Week 4

- Tuesday
  - KW Chapter 4 : Neurons
  - KW Chapter 5 : Neurotransmitters
  - Midterm Study Guide
- Thursday
  - KW Chapter 10: Neocortex
  - Exercise 1: Brain Anatomy

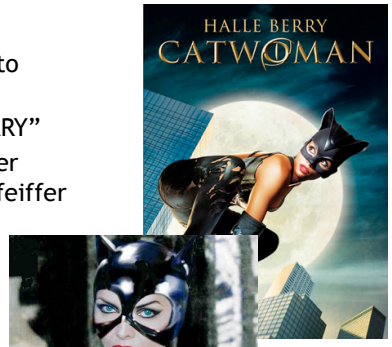
Chapter 4 : Neurons

Case Report : Single Cell Recording

- History:
  - Subject with epilepsy volunteered for research study
    - Goal: find location where seizure originates and remove it
  - Recordings of electrical potential on surface of skull failed to find location
  - Single Cell recordings were used

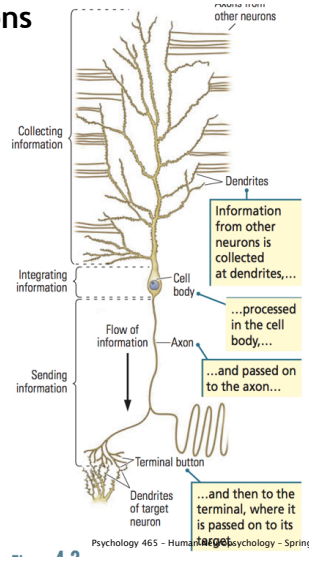
Grandmother Neurons?

- Findings:
  - Some neurons responded to Picture of Halle Berry
  - To the letters “HALLE BERRY”
  - But not to pictures of other actresses, e.g. Michelle Pfeiffer



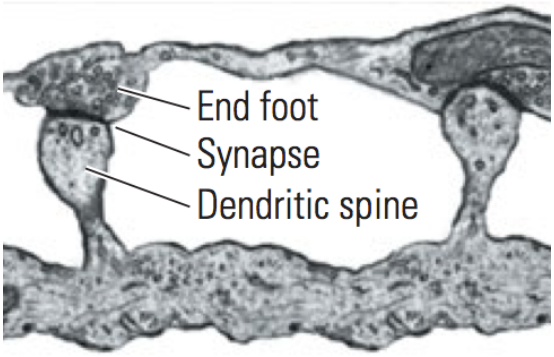
Neurons

- Function
  - information processing
- Structure
  - Dendrite
    - inputs
  - Cell Body
    - calculation
  - Axon
    - output



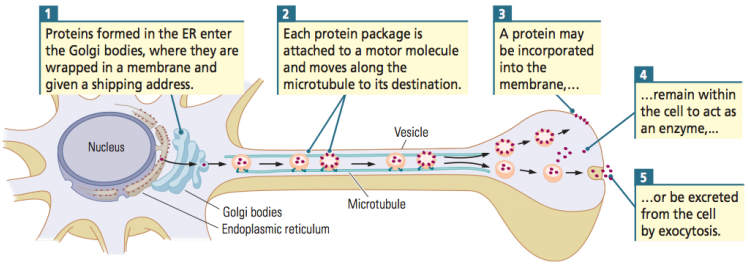
Synapse

- Gap between dendrite and axon



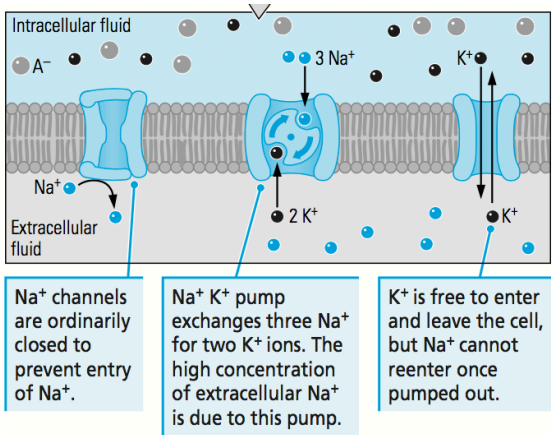
Vesicles and Neurotransmitters

- Neurotransmitters bridge the synapse between axon and dendrite
- Vesicles are created in cell body and hold neurotransmitters



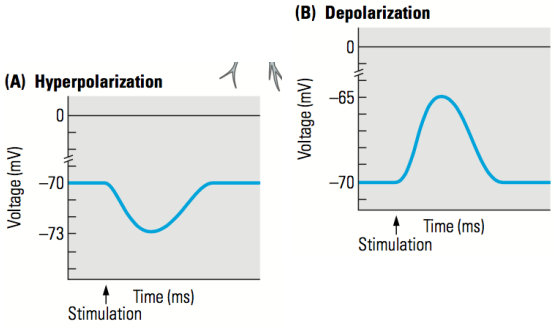
The Resting Potential: -70mV

- Sodium / Potassium Pump (NA^+/K^+ Pump)



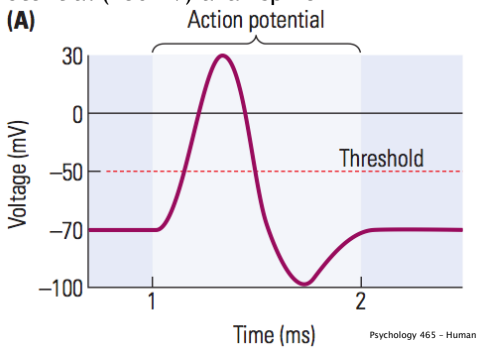
Polarization

- Hyperpolarization (more negative)
- Depolarization (more positive)



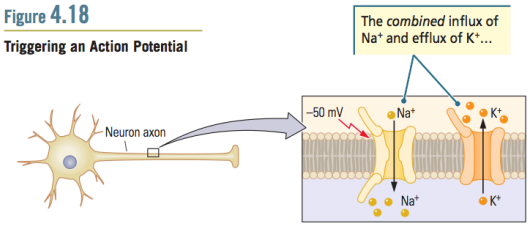
Axons are Electro-Chemical computers

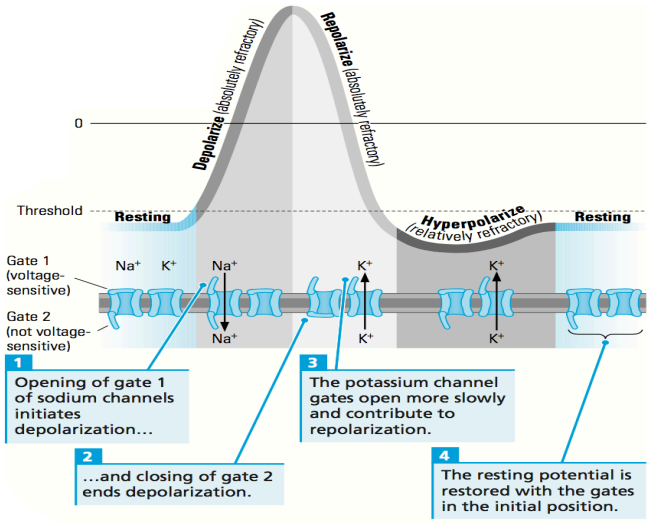
- Electrical potential (Voltage)
- Resting voltage (-70mV)
- Stimulation from dendrites -> increases voltage
- Threshold (-50mV)
- Action Potential (+30mV) aka "spike"



The Action Potential

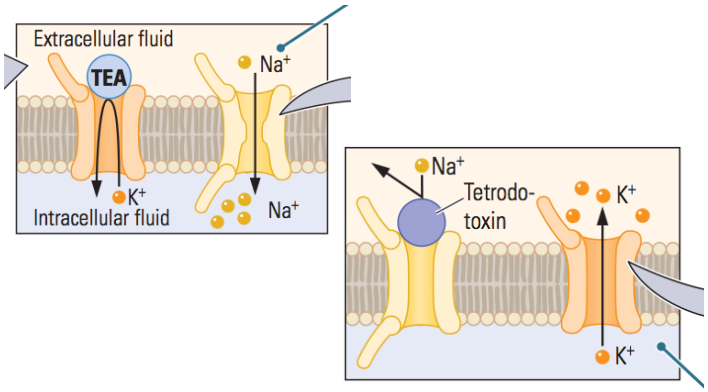
- Sodium (Na) ions enter cell, Potassium (K) ions exit
- Cell voltage changes





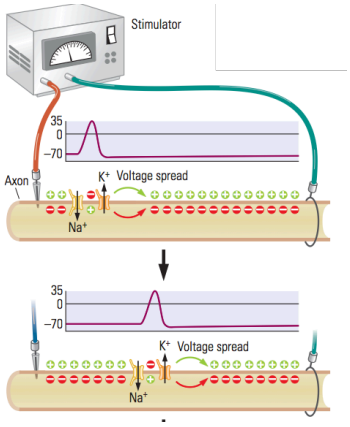
Research methods

- TEA (tetra-ethyl-ammonium) blocks K channels
- Tetrodotoxin blocks Na channels



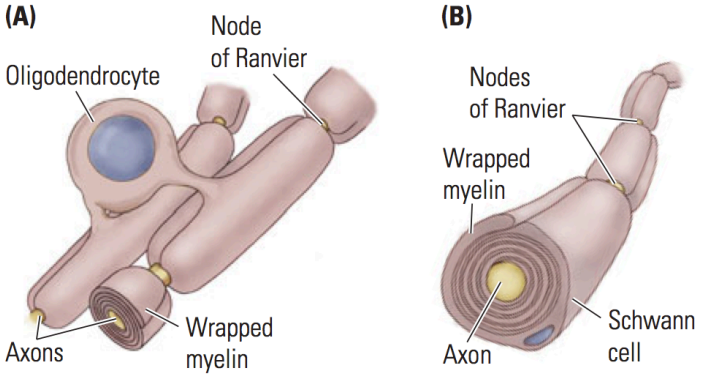
The Nerve Impulse

- Action Potentials travel along the axon
- aka "propagation"
- Domino Analogy



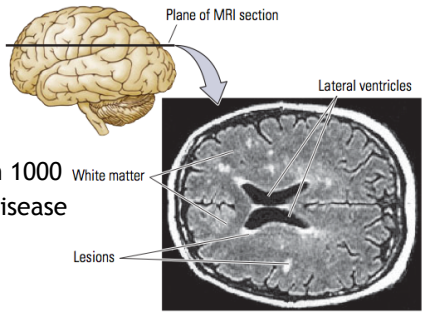
Going Faster

- Nerve impulse speed related to axon size (bigger -> faster)
- Problem: too big = too crowded. Solution: Myelination
  - "saltatory conduction" (*to leap*)



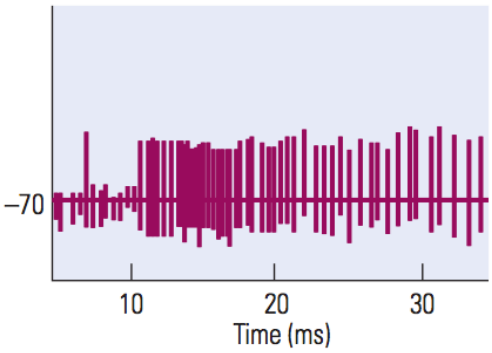
Disease: Multiple Sclerosis

- Sclerosis = *hardness*
- MS : myelin is attacked, causing inflammation and damage / destruction of myelin
- Unpredictable / Disabling
- Remissions & Relapses
- often mis-diagnosed
- Epidemiology
  - typically age 15-40
  - 2x more F than M
  - prevalence about 1 in 1000
- Possibly auto-immune disease
- Lesions visible on MRI



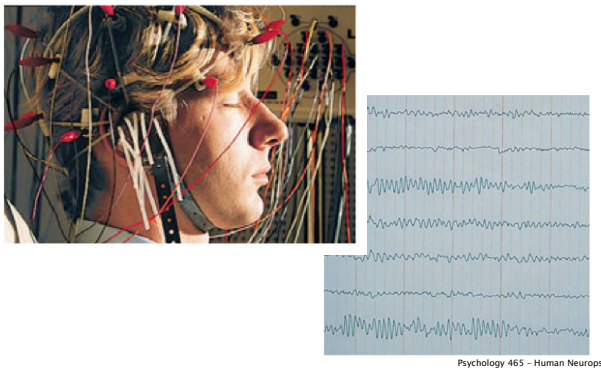
Information is coded in Spike Trains

- Neurons can have multiple action potentials
- Information is coded in timing & pattern of spikes



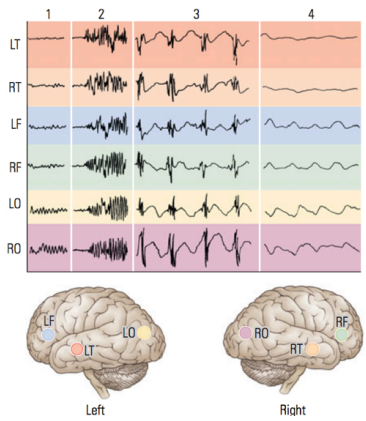
Multiple neurons are synchronized

- Waves and patterns of thousands of neurons firing together
- Strong enough that voltage can be detected on scalp
- Electro Encephalograph (EEG)



Epilepsy

- Seizure
  - large groups of neurons firing all at once
  - out of control
  - pattern spreads
  - can involve entire brain



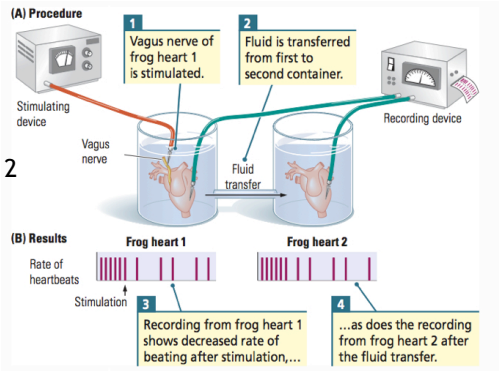
- Key
  - 1=pre
  - 2=onset
  - 3=clonic
  - 4=coma

Chapter 5 : Neurotransmitters

Otto Loewi's Experiment

- Frog hearts in bottles
- Stimulate vagus nerve of heart 1
  - heart 1 slows down
- Pass fluid to heart 2
  - heart 2 slows down
- Conclusion : must be chemical

- Acetylcholine



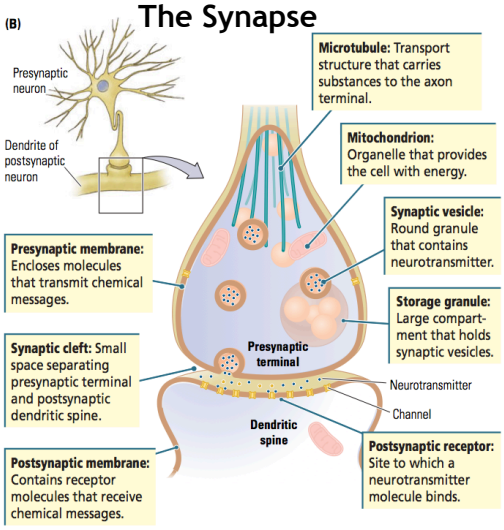
Neurons and neurotransmitters

- Neurons generally release only 1 specific NT
- Neurons are named for the NT they release
  - Neurons that release Acetylcholine
    - "cholinergic"
- Some NTs function in both CNS and PNS
- Some don't
  - epinephrine : PNS
  - nor-epinephrine : CNS
- Hundreds of NTs
- NTs can be excitatory OR inhibitory depending on specific neuron
  - but more typically have a single action (+ or -)

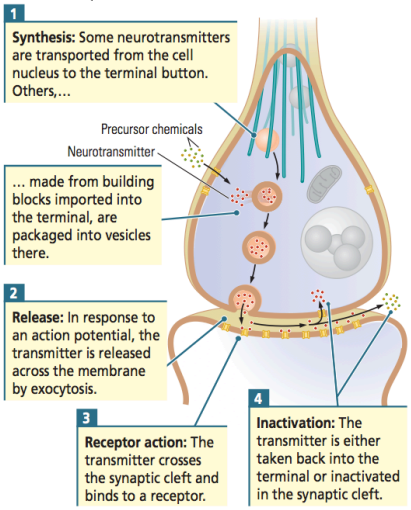
NT Synthesis

- Two classes
  - Large Proteins
    - synthesized in cell body from DNA/RNA
    - transported to axon terminal in vesicles
    - slower acting
  - Smaller molecules
    - synthesized from nutrients
    - absorbed directly through cell wall
    - faster acting

The Synapse



Neurotransmission



Neurotransmission

- Synthesis
- Release
- Receptor Action
  - depolarize (excitation)
  - hyper-polarize (inhibition)
  - creates new synapses
  - other cascaded processes
- Inactivation
  - Reuptake
  - Degradation

- Autoreceptors
  - pre-synaptic cell may also be affected

Categories of Neurotransmitters

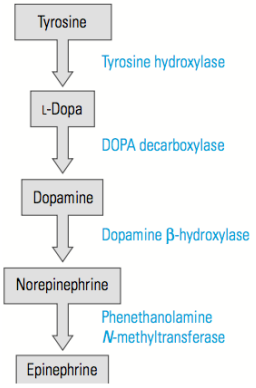
- More than 100
- More than one NT may be in single vesicle

- Small-molecules
  - organic chemicals
- Neuropeptides
  - short amino acid chains
- Transmitter gasses
  - tiny water-soluble gas molecules such as NO and CO

Small Molecule Neurotransmitters

- Acetylcholine

- Amines
  - Dopamine (DA)
  - Norepinephrine (NE)
  - Epinephrine (EP)
  - Serotonin (5HT)



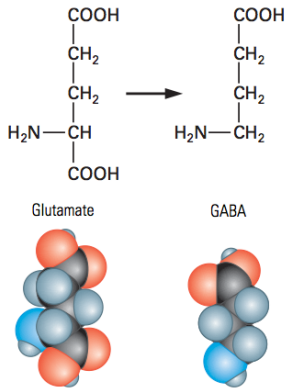
- Amino Acids
  - Glutamate (Glu)
  - Gama-aminobutyric acid (GABA)
  - Glycine (Gly)
  - Histamine (H)

NTs and Behavior in PNS

- PNS
  - SNS
    - motor neurons: cholinergic (ACh), excitatory, produce muscle contractions
  - ANS
    - Sympathetic: Fight or Flight
      - epinephrine (EP) aka Adrenaline
    - Parasympathetic : Rest and Digest
      - acetylcholine (ACh)

NTs and Behavior in CNS

- Glutamate (Glu)
  - major excitatory NT
- Gama-aminobutyric acid (GABA)
  - major inhibitory NT

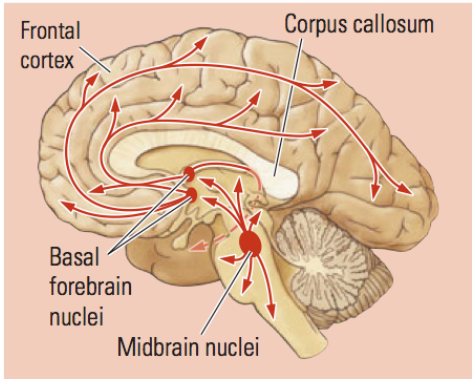


CNS Activating Systems

- In brain, NT systems have large-scale effects
- Major Ones:
  - Cholinergic
  - Dopaminergic
  - Noradrenergic
  - Serotonergic
- Functions are complex, interlinked
- Generally not possible to have 1:1 relationship between system and disease/disorder

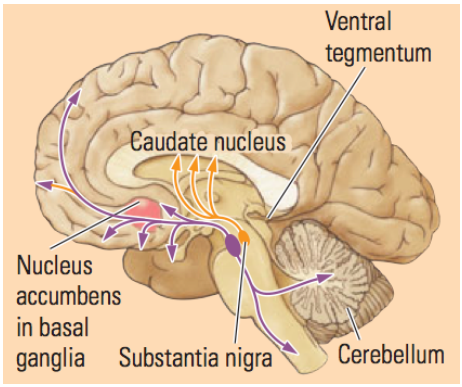
Cholinergic Activating System

- Functions:
  - Waking EEG
  - Memory
- Damage/Disease:
  - Alzheimer's Disease



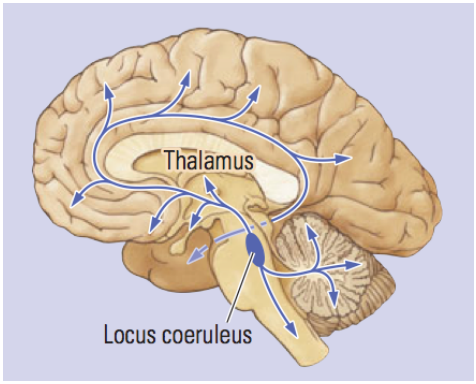
Dopaminergic Activating System

- Nigrostratial
  - Functions:
    - normal motor behavior
  - Damage/Disease:
    - Parkinson's
- Mesolimbic
  - Functions:
    - reward & pleasure
  - Damage/Disease:
    - addiction
    - schizophrenia



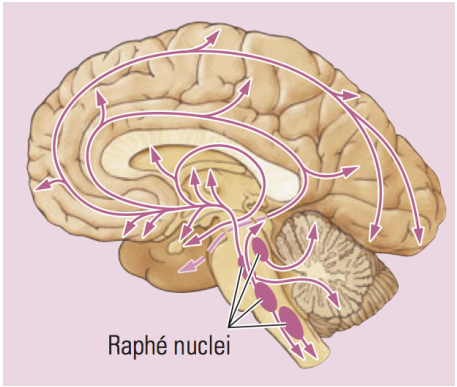
Noradrenergic Activating System

- Functions:
  - emotional tone
  - cognitive functioning
- Damage/Disease:
  - impaired thinking
  - depression

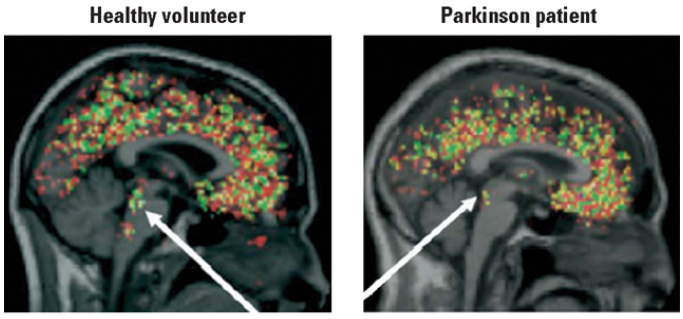


Serotonergic Activating System

- Functions:
  - waking EEG
  - resistance to stress
- Damage/Disease:
  - depression
  - anxiety
  - OCD
  - tics
  - schizophrenia



Serotonergic Activating System



Brooks, D.J., Piccini, P. Imaging in Parkinson's disease. The role of monoamines in behavior, *Biological Psychiatry*, 59:908–918, 2006

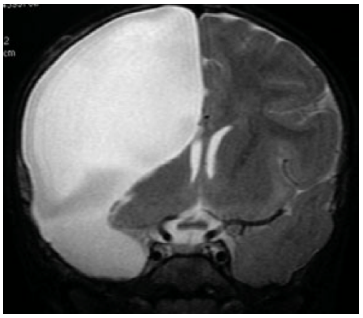
Chapter 10 : Neocortical Function

Case Report : Hemispherectomy

- AR, an 11 year old boy began developing seizures
  - right-sided weakness, difficulty talking (dysphasia)
- Over next six years, hospitalized many times
  - Right handed -> left handed
  - by age 15, IQ dropped 30 points (from 100 to 70)
  - by age 17, he was not testable due to emotional & language problems
- Dx : Rasmussen's Encephalitis
- Tx : removal of most of left hemisphere

Case Report : Hemispherectomy

- Note: image is from another patient with a Right-hemispherectomy



Case Report : Hemispherectomy

- Recover post hemispherectomy
- 10 years later
  - oral language skills : vastly improved (to average)
  - unable to read or write
  - motor skills : improved
    - could walk (with limp)
    - could raise right arm to shoulder level and grasp objects with right hand

How did AR recover?

- Levels of Function
  - Subcortical areas manage, direct, and control cortical areas
- Brain Plasticity
  - brain can respond to injury / damage / dysfunction
  - in AR's case: dysfunctional LH blocking language functions in RH. With LH removed, RH could work better and grow back some functions.

Levels of Function

Level	Function
Cortex	**Control and Intention:** Sequences of voluntary movements. Cognitive maps, relationships between objects, emotional values, motivation, long term planning
Basal Ganglia	**Self Maintenance:** Coordinates voluntary and automatic movements for self-preservation (simple eating, drinking, sex)
Diencephalon hypothalamus thalamus	**Affect and Motivation:** Voluntary movements, but without purpose. Integrated emotional behavior, but mis-directed. Thermoregulation.
Midbrain	**Spontaneous Movement:** Simple motor responses to visual/ auditory stimuli. Automatic behavior (grooming). Stand, walk, turn, jump in response to stimuli.
Hindbrain	**Postural Support:** hiss, bite, growl, chew, lick in response to stimuli. Standing, postural reflexes, sleepwalking.
Spinal cord	**Reflexes:** stretch, withdraw, scratch in response to stimuli

Decorticate Rats

- Decorticate rats behave in many ways normally
  - eat, drink
  - can run simple mazes
- Untrained observers have difficulty telling them apart from a rat with a cortex

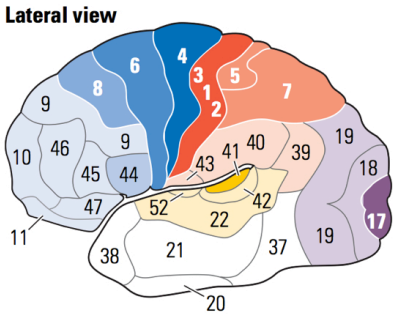
- Decorticate rats
  - don't build nests
  - do not hoard food
  - can't do skilled movements with tongue & mouth
  - can do simple learning

Cortex - what is it good for?

- Conclusions : Neocortex not necessary for basic survival
- Neocortex is a "new layer" evolutionarily developed
- Manages complex and new combinations of behavior

Cortical Mapping Ideas

- Brodmann's Map
- Primary/Secondary/ Tertiary
- Developmental
- Primordial zone
  - myelinates early : part of motor & somatosensory cortex
- Secondary zone (borders primordial zone)
  - myelinates next
- Tertiary zone (association)



Cortical Neuron Types

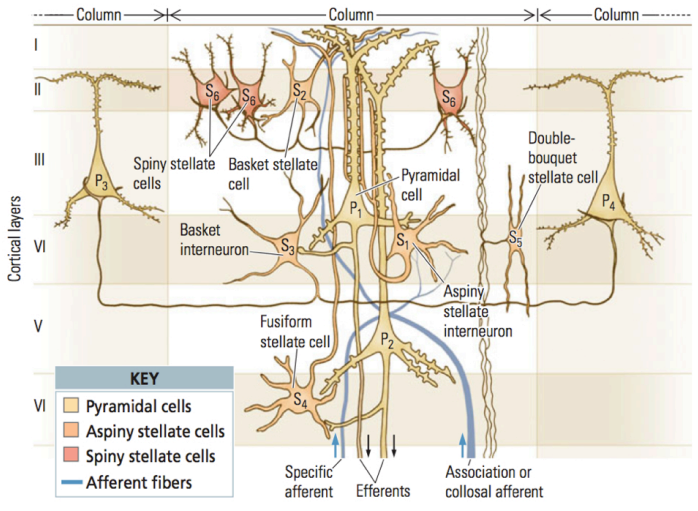
- Spiny
  - has dendritic spines
  - Examples:
    - Pyramidal cells
      - pyramid-shaped
      - 75% of all neurons
      - efferent (project out of brain, e.g. motor neurons)
    - Stellate cells
      - star-shaped

Cortical Neuron Types

- Aspiny
  - no dendritic spines
  - Inhibitory, use GABA and also use other NTs
  - diverse shape & chemistry
  - Examples:
    - basket cell

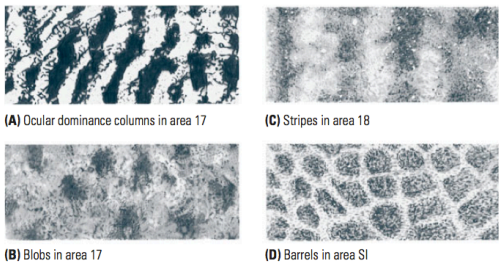
- Columns:
  - cells in vertical arrangement mostly talk to each other

Cortical Columns



Cortical Columns, Spots & Stripes

- Cortical neurons function in narrow columns
- Up to 300 neurons in 1mm wide strip
- "Column" or "Module"
- How determined?
  - radioactive staining - inject tagged AA into eyeball
- Not widespread agreement on definition or function



(A) Ocular dominance columns in area 17 **(C)** Stripes in area 18

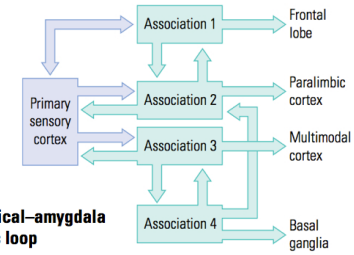
(B) Blobs in area 17 **(D)** Barrels in area SI

Representation & Mapping

- Early views
  - brain areas have mapping to specific topics
  - e.g. motor cortex maps to body muscles
    - sensory cortex maps to skin receptors
- Later research
  - found multiple maps in many parts of the brain
    - e.g. monkeys: approx 30 areas mapping to vision
  - found multimodal / polymodal areas
    - combining sensory / motor information
  - found maps are widely distributed / general (not as localized as thought)
- Conclusion:
  - # of maps --> amount of "intelligence" ?

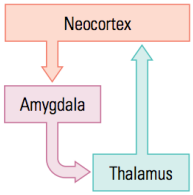
Cortical Systems & Subcortical Loops

- Cortex connections can be divided into 5 major areas



- Subcortical connections form loops between subcortical and cortex (6 major ones discovered)

(D) Cortical–amygdala thalamic loop



The Binding Problem

- How does the brain integrate sensory perception into a *gestalt* (a "whole")
- Possible solutions
- 1. A top-level cortical area binds them together
  - problem - this doesn't seem to exist
- 2. All areas are interconnected and share information
  - problem - not all areas are connected
- 3. Intracortical networks among subsets of regions
  - may actually be how the brain works?
  - called "integration"

- Still not really solved

A Hierarchical Model : Structure

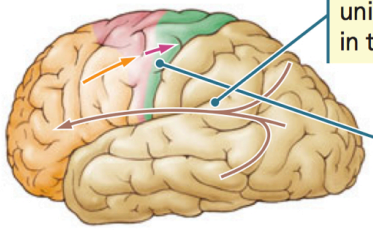
- Alexander Luria's model
- Cortex : two parts
  - posterior : sensory
  - anterior : motor

- Each part has 3 zones:
  - primary
  - secondary
  - tertiary (association)

A Hierarchical Model : Function

- Processing is serial:
  - posterior (1,2,3) --> anterior (3,2,1)

(B) Motor unit

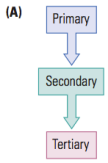


3 Symbolic processes from the sensory unit are translated into intentions in the tertiary motor zones...

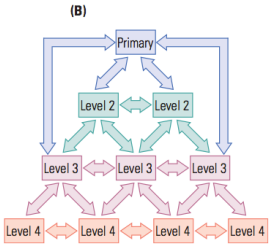
4 ...and then into patterns of action in the secondary and primary motor zones.

Luria's model : accurate?

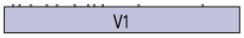
- Problems
  - serial connections may not exist
  - subcortical connections bypass cortex



- Newer models:
  - still hierarchy, but some levels bypass each other
  - includes parallel processing.
- "Distributed Hierarchy"



Modern Distributed Hierarchical Models



Are Humans Special?

- Do Human brains have any unique properties?
- Biological, Psychological and Theological Question

- Human brains have
  - High density of neurons with fast conduction velocity
    - --> increased processing capability
  - Von Economo Neurons
    - large bipolar neurons in cingulate cortex (also seen in great apes, but to a lesser extent)
    - develop around age 4
      - might hold "theory of mind"?
      - defective in Autism?