development

primary neurulation: neural plate >>> neural groove >>> neural tube
neural tube - CNS glial cells and neurons (axons of somatic motor neurons and preganglionic neurons in PNS)
neural crest - PNS glial cells (Schwann cells) and neurons (sensory afferent cell bodies in CN and spinal ganglia, postganglionic autonomic soma in autonomic ganglia)
(axons of sensory afferent neurons terminate in CNS)
(neuron cell bodies = “soma” = “somata” = “perikarya”)

neural tube defects: anencephaly spina bifida occulta/cystica meningocele myelomeningocele associated with Arnold-Chiari malformations hydrocephalus encephalocele meningocele meningoencephalocele meningohydroencephalocele

prosencephalon

telencephalon - cerebral cortex, basal ganglia
diencephalon - dorsal thalamus, hypothalamus, epithalamus

mesencephalon - midbrain structures
rhombencephalon
metencephalon - pons and cerebellum
myelencephalon - medulla

alar plate - sensory
basal plate - motor
sulcus limitans

gross anatomy

telencephalon: lateral surface - central and lateral sulci precentral and postcentral gyri supramarginal and angular gyri superior temporal gyrus parietal lobule

medial surface - cingulate gyrus and sulcus parahippocampal gyrus calcarine sulcus

corpus callosum
ventricles

brain section anatomy

coronal
sagittal
horizontal
brain stem cross-section anatomy

tegmentum ("covering," think of it as a floor) and tectum ("roof")
tectum is small in pons and medulla, but appreciable in the midbrain

medulla
motor decussation - at lower end of medulla
pyramids - along anterior medial surface of medulla
dorsal column nuclei (gracile medial and cuneate lateral) at lower end of medulla near obex
sensory decussation - just above motor decussation in lower medulla
internal arcuate fibers decussate and form medial lemniscus
anterolateral system
inferior olivary nucleus (major input to cerebellum via climbing fibers)

motor centers in basal plate
  hypoglossal nucleus (somatic motor)
  nucleus ambiguus (somatic and possibly autonomic (cardiac) motor)
  vagal motor nucleus (CN X, autonomic motor)
  inferior salivatory nucleus (CN IX, autonomic motor)

t sensory centers in alar plate
  solitary nucleus and tract (general visceral sensory and taste)
  descending trigeminal tract and nucleus (somatic sensory)
  vestibular nuclei (special sensory)
  cochlear nuclei (special sensory)

reticular nuclei ("reticular formation")
raphe (serotonin)

inferior cerebellar peduncle (major input to cerebellum from medulla and spinal cord)

fourth ventricle
brain stem cross-section anatomy

pons
medial lemniscus - “sags” horizontally
anterolateral system
corticospinal and corticobulbar axons among pontine nuclei
pontine nuclei
motor centers in basal plate
  abducens nucleus (somatic motor)
  facial nucleus (somatic motor)
  trigeminal motor nucleus (somatic motor)
  superior salivatory nucleus (CN VII, autonomic motor)
  nucleus ambiguus (somatic and possibly autonomic (cardiac) motor)
sensory centers in alar plate
  solitary nucleus and tract (general visceral sensory and taste)
  vestibular nuclei (special sensory)
  descending trigeminal tract and nucleus (somatic sensory)
  primary trigeminal sensory nucleus (somatic sensory) lateral to trigeminal motor nucleus
reticular formation
  raphe (serotonin)
middle cerebellar peduncle
superior cerebellar peduncle
locus ceruleus (norepinephrine)
fourth ventricle
brain stem cross-section anatomy

midbrain
medial lemniscus - “tips” almost up-side-down
anterolateral system
cerebral peduncles (axons of corticospinal and corticobulbar axons on surface of midbrain)
periaqueductal gray (part of a descending system along with raphe for pain control)
motor centers in basal plate
trochlear nucleus (somatic motor)
oculomotor nucleus (somatic motor) (decussates and emerges on top of midbrain)
Edinger-Westphal nucleus of oculomotor complex (autonomic motor)
sensory centers in alar plate
inferior colliculus ( audition)
superior colliculus (primarily vision, also somatosensory and audition)
mesencephalic trigeminal components
reticular formation
raphe (serotonin)
decussation of superior cerebellar peduncle
red nucleus
substantia nigra (pars compacta) and ventral tegmental area (dopamine)
  SN pars compacta - cells with melanin
  SN pars reticulata
cerebral aqueduct (narrowest of major ventricular spaces in brain)
spinal cord cross-section anatomy

white matter
funiculus
dorsal (posterior)
lateral
ventral (anterior)

anterior white commissure
dorsal columns

gracile fasciculus (medial, entire length of cord)
cuneate fasciculus (lateral, above T6)

gray matter
dorsal horn

entrance of sensory afferent axons
dorsolateral fasciculus (Lissauer’s tract)
substantia gelatinosa (synapses for pain and temp)

intermediate gray matter
Clarke’s nucleus (dorsal nucleus of Clarke)
intermediolateral column gray matter “lateral horn”
autonomic preganglionic cell bodies

ventral horn
somatic motor neurons (alpha motor neurons, lower motor neurons)

Rexed lamina

<table>
<thead>
<tr>
<th>Cutaneous Area</th>
<th>Cord Segment</th>
</tr>
</thead>
<tbody>
<tr>
<td>upper arm (lateral side)</td>
<td>C5</td>
</tr>
<tr>
<td>thumb, lateral forearm</td>
<td>C6</td>
</tr>
<tr>
<td>middle finger</td>
<td>C7</td>
</tr>
<tr>
<td>little finger</td>
<td>C8</td>
</tr>
<tr>
<td>nipple</td>
<td>T4</td>
</tr>
<tr>
<td>umbilicus</td>
<td>T10</td>
</tr>
<tr>
<td>big toe</td>
<td>L5</td>
</tr>
<tr>
<td>heel</td>
<td>S1</td>
</tr>
<tr>
<td>back of thigh</td>
<td>S2</td>
</tr>
</tbody>
</table>

ratio of gray matter and white matter at major levels of spinal cord

some spinal cord problems

Tabes dorsalis
advanced syphilis
loss of fine touch, proprioception and vibration sense

Anterior cord syndrome
anterior spinal artery
spasticity - bilateral
fine touch, proprio, vib - OK
pain, temp - bilateral

Brown-Sequard syndrome
approx hemisection
spasticity - same side
fine touch, proprio, vib - same side
pain, temp - contralateral side

Charcot-Marie-Tooth disease
dorsal columns and LMNs

ALS
upper and lower MN loss

Freidreich ataxia
dorsal columns with spinocerebellar and corticospinal involvement

Syringomyelia
cavitation
anterior white commissure damaged
may extend into LMNs

Cord Segment

pain, temp loss - both arms
motor weakness - both arms

Back of thigh

C5

Cord Segment

ALS

S1

Brown-Sequard syndrome

S2

Charcot-Marie-Tooth disease

T10

Freidreich ataxia

Upper arm (lateral side)

Syringomyelia

T4

Tabes dorsalis

T6
neurons
anatomy
soma
dendrites
axons
sensory
l la lb
ll “A delta”
lll “C”
physiology
membrane potential
cations and anions
depolarization/hyperpolarization
action potentials
  speed of conduction depends on axon diameter and myelination
demyelination: multiple sclerosis (CNS) Guillain-Barre syndrome (PNS)
degeneration
  anterograde
  retrograde
axonal transport  fast and slow
  anterograde  kinesin  retrograde  dynein
peripheral neuropathy  often symptoms in hands and feet - “gloves and socks”
synapses
anatomy
neurotransmitters
  ACh  muscarinic  nicotinic
  excitatory: glutamate and aspartate
  inhibitory: GABA and glycine
  monoamines: dopamine -> norepinephrine -> epinephrine  serotonin
physiology
  inotropic
  metabotropic
NMDA glutamate receptors  excitatory - Ca++ influx
glial cells
astrocytes - part of blood brain barrier; end feet on capillary walls
  fibrous in white matter
  protoplasmic in gray matter
oligodendrocytes - myelin in CNS (form multiple sheaths); Schwann cell in PNS
microglia
ependymal cells
satellite cells - surround cell bodies in sensory ganglia
Meninges, Ventricles and CSF

dura (innervated in part by trigeminal nerve)
arachnoid
  subarachnoid space
pia
ependyma
leptomeninges (pia and arachnoid)

origin in choroid plexus  500-1000 ml/day  volume: 150ml (most in subarachnoid space)
  pressure: 80-180 mm water  few WBCs  protein: less than 45mg/dl protein  clear

ventricular circulation
  lateral ventricles
  interventricular foramina (of Monro)
  third ventricle
  fourth ventricle
    foramina of Luschka and Megendie
    central canal of spinal cord
in subarachnoid space (most of CSF found here)

absorption
  through arachnoid villi (arachnoid granulations) into dural sinuses
problem: Pseudotumor Cerebri
  most common in heavier, young women
  associated with papilledema due to elevated intracranial pressure
  papilledema (shape of optic nerve head as intracranial pressure rises)

meningitis
  viral
  bacterial
    Streptococcus pneumoniae “pneumococcal” and Neisseria meningitidis “meningococcal”
      cloudy or colored
      higher pressure
      less glucose
      higher cell count
      more protein

hydrocephalus
  communicating: blockage of arachnoid granulations
  non-communicating: blockage of flow in CNS (for example, through aqueduct or formena of Luschka and Megendie fourth ventricle to subarachnoid space)
Blood Flow and Nervous System

arterial supply / venous drainage

- **anterior, middle and posterior cerebral arteries**
  - (strokes affecting primary somatosensory cortex and primary motor cortex)

- **hemorrhagic**
  - epidural hematoma
  - subdural hematoma
  - subarachnoid hemorrhage
  - arteriovenous malformations (arterioles directly to venules)

- **ischemic** (most common)
  - TIA's

- **stroke**
  - core infarct
  - penumbra

- **TIA's**

- **aneurysm**

- **arteriovenous malformations**

- **meningeal artery damage**
  - damage to venous sinus

- **damage to vein as it enters venous sinus**
cranial nerves

point of entrance/exit from brain

location of sensory and motor nuclei in brain stem and cervical spinal cord (III - XII)

components

I   special sensory: tiny, short axons of olfactory receptor neurons; terminate in olfactory bulb

II  special sensory: axons of retina ganglion cells; terminate in LGN, superior colliculus, pretectum, and suprachiasmatic nucleus in hypothalamus

III somatic motor: innervate four extraocular muscles, including medial rectus, as well as Lev Palp Sup

   autonomic motor: Edinger-Westphal to ciliary ganglion (then to pupillary constrictor and ciliary muscles)

IV  somatic motor: innervate contralateral superior oblique

V   somatic sensory: face and top of head (ophthalmic (V1), maxillary (V2) and mandibular (V3)

   to primary trigeminal nucleus and to desc trig tract/nucleus

   somatic motor: trigeminal motor nucleus via mandibular (V3) to jaw muscles

VI  somatic motor: innervate lateral rectus muscle

VII somatic sensory: external ear - terminates in desc trig tract/nucleus

   visceral sensory: taste buds on front of tongue - terminates in solitary tract/nucleus

   autonomic motor: superior salivatory nucleus to pterygopaltiline ganglion (then to lacrimal and nasal glands)

   autonomic motor: superior salivatory nucleus to submandibular ganglion (then to submandibular

   somatic motor: facial nucleus to muscles of facial expression

   and stapedius in middle ear

VIII special sensory: cochlea of inner ear to cochlear nuclei

   semicircular ducts and otolithic organs (utricle and saccule) of inner ear to vestibular nuclei

IX somatic sensory: external ear - terminates in desc trig tract/nucleus

   visceral sensory: viscera and taste buds on back of tongue - terminates in solitary tract/nucleus

   autonomic motor: inferior salivatory nucleus to otic ganglion (then to parotid gland)

   somatic motor: nucleus ambiguus to stylopharyngeus muscle

X   somatic sensory: external ear - terminates in desc trig tract/nucleus

   visceral sensory: viscera and pharyngeal taste buds - terminates in solitary tract/nucleus

   autonomic motor: vagal motor nucleus to intramural ganglia in thoracic and upper abdominal organs

   autonomic motor: intramural ganglia in heart

   somatic motor: nucleus ambiguus to pharyngeal and laryngeal muscles

XI  somatic motor: innervates sternocleidomastoid and trapezius

XII somatic motor: innervates tongue muscles

some CN problems

oculomotor paresis/palsies/strabismus anopias anisocoria

Argyl Robertson pupil Adie-Holmes syndrome tic douloureux (trigeminal pain)

Bell's palsy acoustic neuroma (begnign Schwann cell tumor on CN VIII) Meniere's disease

IN O P (intranuclear ophthalmoplegia) - eyes adduct during accommodation

D O N OT adduct on viewing an object to the side
diencephalon

epithalamus

pineal secretes more melatonin during dark, antiguonadotropin effect
receives information from retina (through a very indirect route)
landmark - calcification shifted position to side may indicate growing mass

dorsal thalamus

specific relay nuclei

<table>
<thead>
<tr>
<th>hippocampus</th>
<th>mamm body</th>
<th>anterior</th>
<th>cingulate gyrus</th>
</tr>
</thead>
<tbody>
<tr>
<td>cerebellum, basal ganglia</td>
<td>VA / VL</td>
<td></td>
<td>motor areas of cortex</td>
</tr>
<tr>
<td>med lemnis, ant lat system</td>
<td>VPL</td>
<td></td>
<td>somatosensory cortex</td>
</tr>
<tr>
<td>trig tract nucleus, prin trig nuc</td>
<td>VPM</td>
<td></td>
<td>somatosensory cortex</td>
</tr>
<tr>
<td>solitary nucleus</td>
<td>VPM</td>
<td></td>
<td>insula (taste)</td>
</tr>
<tr>
<td>inferior colliculus</td>
<td>MGN</td>
<td></td>
<td>auditory cortex</td>
</tr>
<tr>
<td>retina</td>
<td>LGN</td>
<td></td>
<td>visual cortex</td>
</tr>
</tbody>
</table>

association nuclei

<table>
<thead>
<tr>
<th>prefrontal cx, olfactory cx</th>
<th>DM (or MD)</th>
<th>association cortex in prefrontal cortex</th>
</tr>
</thead>
<tbody>
<tr>
<td>parietal, temporal, occipital cx</td>
<td>pulvinar</td>
<td>association cortex in parietal, temporal, occipital cortex</td>
</tr>
</tbody>
</table>

intralaminar nuclei

| cerebral cx, basal ganglia, reticular nuc, spinal cord | CM, PF | cerebral cortex, limbic structures, basal ganglia |

hypothalamus

suprachiasmatic: entraining circadian rhythm
supraoptic and paraventricular: secretion of ADH and oxytocin
arcuate: secretion of releasing hormones, affect anterior pituitary
mammillary bodies: memory (Korsakoff/Wernicke syndrome)

anterior of hypothalamus: parasympathetic and heat dissipation

posterior region of hypothalamus: sympathetic and heat/conservation and production
dorsomedial and ventromedial nuclei: nutritional status, “satiety center”
lateral region of hypothalamus: “feeding center”

blood supply

mostly via posterior cerebral artery
(and posterior communicating artery to anterior part)
telencephalon
frontal, parietal, occipital, temporal and limbic lobes
insula
primary visual cortex (Brodmann area 17)
primary auditory cortex (Brodmann area 41)
primary somatosensory cortex (Brodmann areas 3, 1, 2)
gustatory cortex (insula)
estibular cortex (insula)
primary motor cortex (Brodmann area 4)
premotor and supplemental motor cortices (Brodmann area 6)
frontal eye fields (Brodmann area 8)
area supplied by anterior, middle and posterior cerebral arteries
maps of primary somatosensory and primary motor cortices
upper part of body on lateral surface; lower part of body on medial surface
granular cortex: sensory, many small cells in layer IV
agranular cortex: motor, larger pyramidal cells in layers V and VI
isocortex (“neocortex”) six layers vast majority of cortex
allocortex (“archi- and paleocortex”) three layers olfactory cortex hippocampus
“prefrontal cortex” = cerebral cortex in frontal lobes, especially in front portions of lobes
lamina
afferents (sensory) to layer IV, (cortical) to layer III
efferent to cerebral cortex from layer III; to thalamus from layer VI,
to basal ganglia, brain stem. cerebellum and spinal cord from layer V
pyramidal cells are characteristic projection cells of cerebral cortex
huge pyramidal Betz cells in layer V of motor cortex
columnar organization of cerebral cortex
efferent projections to brain stem and spinal cord
corona radiata >>> internal capsule >>> cerebral peduncle >>> through pons >>> pyramids >>> corticospinal tract
contralateral neglect of left side due to damage of parietal lobe of right cerebral hemisphere
aphasia
Broca (expressive, motor, anterior) aphasia
Wernicke (receptive, sensory, posterior) aphasia
conductive aphasia - damage to arcuate fasciculus
global aphasia - damage to large area of cortex in dominant hemispheres
transcortical - damage to regions that provide input to language areas
sensory systems

olfactory epithelium → olfactory bulb → olfactory cortex → DMN → association olfactory cortex

retina → LGN → visual cortex → visual association cortices
superior colliculus → suprachiasmatic nucleus

visual cortex

more dorsal pathway for motion
more ventral pathway for form, color

taste buds → solitary nucleus → VPM → gustatory cortex

cochlea → cochlear nuclei → superior olivary nucleus → nucleus of lateral lemniscus → inferior colliculus → MGN → auditory cortex

saccule utricle → vestibular nuclei → cerebellum → VPI and VPL → nuclei of CNs III, IV, VI → vestibular cortex

body → dorsal column nuclei → VPL → somatosensory cortex
spinal cord gray matter → VPL

head → principle trigeminal nuc → VPM → somatosensory cortex
nucleus of trigeminal tr → VPM

some tests

nystagmus (named for the direction of fast movement)
optokinetic
vestibular
caloric (COWS)
positive Romberg
Rinne
Weber
direct and consensual pupillary constriction
eyes, eye movement, pupils, vision

- anisocoria
- pupillary dilation  pupillary constriction
- miosis
- mydriasis
- Adie pupil (Holmes-Adie syndrome)
- Argyl Robertson pupil
- Marcus Gunn pupil
- third nerve palsy
- sixth nerve palsy
- internuclear ophthalmoplegia (INOP)
- lateral gaze paralysis
- damage to frontal eye field in cerebral cortex
- papilledema

### Visual Field Changes

- Visual field of left eye
- Visual field of right eye

1. **ipsilateral blindness**
2. **bitemporal hemianopia**
3. **ipsilateral nasal hemianopia**
4. **contralateral homonymous hemianopia**
5. **contralateral superior quadrantanopia**
6. **contralateral homonymous hemianopia**
7. **contralateral superior quadrantanopia**
8. **contralateral inferior quadrantanopia**

Lesions may involve “macular sparing.”

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**Diagram Notes:***

- CG: ciliary ganglion
- E-W: Edinger-Westphal
- SC: suprachiasmatic nucleus
- LGN: lateral geniculate nucleus
- Foveal info projects to posterior portion of primary visual cortex
brain stem

in MEDULLA
medial medullary syndrome
(Ant Spinal Art)

lateral inferior pontine syndrome
(PICA)

in PONS
medial inferior pontine syndrome
(Basilar Art)

lateral inferior pontine syndrome
(AICA)

in MIDBRAIN
dorsal midbrain - Parinaud syndrome
(tumor in pineal region)

paramedian midbrain - Benedikt syndrome
(PCA)

medial midbrain - Weber syndrome
(PCA and circle of Willis)

reflex arcs (afferent and efferent limbs)
corneal
acoustic (stapedius muscle)
gag
brain stem

tectum - from alar plate
tegmentum - from basal plate
medulla - negligible tectum; pyramids anterior to tegmentum
pons - negligible tectum; pontine nuclei and corticospinal/corticobulbar axons anterior to tegmentum
midbrain - thick tectum (inferior and superior colliculi); cerebral pedicles (crus cerebri) anterior to tegmentum

Brain Stem Monoamine Systems
norepinephrine - locus ceruleus (pons), solitary nucleus, and reticular formation
vigilance/changes in attention?
dopamine - substantia nigra pars compacta and ventral tegmental area (midbrain)
cognition/motivation?
serotonin - raphe (nuclei) throughout brain stem, especially pons and medulla
general arousal?
corticobulbar input to cranial nerve motor nuclei
possibly special emphasis on CNs VII (upper and lower divisions), CN X (uvula), CN XI (trapezius and SCM) and CN XII (genioglossus)

decorticate rigidity (posture): lesion above rostral midbrain, corticospinal gone, rubrospinal, reticulospinal and vestibulospinal remain
decerebrate rigidity (posture): lesion includes rostral midbrain, corticospinal and rubrospinal gone, reticulospinal and vestibulospinal remain

spinal cord

tracts
- ascending
- descending
location of tracts
information carried
pathway - decussation (in some cases)
- termination

the big three
dorsal column/medial lemniscus
ALS (spinothalamic)
lateral corticospinal
reflex arcs
motor system

upper motor neurons (UMN)

lower motor neurons (LMN)
  alpha motor neurons
  (gamma motor neurons)

UMN injury signs: weakness and eventual spasticity
  hyperreflexia and unusual reflexes - Babinski, Hoffmann, clasp-knife clonus

LMN injury signs: weakness, flaccid paralysis, fasciculations (early), atrophy (later)

UMN and LMN involvement
  one approach, consider a particular LMN (for example in the spinal cord or in the hypoglossal nucleus)
  if lesion above the level of the LMNs, can be an UMN problem
  lesion at the level of the LMNs, can be an LMN problem
  lesion below the level of the LMNs, not a problem
  superior alternating hemiplegia
    midbrain
    posterior cerebral artery
  middle alternating hemiplegia
    pons
    basilar artery
  inferior alternating hemiplegia
    medulla
    anterior spinal artery

basal ganglia
  Parkinson disease: loss of nigrostriatal pathway, neurons in substantia nigra pars compacta
    rigidity, resting tremor, hypokinesia, sometimes cognitive and affective signs/symptoms
    inclusions in nerve cell bodies (Lewy bodies) in PD and some neurodegenerative diseases
  Huntington disease: loss of neurons in caudate (and in cerebral cortex)
    choreiform (jerky) movements, dementia, depression
    ballismus (hemiballismus) - damage to (ipsilateral) subthalamic nucleus

cerebellum
  cerebral cortex and deep nuclei
  medial zone damage - postural difficulties nystagmus
  lateral zone damage - limb ataxia (on same side as cerebellar damage)
  “falls to same side (due to leg apraxia) as lesion to lateral part of cerebellum
  signs are worse when damage involves deep nuclei as well as cerebellar cortex
Pathways:

**Brainstem**
- **Vestibular nuclei**
- **Posterior spinocerebellar tract**
- **Dorsal columns**
- **Dorsal nucleus of Clarke (T1 - L3)**

**Spinal Cord**
- **Inferior olivary nucleus**

**Cerebellum**
- **Via middle cerebellar peduncle**

**Cerebral Cortex**
- **Pontine nuclei**

**Red nucleus**
- **Via superior cerebellar peduncle**

Lesion in lateral part of cerebellum is seen as problems in limbs on side of the cerebellar lesion.
headaches

stimulation of receptors:
in dura mater above tentorium cerebelli
  innervated by trigeminal
  pain referred to face and forehead

stimulation of receptors:
in dura mater below tentorium cerebelli
  innervated by cervical nerves
  pain referred to back of head and neck

cerebral tumor: raises intracranial pressure, can stretch and irritate dura
  continuous and progressive headache

meningitis: results in severe pain over all of head and back of neck

“maps” in primary somatosensory cortex
  and primary motor cortex

review sleep from Dr. Martin’s notes

knowing peripheral nerves in arm, leg, neck and face has helped in prior years