FINAL INFO

80 questions

- 40 questions from new material (lectures 34 – 41)
  - ~ 20 recycled from old quizzes/exams
- 40 questions from old material (lectures 1 – 31)

8:00am – 11:00am, Saturday May 11th

Office hours:

- Either Dr. McLoon, Chloe, or I will be available:

  Angie: Thursday 2pm – 4pm, Jackson 6-135

  Chloe: Tuesday – Thursday 10am-11am, Jackson 3-159

  Steve: Friday 9:30am – 11:30am, Jackson 4-158

  Angie will answer emails through Friday evening

Review

-cerebral cortex 1 & 2 (Heilbronner)
-language & speech (Heilbronner)
-drug abuse/addiction (Thomas)
-memory and decision making (Redish)
-neurodegenerative disorders (Lesne)
-injury and regeneration (McLoon)
-adult neurogenesis and stem cells (McLoon)

Cerebral Cortex 1 (Lecture 34): Goals

1.review gross anatomy of the cerebral cortex

 -position of the cerebral cortex within the whole brain

 -lobes

 -major regions of each lobe

3.understand topographic organization of the sensory cortex

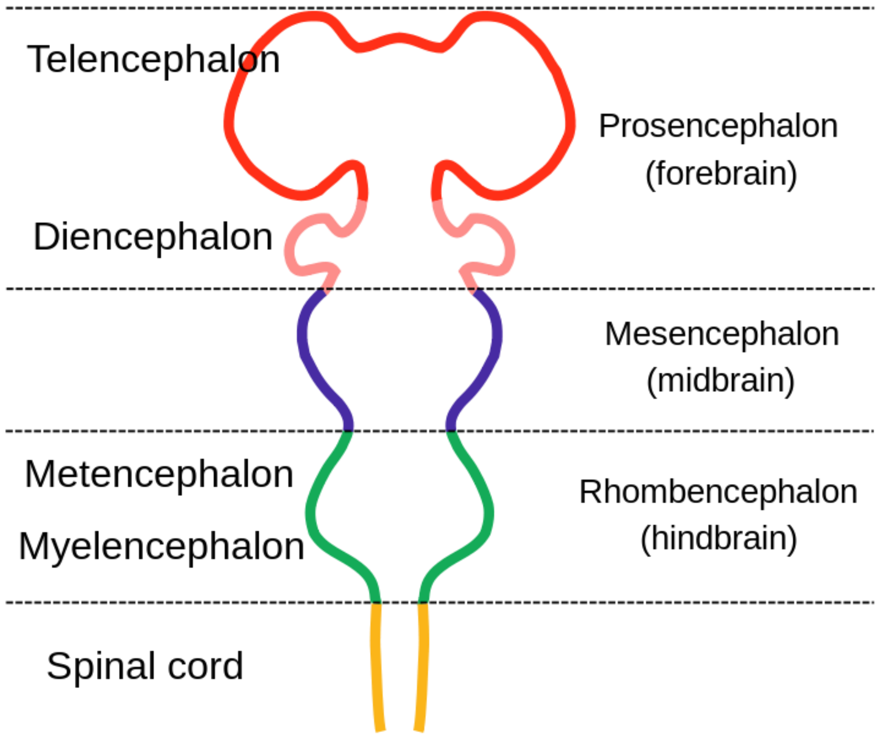
4.understand microscopic anatomy of the cerebral cortex

 -layers

 -major cell types in each layer

 -input and output connections

Where is the cerebral cortex?

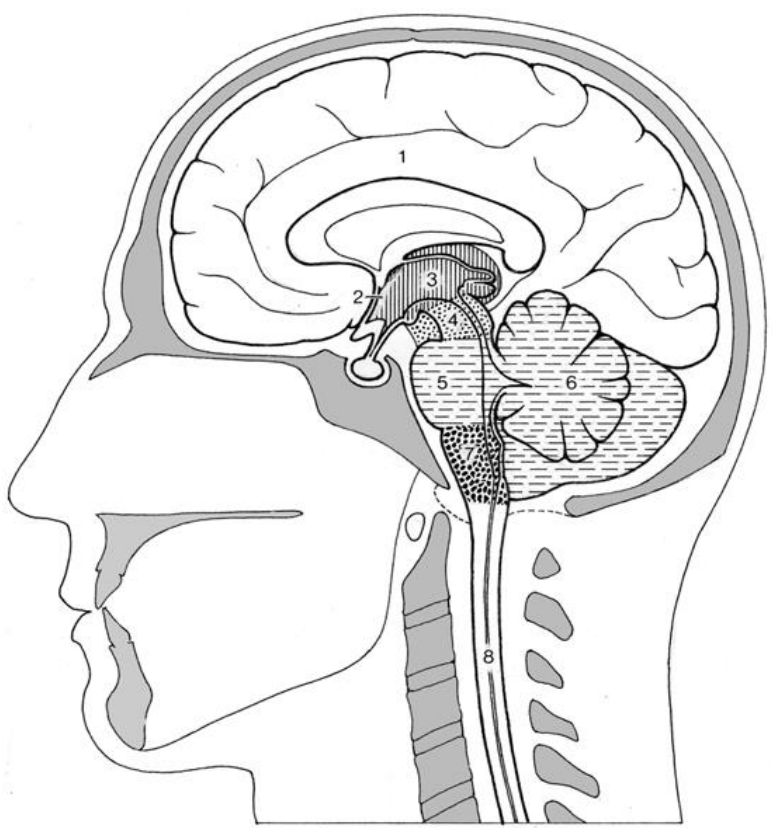


prosencephalon (forebrain)

telencephalon   diencephalon

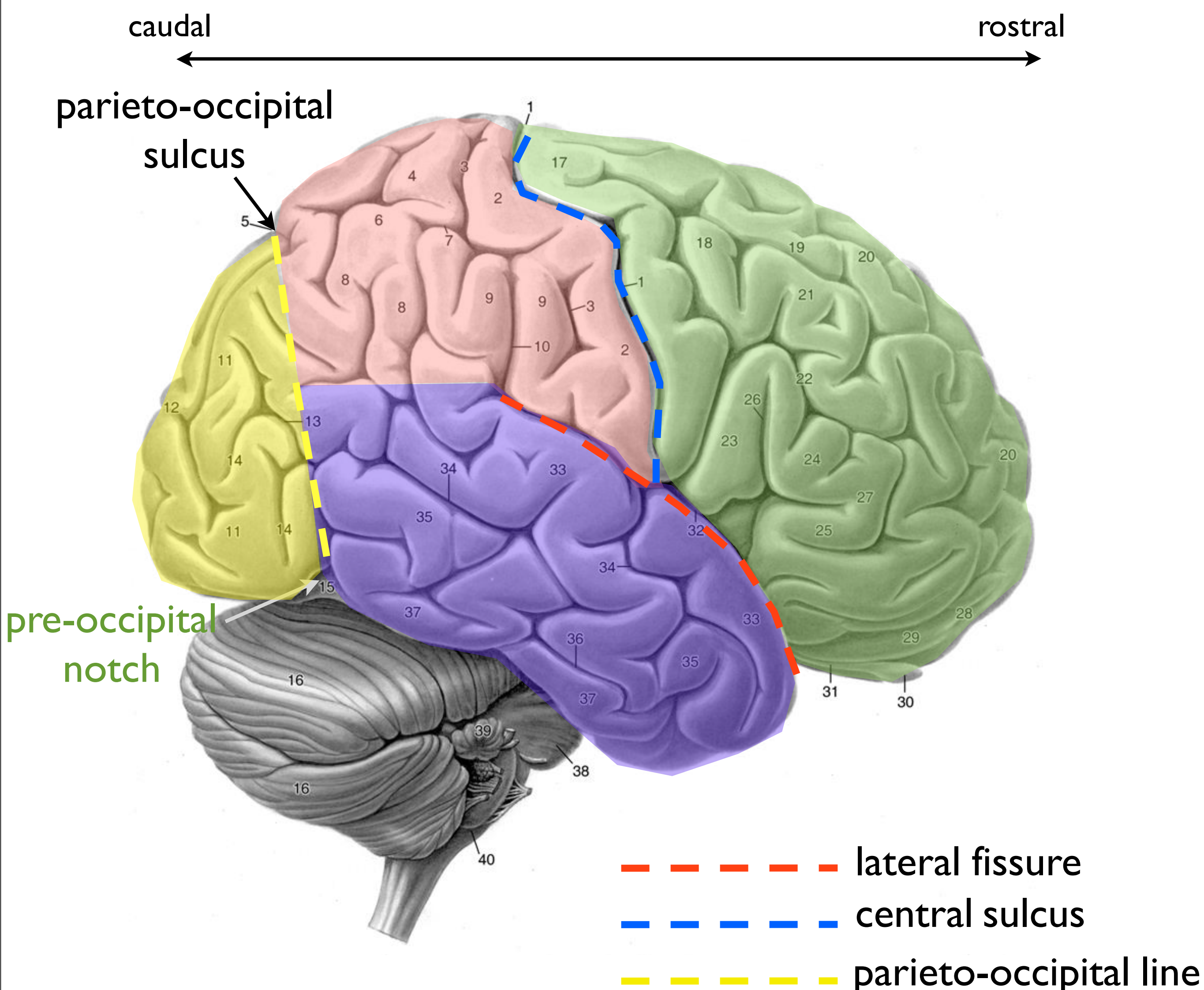
ventral telencephalon
=part of basal ganglia
-putamen
-caudate
-nucleus accumbens
-globus pallidus

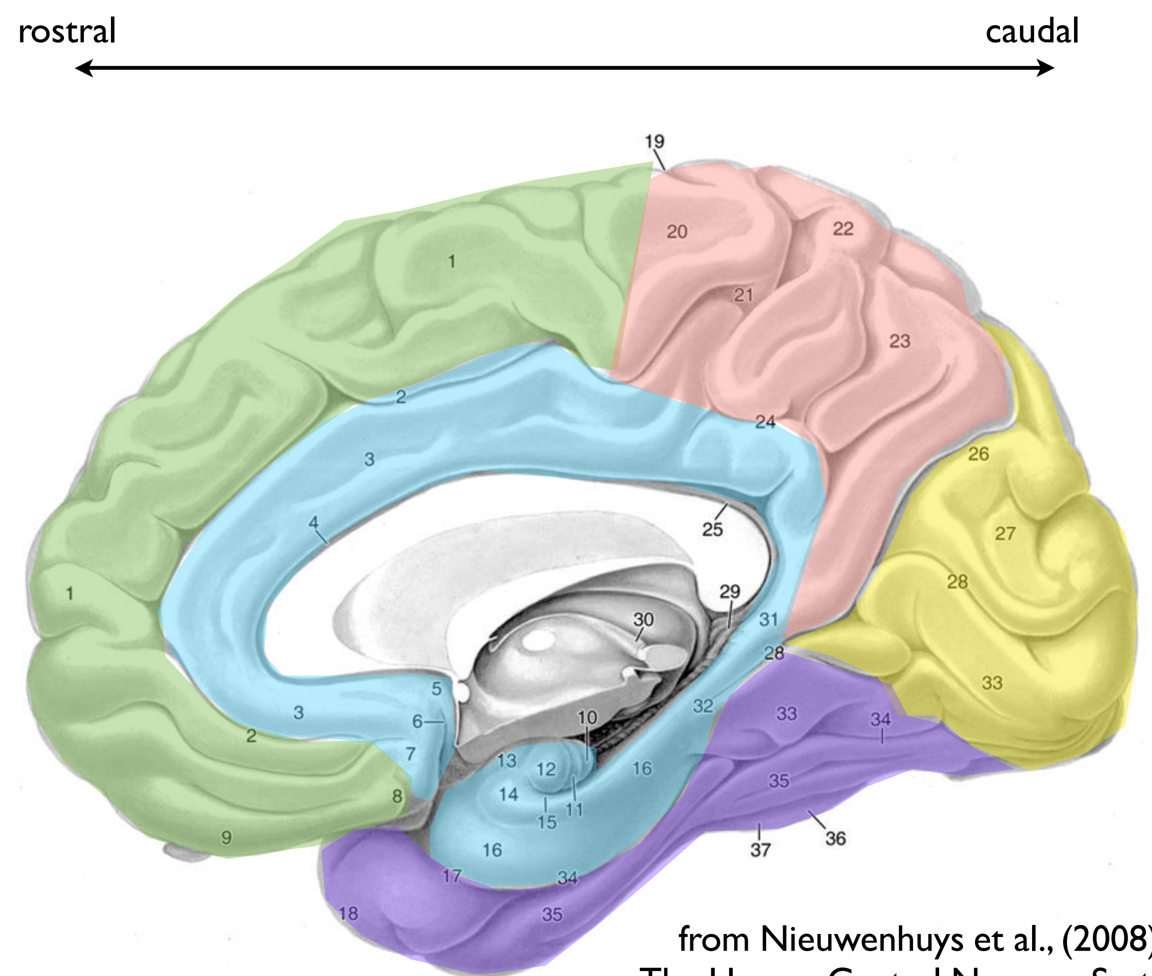
dorsal telencephalon
=cerebral cortex
-neocortex
-hippocampus
-olfactory cortex



The overall organization is conserved in all vertebrate brains. The six-layered organization is found only in mammalian neocortex.

Lobes of the cerebral cortex



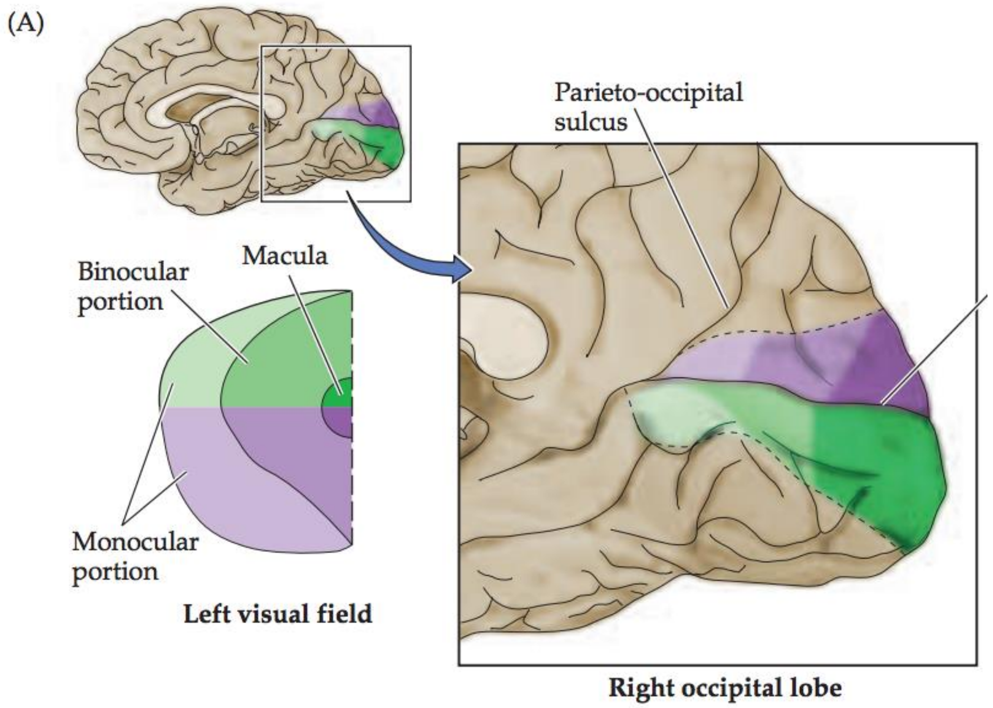


from Nieuwenhuys et al., (2008)
The Human Central Nervous System

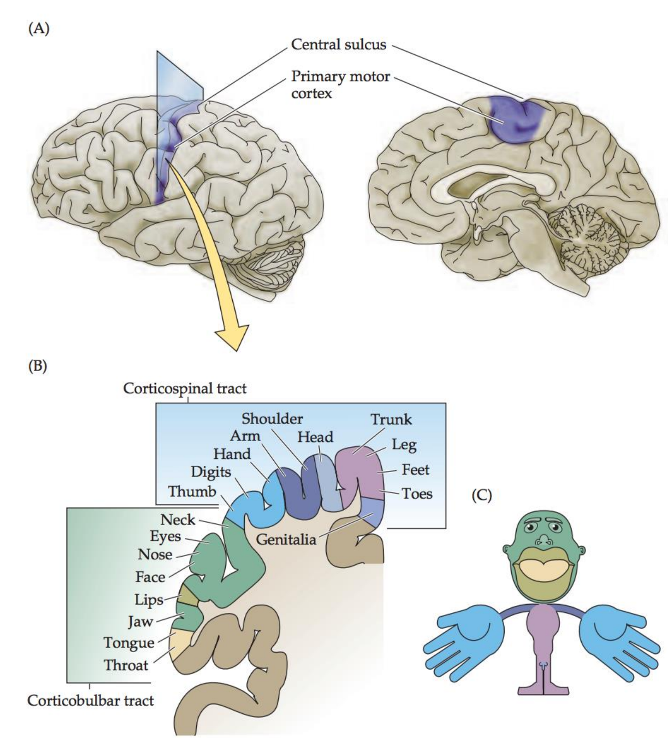
-major areas in each lobe (you do not need to remember the Brodmann's area numbers)
-sources of afferent input for each of the major cortical areas

Topographic organization of the sensory cortex

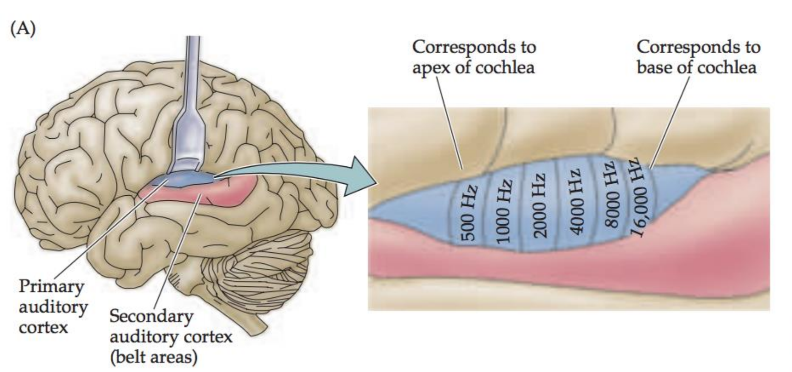
retinotopy (visual system)...location/orientation of the visual object



somatotopy (sensory/motor system)...location of the body surface

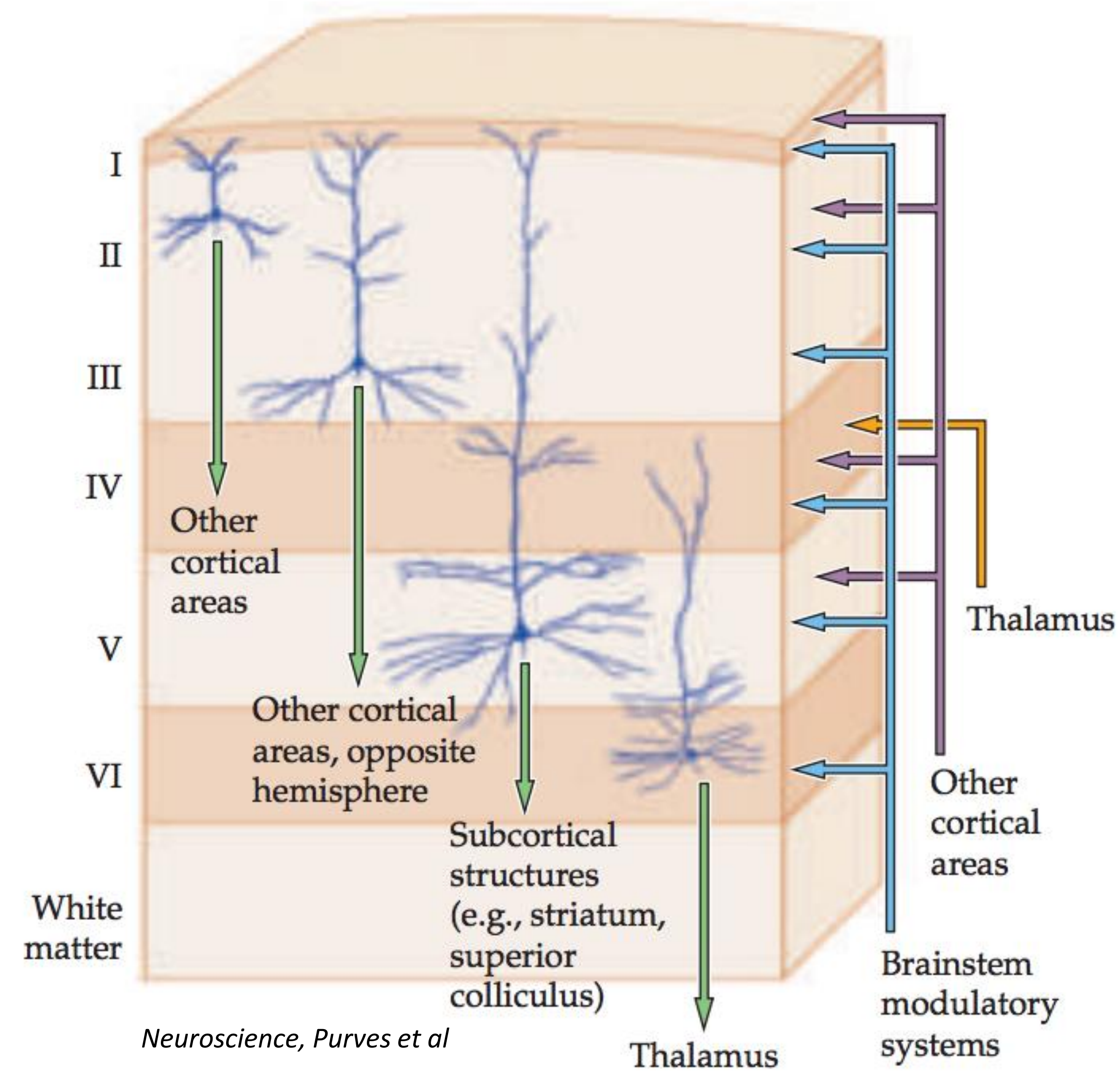


tonotopy (auditory system)...frequency of sound



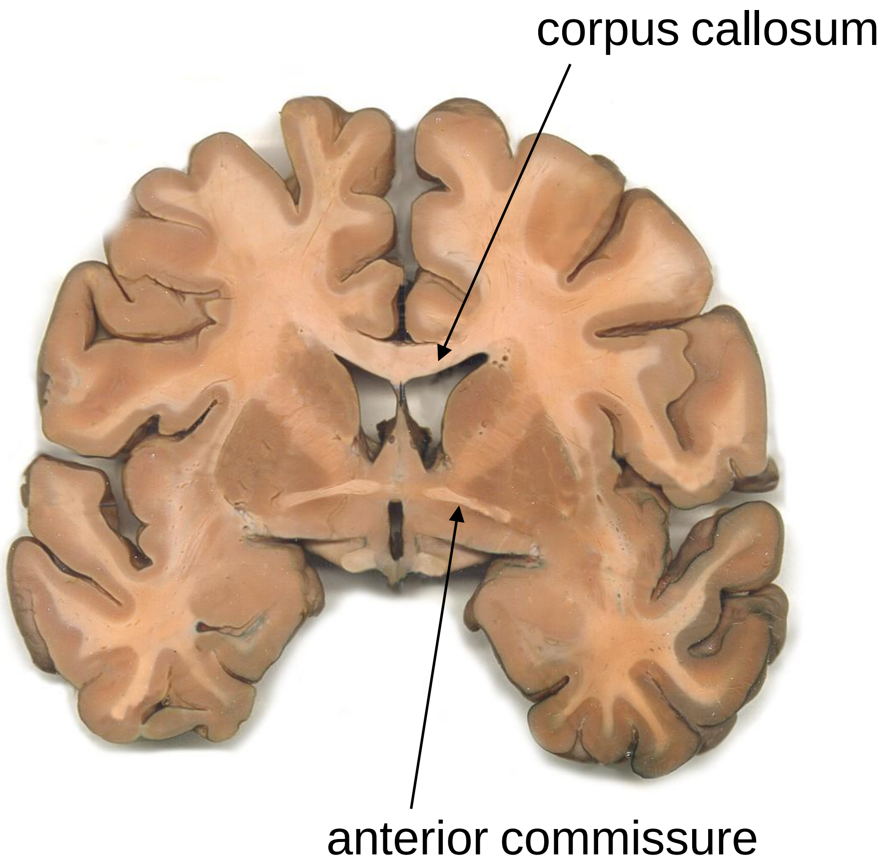
Cellular Organization of Cortex

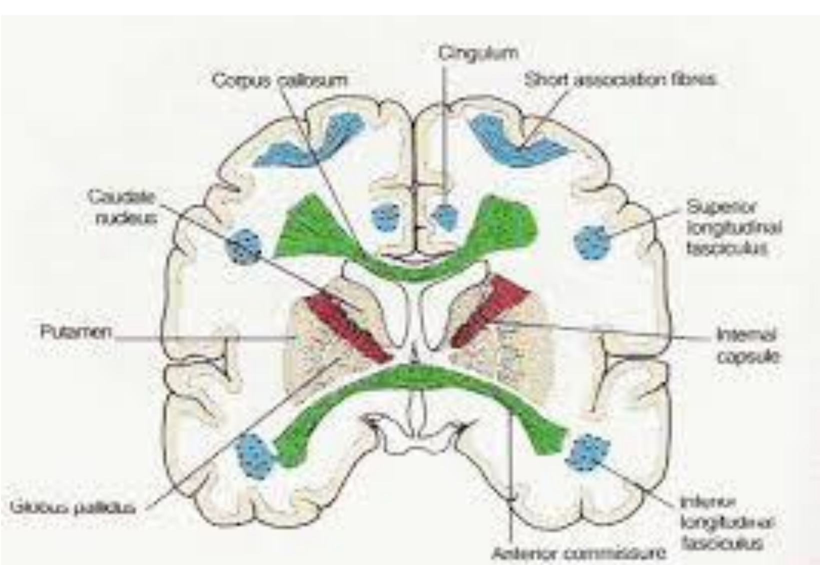
Green arrows indicate outputs to the major targets of each of the neocortical layers in humans; orange arrow indicates thalamic input (primarily to layer IV); purple arrows indicate input from other cortical areas; and blue arrows indicate input from the brainstem modulatory systems to each layer.



Neuroscience, Purves et al

Cortical white matter tracts





1.Two major axon bundles connect the two sides of the cortex (commissural connections)
-corpus callosum (dorsal part of the cortex)
-anterior commissure (temporal lobes)

2. Uncinate fasciculus connects the frontal and temporal lobes

3. Cingulum bundle and longitudinal fasciculi run rostral-caudal and connect the frontal, parietal, and occipital lobes

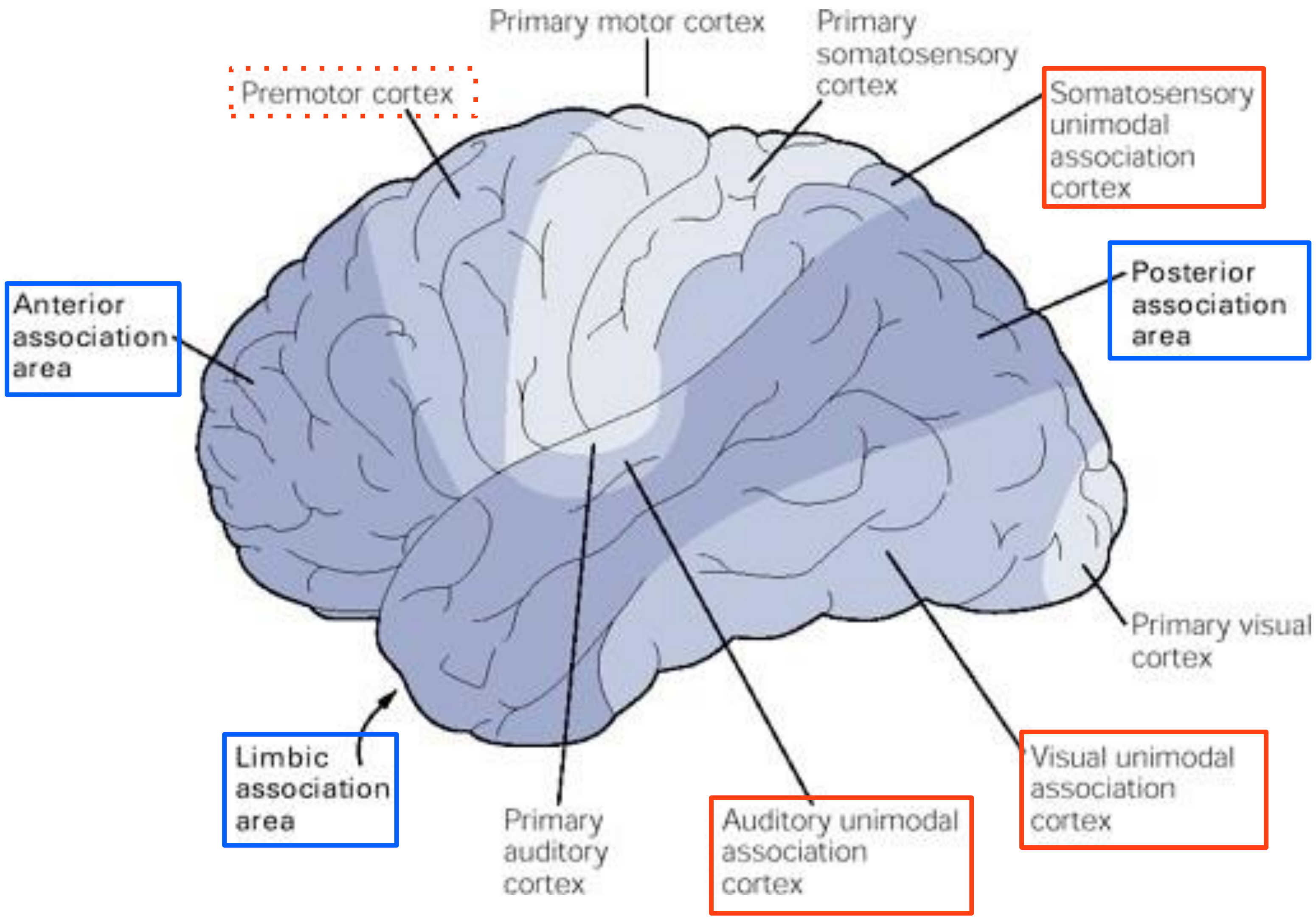
4. Internal capsule connects cortical regions with thalamus, subthalamic nucleus, and brainstem

Cerebral Cortex 2 (lecture 35): Goals

1. Review types of brain imaging
    - -structural
    - -functional
    - -advantages/disadvantages
2. Association areas
    - -modularity
    - -what happens when these are damaged

Definition of association areas

-parts of the cortex that neither receive direct sensory information through the major sensory pathways (somatosensory, auditory, visual) or motor thalamic nuclei (ventro-lateral, ventro-anterior).



unimodal association areas:

-located adjacent to their respective primary sensory cortical areas; process one type of information

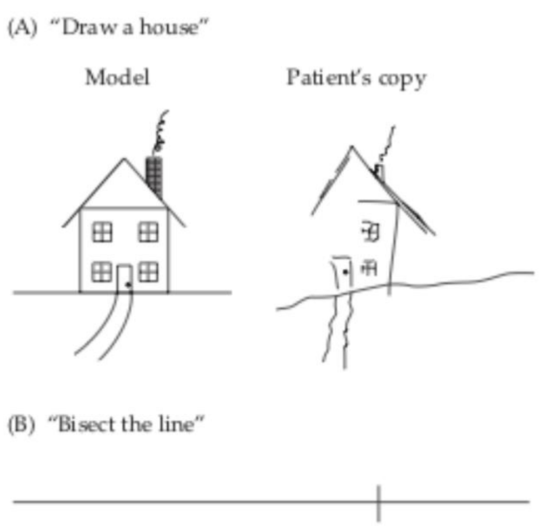
multimodal association areas:

-process many types of information in complex ways

Quizzlet.com

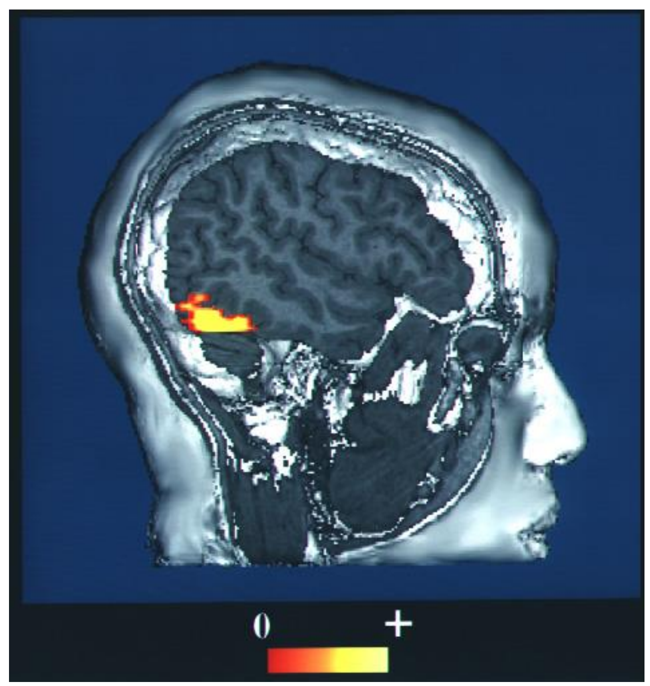
Modularity

-certain brain areas are specialized for specific functions



Parietal association cortex:

-involved in visual attention, especially the right parietal cortex responding to left visual field, damage results in **parietal neglect**



Temporal association cortex:

--contains fusiform face area for recognition of faces, also involved in recognizing objects/things, damage results in **agnosias** – difficulty recognizing/naming things

Smithsonianmag.com

Frontal association cortex:

-damage causes deficits in planning, decision-making, and personality

Brain imaging

How can we understand biological basis of cognitive functions?

-use lab animals for invasive experiments (e.g., electrophysiology and tract tracing on monkey)
-clinical studies of patients with cognitive disorders

-structural imaging
obtain detailed anatomical images of the brain

-functional imaging
non-invasive methods used to observe the areas of the human brain during cognitive processes

Structural

CT (X-ray computerized tomography)

- Used medically; less distortion; lower resolution

MRI (magnetic resonance imaging)

- Used mostly in research; high resolution; finer detail

DTI (diffusion tensor imaging)

- Used to visualize whit matter tracts; tracks diffusion of water along white matter

Functional

PET (positron emission tomography)

- A radioactive tracer is used to visualize brain regions that are more active
- Limited temporal resolution; requires tracer injection

fMRI (functional magnetic resonance imaging)

- Tracks changes in blood oxygenation level dependent (BOLD) signal; BOLD correlates with neural activity levels; can be done over a longer time frame

Cortical Diseases, Language & Speech (lecture 36): Goals

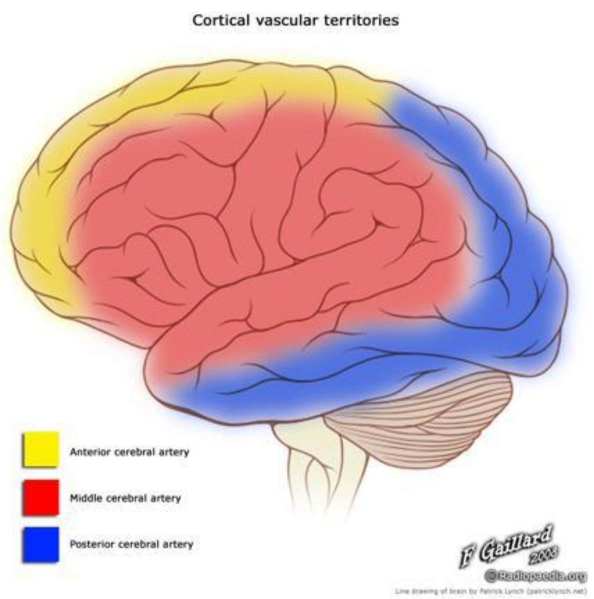
1. Understand primary cortical diseases and their categories
   -vascular (stroke)
   -developmental (epilepsy)
   -mental illness (depression, OCD)

2. relationship of language to the brain
   -definition and types of aphasia
   -lateralization
   -acquisition
   -evolution

Cerebral Cortical Diseases

Vascular: Stroke

1. Blood supplies
   - Anterior cerebral artery (ACA)
   - Middle cerebral artery (MCA)
   - Posterior cerebral artery (PCA)



2. Ischemic stroke
   - block in the blood vessel
   - thrombosis or athrosclerosis
   - treatable with TPA

3. Hemorrhagic stroke
   - rupture of a blood vessel
   - aneurysm
   - arteriovenous malformation (AVM)

Developmental: Epilepsy

Imbalance of excitation/inhibition

Cortical malformation

Mental Illness:

Abnormal cortical activity

Depression – reduced activity in the prefrontal cortex

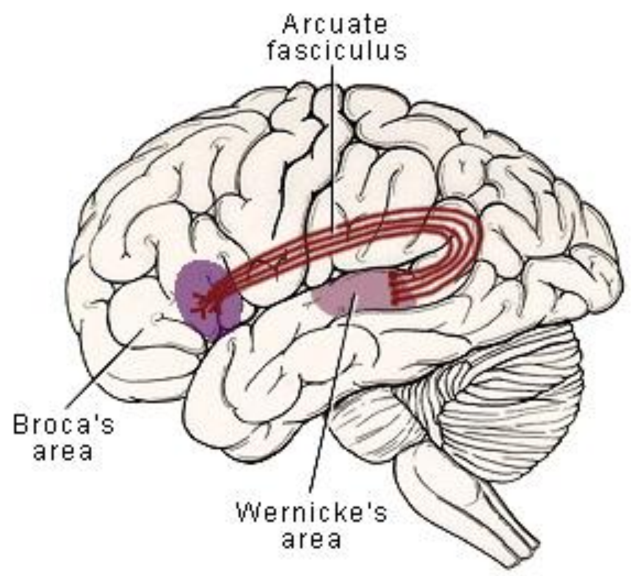
OCD – increased activity in the anterior cingulate gyrus

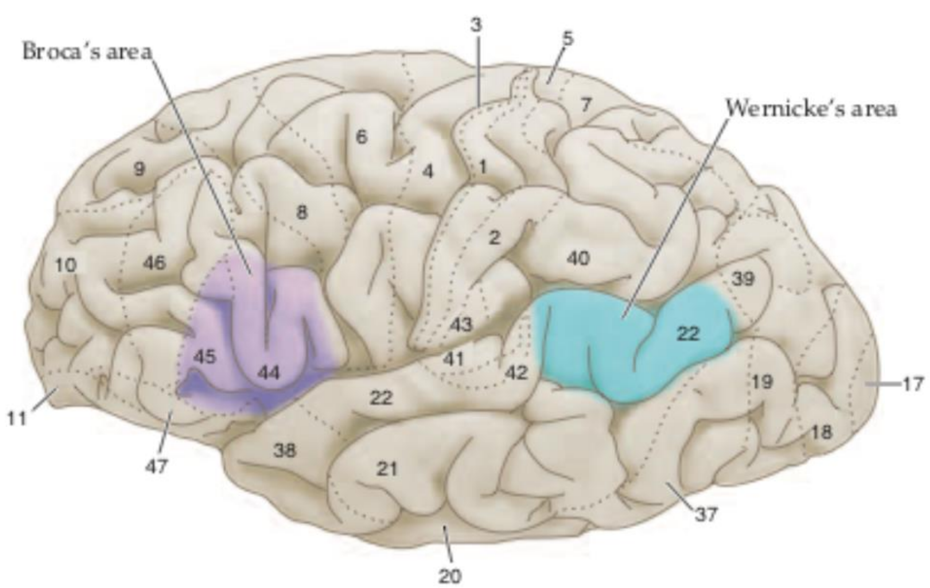
Aphasia

Broca’s aphasia – can’t produce meaningful language, can understand it, and produce words

Wernicke’s aphasia – can’t understand language, can still produce sentences/words

Conduction aphasia – can’t produce appropriate responses to language, can comprehend it, impairment in repeating words





Hemispheric differences

Language is lateralized and localized in the left hemisphere

Although the emotion of language is processed by the right hemisphere

Split-brain patients (had their corpus callosum severed) have a hard time naming things presented to the left visual field

Language acquisition

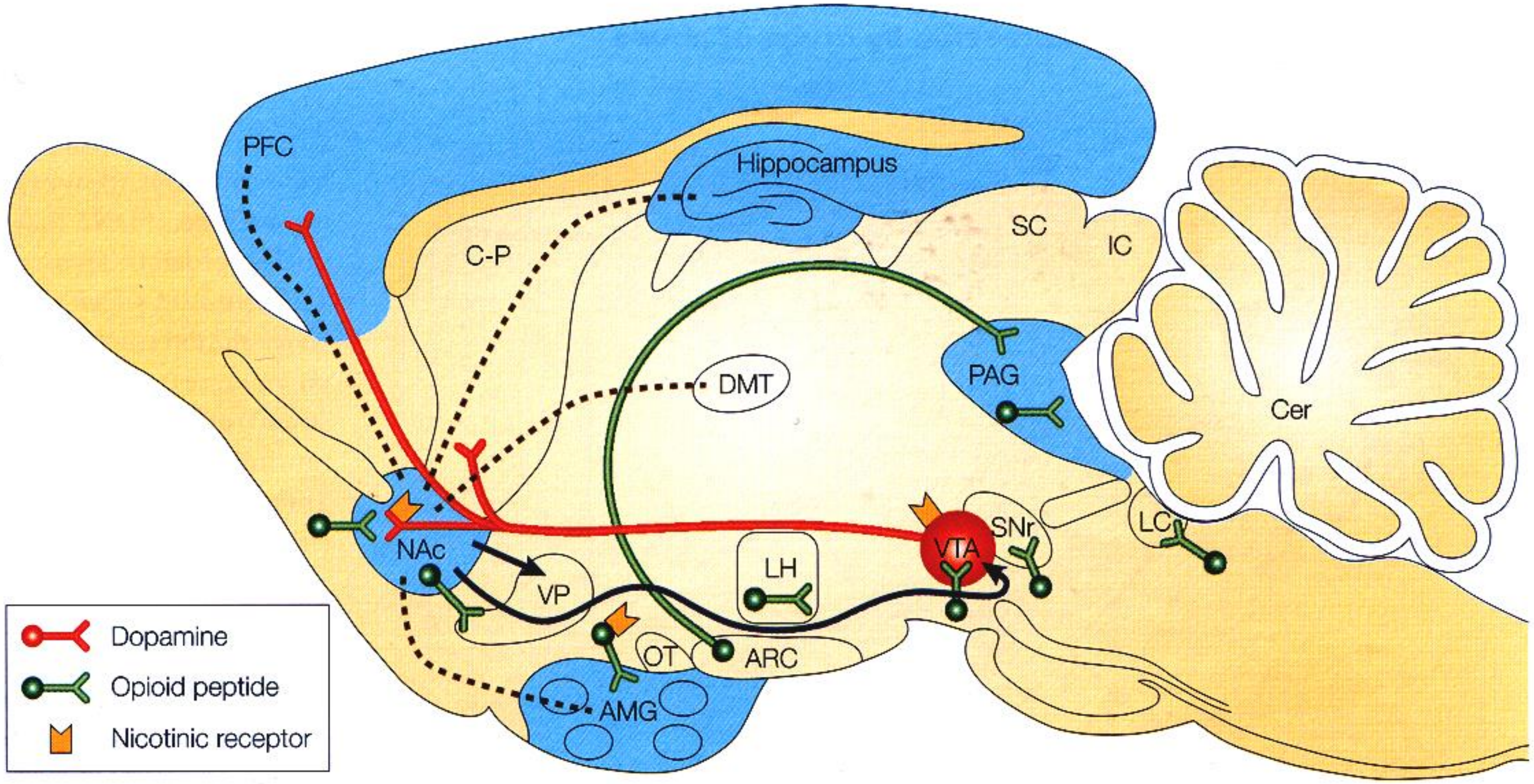
Critical period (0 to 5-12 years old)
FOXP2 is an important gene
Non-human animals do communicate (monkey vocalizations when different threats are presented)

Drug Addiction/Abuse (lecture 37): Goals

-What is the reward system good for?
  -guides us to seek-out advantageous stimuli (food, sex, community, survival)
-Which areas of the brain are involved in the reward system?
-Which neurotransmitters are key players in the reward system?
-How does cocaine act at the cellular level (how does it change dopamine levels)?
-How can we study addiction in animals?
-What changes can happen at the cellular level after drug use?

Addiction in the brain

Nucleus Accumbens: motivation, reward, reinforcement
Ventral Tegmental area: reward, motivation
Prefrontal Cortex (PFC) : decision-making
Hippocampus: learning and memory
Amygdala: emotion
Dorsal Striatum (caudate/putamen): motor function, stimulus-response learning

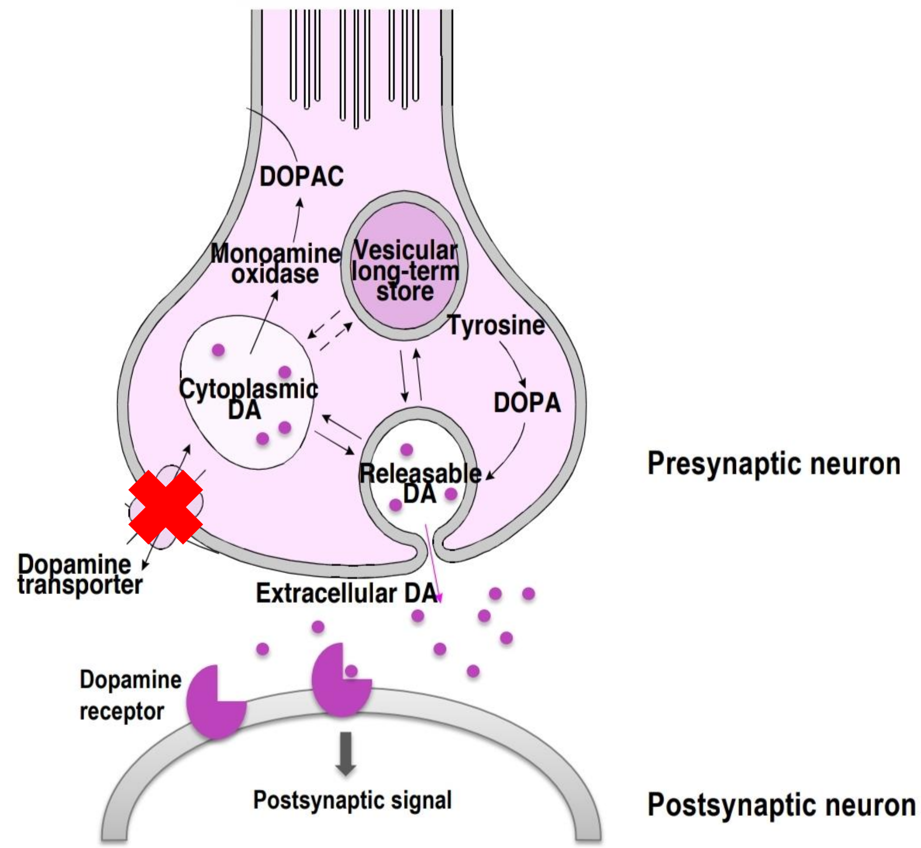


- **Dopamine**
- Glutamate
- Endogenous opioids
- Acetylcholine

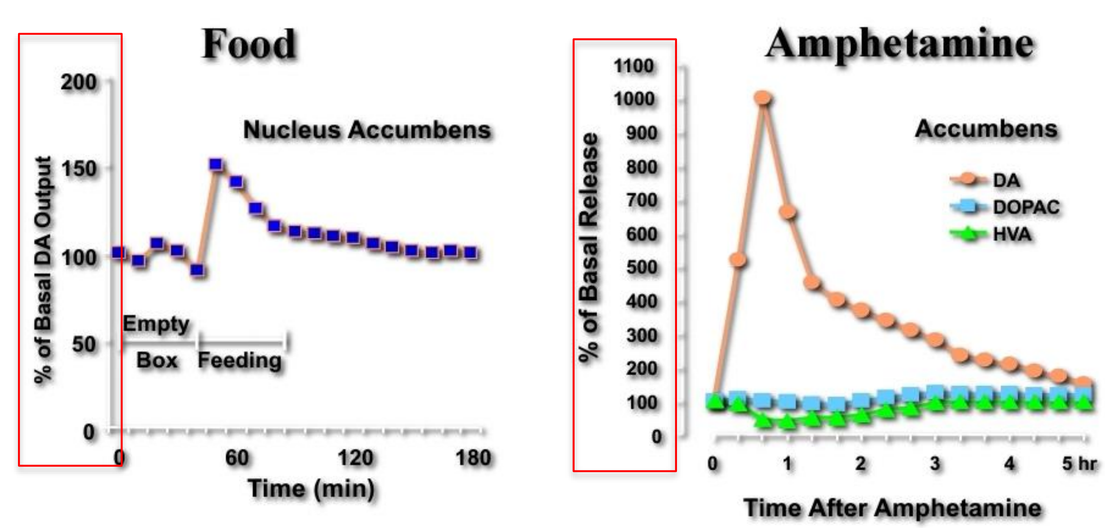
The dopamine synapse on drugs

- Dopamine synapses have the same properties as any other typical synapse:
  - Neurotransmitter
  - Neurotransmitter vesicles
  - Machinery to release vesicles into extracellular space
  - Reuptake transporters
  - Postsynaptic terminal with receptors

  - Cocaine blocks dopamine transporters increasing the time dopamine remains in the extracellular space



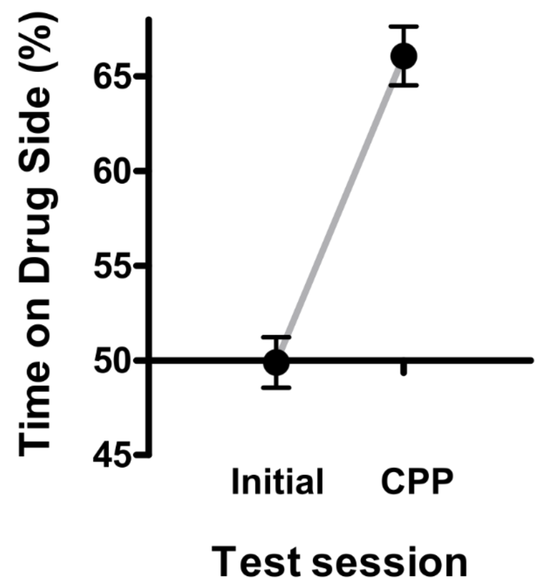
Dopamine release:
"natural" vs. drug reward



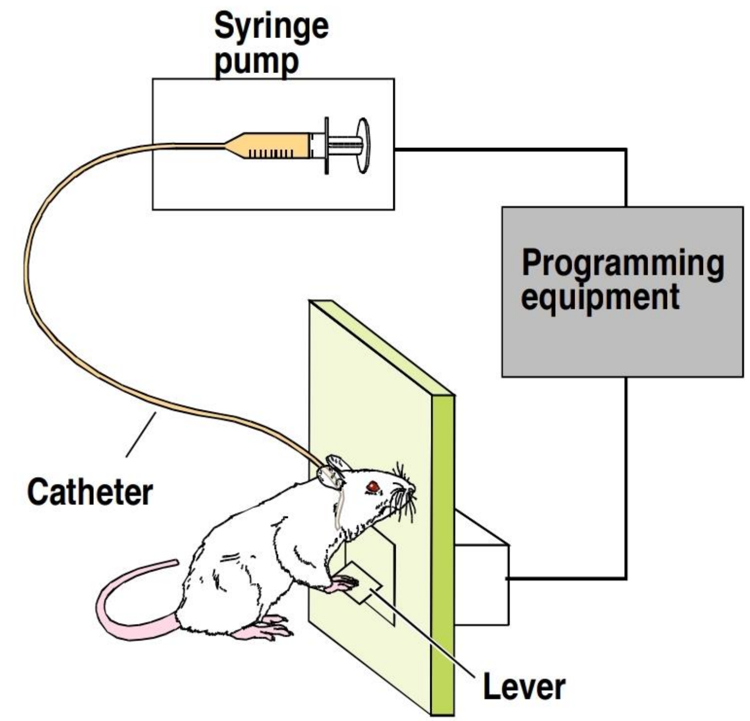
Source: Di Chiara et al.

Animals models of addiction & cellular changes

- Conditioned Place Preference (CPP)

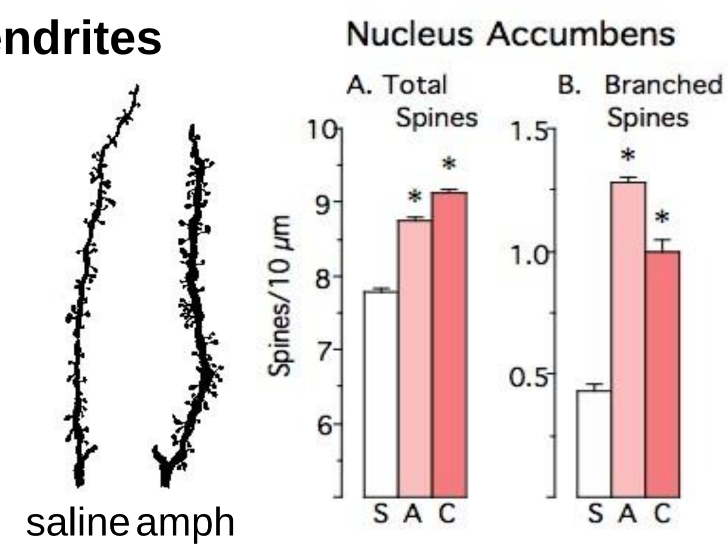


- Self-administration



Rosenzweig/Leiman (Sinauer)

Terminal tips of medium spiny dendrites



T.E. Robinson & B. Kolb, J. Neurosci., 1997

Injury and regeneration (lecture 38): Goals

-What happens to neurons after axon severing (axotomy)?

- Loss of function distal to cut, Na^+/Ca^{2+} influx, resealing of ends (2 hrs)

-What is Wallerian degeneration (rough time course, cellular events)?

- Axonal swelling (12 hrs), cell membrane fragmentation (3 days), myelin fragmentation and glial proliferation (1 wk), phagocytosis of debris by microglia/glia (1+ months)

-What are retrograde response of neurons to axon injury?

- Loss of neurotrophin supply (BDNF), chromatolysis (3 days), downregulation of molecules for synaptic transmission, upregulation of axonal growth molecules, axon begins regeneration (1-2 wks).

-What are transneuronal effects of axon injury?

- Neurons can die without synaptic input, muscles atrophy without innveration

-What are the differences between PNS and CNS in terms of their response to axon injury?

How do axons regenerate in the PNS?

What limits axon regeneration in the CNS?

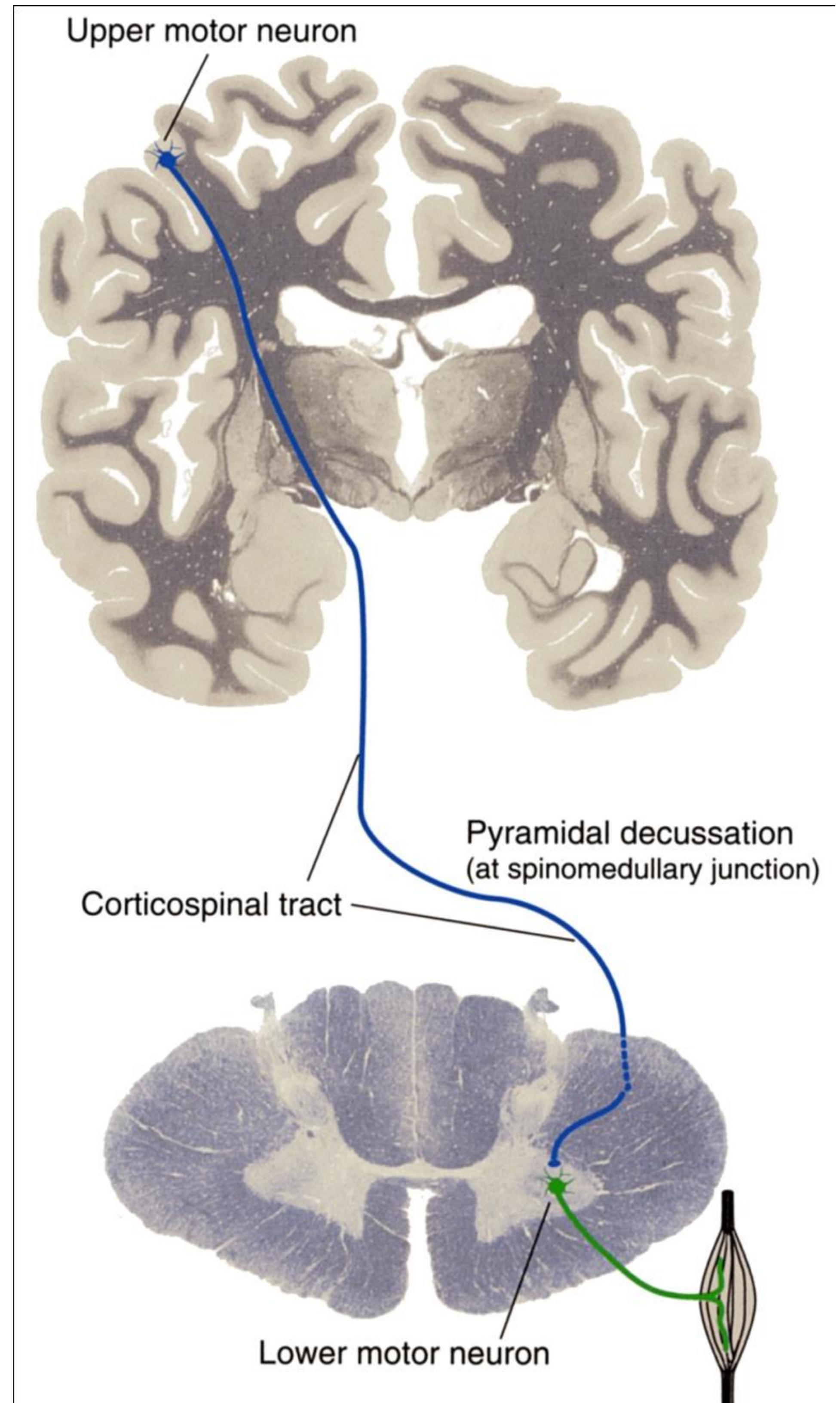
Effects of Upper vrs. Lower Motor Neuron Loss on Muscle

upper motor neuron loss (CNS):

- slow & mild atrophy

lower motor neuron loss (PNS):

- rapid & sever atrophy



Axons in the PNS regenerate.

- Axons grow 2-4 mm/day
- Axons grow within the connective tissue sheath along channels formed by Schwann cells.
- Optimal regeneration requires the nerve sheath to be intact; ends of a cut nerve can be connected surgically with sutures in the connective tissue sheath.
- Regeneration is never perfect:
    - strength & dexterity is reduced
    - sensory discrimination is poor
    - motor units are larger than normal
    - conduction velocity is 80% of normal

Axons in the CNS fail to regenerate.

- Research on the failure of axons to regenerate in the adult CNS has focused on three main issues:
  - Glial scar
  - Myelin inhibitory molecules
  - Intrinsic inability of mature CNS neurons to grow axons

Neurodegenerative diseases (lecture 39): Goals

For each disorder, study the following:
-Which parts of the brain are predominantly affected?
-Specific types of neurons are affected?
-What is known about the genetics? Any other risk factors?
-Any treatments?

Alzheimer's Disease

Regions/neurons affected:

-cerebral cortex

Genetic risk factors:

Mutations/variations in:

-APP

-PSEN1

-PSEN2

-ApoE4

Symptoms:

- Memory loss that interferes with daily life
- Difficulty solving problems
- Difficulty finding words/speaking
- Confusion with time/place
- Mood/personality changes

Treatments

-cholinesterase inhibitors

-NMDA receptor antagonists

Frontotemporal Dementia (FTD)

Regions/neurons affected:

-frontal lobe & temporal lobe

risk factors:

-Aging

- Mutations in several genes including MAPT

Symptoms:

- Speech/language impairments
- Extreme personality/behavioral changes

Parkinson's Disease (PD)

Regions/neurons affected:

-Substantia nigra loss of dopaminergic neurons

risk factors:

- Aging
- Mutations in several genes (SNCA)
- Exposure to pesticides

Symptoms:

- Resting tremor
- Rigidity
- Slowed movement
- Impaired balance/coordination

Treatment

- L-DOPA
- Dopamine receptor agonists
- Deep brain stimulation

Amyotrophic Lateral Sclerosis (ALS)

Regions/neurons affected:

-Brain and spinal cord loss of motor neurons

risk factors:

- Aging
- Gender (males more prone)
- Genetic mutations

Symptoms:

- Progressive weakness/paralysis
- Muscle atrophy
- Difficulty speaking/swallowing
- Difficulty breathing

Treatment

- Sodium channel blockers

Adult neurogenesis and stem cells (Lecture 40): Goals

-Where do adult stem cells reside in the mammalian brain?

-What type(s) of neurons are generated from these stem cells and where do they eventually get settled?

-What regulates adult neurogenesis?

-What are the roles of gliogenesis in the adult brain?

-Therapeutic neuron replacement
  rationale
  sources of cells for replacement

-What are inducible pluripotent stem cells?

Memory & Decision Making (Lecture 41): Goals

- Different memory systems: function, structure, damage
- Synaptic memory: LTP
- "reading memory" examples (fusiform gyrus, place cells)
- Content Addressable Memory: basis of memory activation (pattern completion), memory as categorization
- Creative memory: fallibility of memory, implications thereof

- Types of decision making: Reflex, Pavlovian, Deliberative, Procedural
- Pros and cons of each system (fast/slow, flexible/inflexible)
- Examples of when each is utilized

Decision Making

- Decision is selecting an action
- Memory is only useful because it influences our decisions

Types of Decisions:

- Reflexes
    - Evolutionary, prewired in spinal cord, inflexible, put my hands out to break a fall
- Pavlovian
    - Associate neutral stimulus with a pre-wired action, amygdala, prefronal cortex, periacqueductal gray, inflexible, salivating at the sound of a bell/ freezing in response to a tone
- Deliberative
    - Search and evaluate many potential outcomes, flexible and time consuming, prefrontal cortex, hippocampus, ventral striatum, should I move to Canada or New Zealand?
- Procedural
    - Associate actions with situations/senarios, inflexible and slow, striatum, cerebellum, learning a triple axel jump

Memory

- LTP (long-term potentiation)
- Cells that fire together wire together
- Memory is a pattern of firing across populations of neurons

- "reading memory"
    - Place cells in a mouse fire in a particular spot in an environment
    - If I can listen to when one cell fires, I know where the animal is
- Content-addressable memory
    - Memory can be accessed by a particular neural firing pattern
    - Memory can be accessed by sensory content
    - Ex. The smell of cinnamon triggers a neural pattern of firing to bring up a memory of Christmas (pattern completion)
    - Memory is flexible based on perception/suggestion
        - Car crash experiment

That's it!