment), anhedonia, apathy, poverty of thought (empty mind), social withdrawal
    similar to depression, except no poverty of thought
    these are more difficult to treat (external motivation is hard)
    lack neural structures of goal-directed behavior
cognitive deficits: executive (understand information & use it to make decisions)
working memory: representational knowledge; mental scratch pad; ability to use information immediately after learning it
    guides thought, action, & emotion through inhibition of inappropriate thoughts, actions, & emotions
    dorsolateral prefrontal cortex dysfunction
problems with independent daily life: social deficits similar to autism (emotion & motive perfecptions) & memory deficits similar to Alzheimer's (sequencing, encoding, naming, object construction)

neurodevelopmental hypothesis

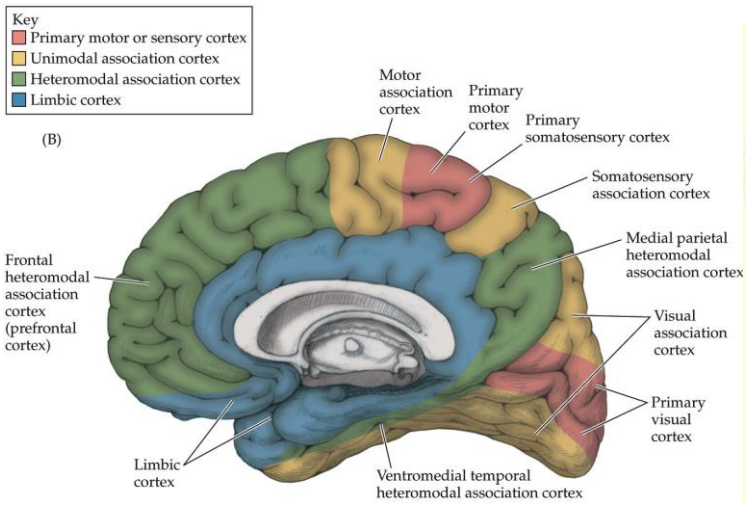
multiple genes act in concert with adverse environmental factors (neonatal or infantile illness) → pathological changes that remain latent while the prefrontal cortex is developing → manifests in early adulthood (once parents are no longer acting as your PFC)
evidence: correlation with obstetrical complications; presence of symptoms before illness; no neurodegredation
heritability: 10% from parent to child
    microenvironment of identical twins (one with lower birth weight or second delivered) is different enough that concordance is only 48%
genome-wide association studies → 80 candidate genes related to synaptic signaling machinery
1944 Netherlands malnutrition study → 3-4x increase in schizophrenia incidence in children
    genetic risk amplified by environmental conditions
    similar spikes observed in other regions with famine

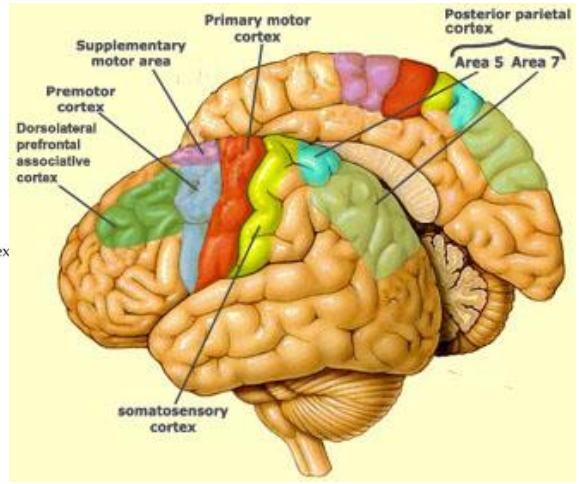
treatment

main method: drugs (new class of atypicals has fewer side effects)
    D2 receptor antagonists which treat psychotic symptoms (from hippocampus/thalamus)
psychosocial interventions help patients form a meaningful life
    some can work part-time, need a support structure to ensure that they get their medication on time
    they are more often the victims of crimes than criminals themselves
when the family is involved, relapse rate is significantly decreased
need case managers (will not seek out help on their own)
comorbidity: mood disorders, nicotine addition (may help the side effects), shizoaffective disorder (with depression or bipolar disorder), alcoholism, drug abuse, obesity/diabetes (from drugs)
genetic benefits: may be oncoprotective (have lower solid tumor incidence rate)
    rarely get lung cancer from smoking or liver cancer from drinking
most patients are not famous because the onset blunts their careers → not enough mental health funds go to this because it's not visible

Cortex

dominant hemisphere: language processing (also praxis, sequential & analytic math/music abilities; following directions in sequence)
non-dominant hemisphere: visual-spatial processing/attention (also prosody, estimation, & orientation)
dominant hemisphere is usually left, (matches motor dominance in general population) but language dominance is less lateralized in left-handed people

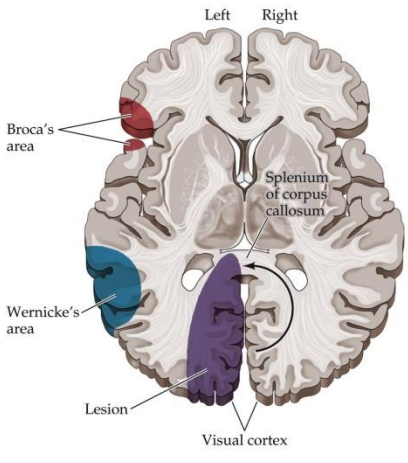


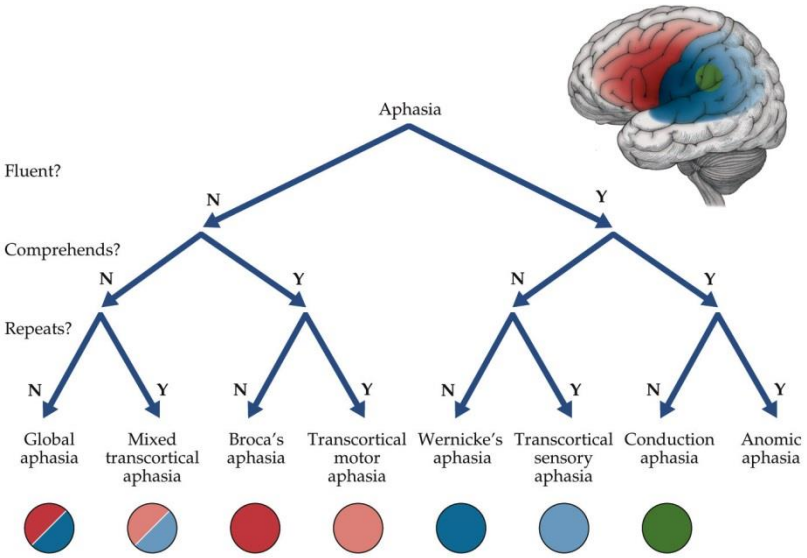


heteromodal areas: eg frontal eye fields, frontal cortex
eg exam (tell me about your childhood): hear & process question, pull memories, select information relevant to context, process language & related motor program
apraxia – inability to perform a task due to a higher-order processing deficit
eg unable to move arm even though auditory & motor neurons not affected
complexity of underlying circuits makes false localization a problem
disconnection syndromes can interrupt connections between relevant areas
hemispheric dominance develops postnatally
handedness does not always correlate with dominance in other areas (eg left hemisphere is dominant in language in left-handed people, but right hemisphere is dominant in motor areas)

cortical aphasias

Wernicke (receptive aphasia): sounds to words (auditory processing deficit) [happy man]
impaired comprehension; speech sounds normal but makes no sense
Broca (expressive aphasia): neural representations of words to sounds, syntax, motor (speech production) deficit [grumpy man]
comprehension is intact; speech is labored, affectless, syntaxless, & perseverated; could also be apraxia, hemiparesis, & disarthria
visual → (angular gyrus) → Wernicke's area → (arcuate fasciculus; layer 2/3) → Broca's area → (thalamus & basal ganglia) → motor
reciprocal connections to many other areas
vascular divisions: MCA superior (Broca's) & inferior (Wernicke's)
Broca's in temporal lobe & Wernicke's in posterior lobe



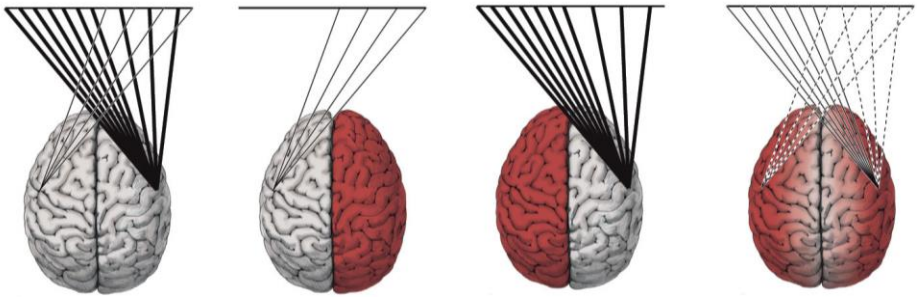


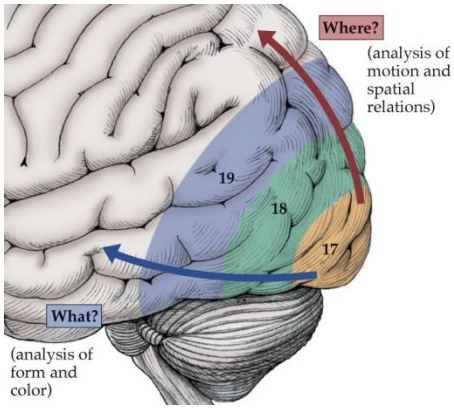
related auditory/motor deficits:
dysarthria: eg basal ganglia disorder (difficultly choosing between motor programs)
apraxia: fine motor control disorder
mutism: psychological disorder
word deafness: inability to differentiate between closely spaced sounds
alexia (loss of reading) & agraphia (loss of writing)

lesion in dominant occipital cortex extending through posterior corpus callosum → right hemianopia prevents visual signals from crossing to language areas → patient can write but can't read what s/he has written

eg ipsilateral apraxia caused by infarct in left MCA, disrupting signals from Broca's area to premotor cortex
language processing is distributed (eg viewing words, listening, speaking, generating word associations)

visual attention/gestalt: non-dominant hemisphere





vision begins in V1 → V2 & V3 (signals & form) → V4 & V5 (color & movement)

dorsal visual stream (where?): posterior parietal lobe to frontal lobe; motion & spatial relations
ventral visual stream (what?): to temporal lobe (auditory & limbic areas); analysis of form & color; facial recognition & movement (different areas respond to different movements & face areas)
attention requires multiple areas acting together
opsias: loss of ability to understand a precept
simultanagnosia: unable to perceive visual scene as a whole (one small region at a time)
optic ataxia: inability to use visual information to reach for an object under visual control

ok with auditory or proprioceptive cues

ocular apraxia: difficulty directing one's gaze toward objects in the peripheral vision through saccades

related to simultanagnosia; can't keep the visual scene all together

prosopagnosia: unable to recognize people from their faces (eg Oliver Sacks)
agnosia: normal perception stripped of its meaning

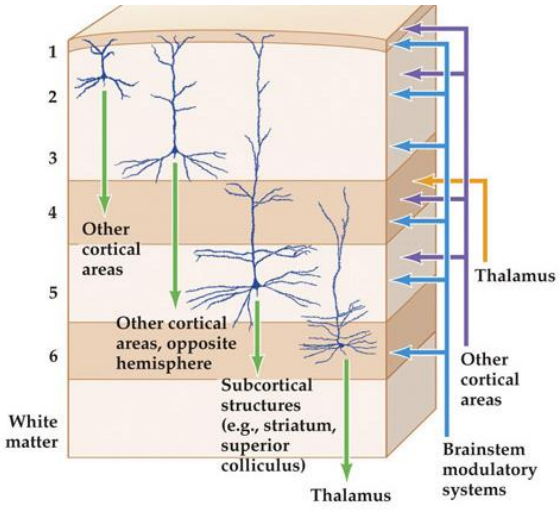
know it's a face, can describe it, but cannot identify the individual

hemineglect: lesions in right parietal association cortex in dorsal stream

primarily posterior parietal lobes (sensory association areas)

exam: extinction of response to stimulus as stimulus moves in space; extinction of motor output

eg bisect the line; circle the letter A



neocortical layers

1 – molecular
2 – external granular; interneurons
3 – external pyramidal; interneurons
4 – internal granular; inputs
5 – internal pyramidal (eg Betz cells in PMC); output to spinal cord
6 – polymorphic/multiform; output to thalamus

perihippocampal cortex has only 4 layers

frontal lobes

all cognitive/emotional processing that characterizes a "human being"

abstract reasoning, working memory, forming perspectives, planning, insight, sequencing, organization, temporal order

planning: cue → delay → response

novel patterns: dorsolateral PFC

lesions produce profound & often contradictory symptoms

depression vs mania, mutism vs confabulation, akinesia vs distractability, abulia vs environmental dependency

abulia – inability to act or make decisions (eg initiate speech, social interaction, movement)

confabulation – formation of false memories, perceptions, or beliefs

frontal lobotomies & Phineas Gage

dorsolateral PFC common in schizophrenia → loss of motivation

frontal cortex: all areas in front of central sulcus

major areas: orbitofrontal cortex (limbic & olfactory); Broca's area, PFC, FEF, motor areas (premotor, supplementary motor, primary motor), micturition inhibitory area (in supplementary motor area)

connections to every region save primary motor & sensory areas

association cortices, limbic & subcortex structures, thalamus (mediodorsal nucleus), basal ganglia (head of caudate)

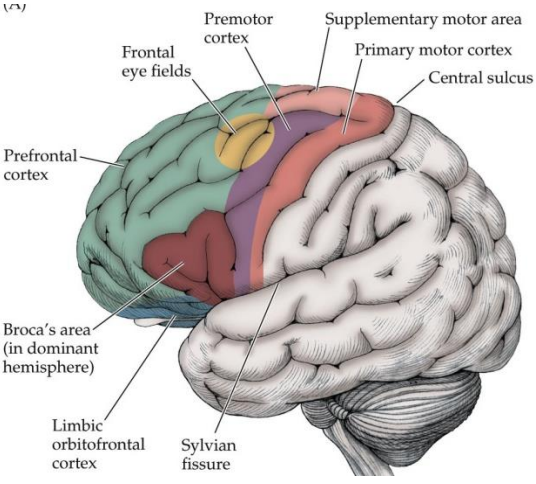
input from all neuromodulatory systems

feneralizations with many exceptions:

- dorsolateral lesions produce an apathetic, lifeless state
- ventromedial orbitofrontal lesions lead to impulsive, disinhibited behavior and poor judgment
- left frontal lesions: depression-like symptoms
- right frontal lesions: behavioral disturbances

patients with lesions may be: catatonic, inappropriate responses to social cues, respond to inappropriate stimuli, give the same answer to multiple questions (perseverate), lack of concentration on single task, lack of abstract reasoning (eg sequencing difficulties)

eg written alternating sequence test – motor perseveration



dementias

grouped by location pathology (cortical vs subcortical) or relationship to pathology (primary vs secondary)
primary dementia: Alzheimer's (cortical) vs Huntington's (subcortical)
secondary dementia: cotical vs HIV-induced
Alzheimer's: sporadic or familial (lipid transport defects, mutations in ApoE4)

cerebral atrophy, neurofibrillary tangles, amyloid plaques

medial temporal lobes (amygdala & hippocampus), basal temporal cortex, frontal lobes, nucleus basalis & locus ceruleus