

KIN 3E03 /Life Sciences 3K03

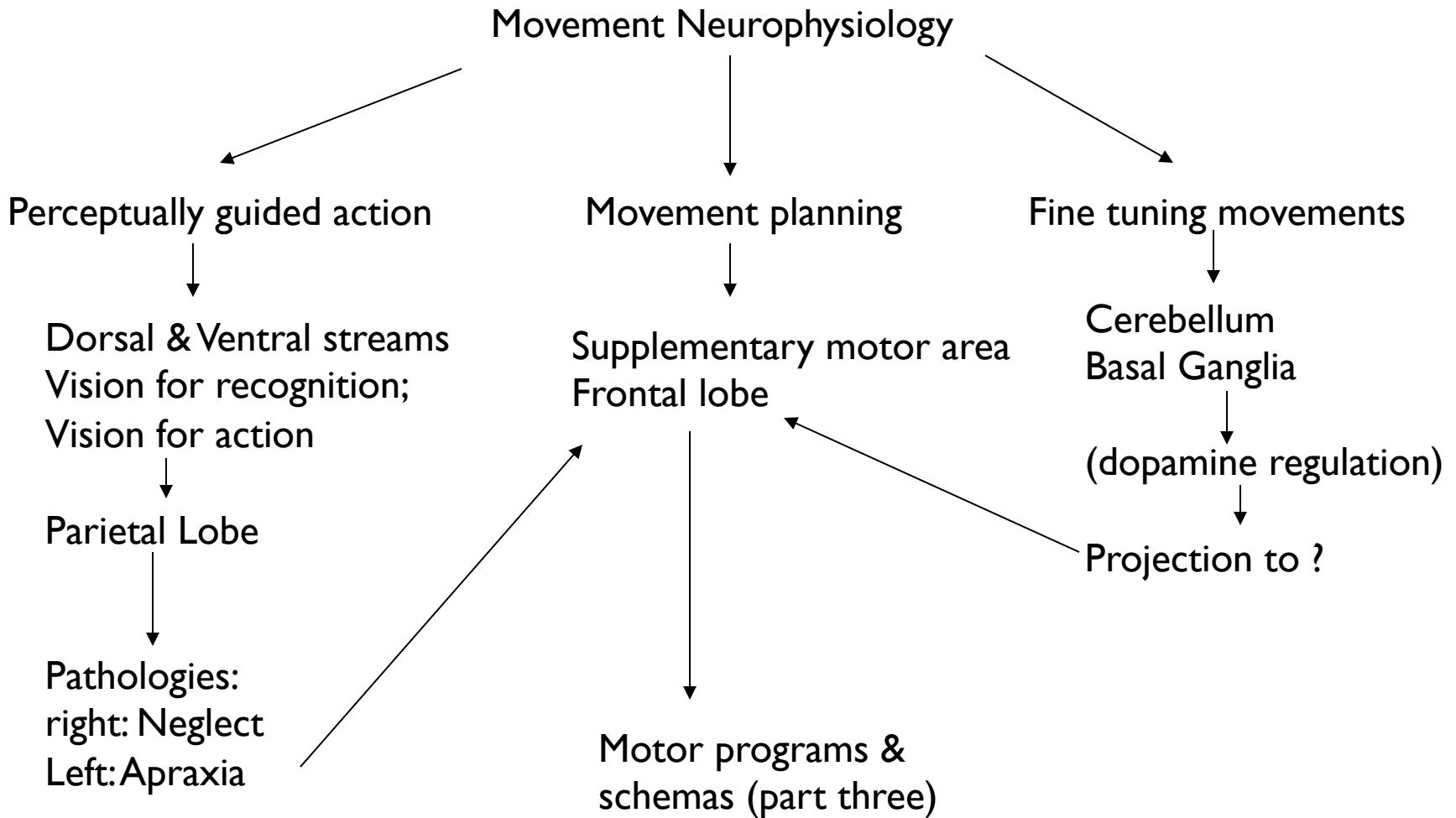
Neural control of human movement

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Fall 2012

NOTES Unit 2

Overview of concepts



Dopamine imbalance

- Too little dopamine = rigidity + tremor (Parkinson's disease)

What happens when there is too much dopamine?

- you may see, hear or imagine things that are not real

What is schizophrenia?

- Most common mental illness
- Affects about 1% of population
- Uniform rate throughout the world
- Adolescent onset
- Name derived by Bleuler (1911) from Greek; *Schizo* = split, *phrenia* = mind
 - Intended to represent the split of the mind from reality

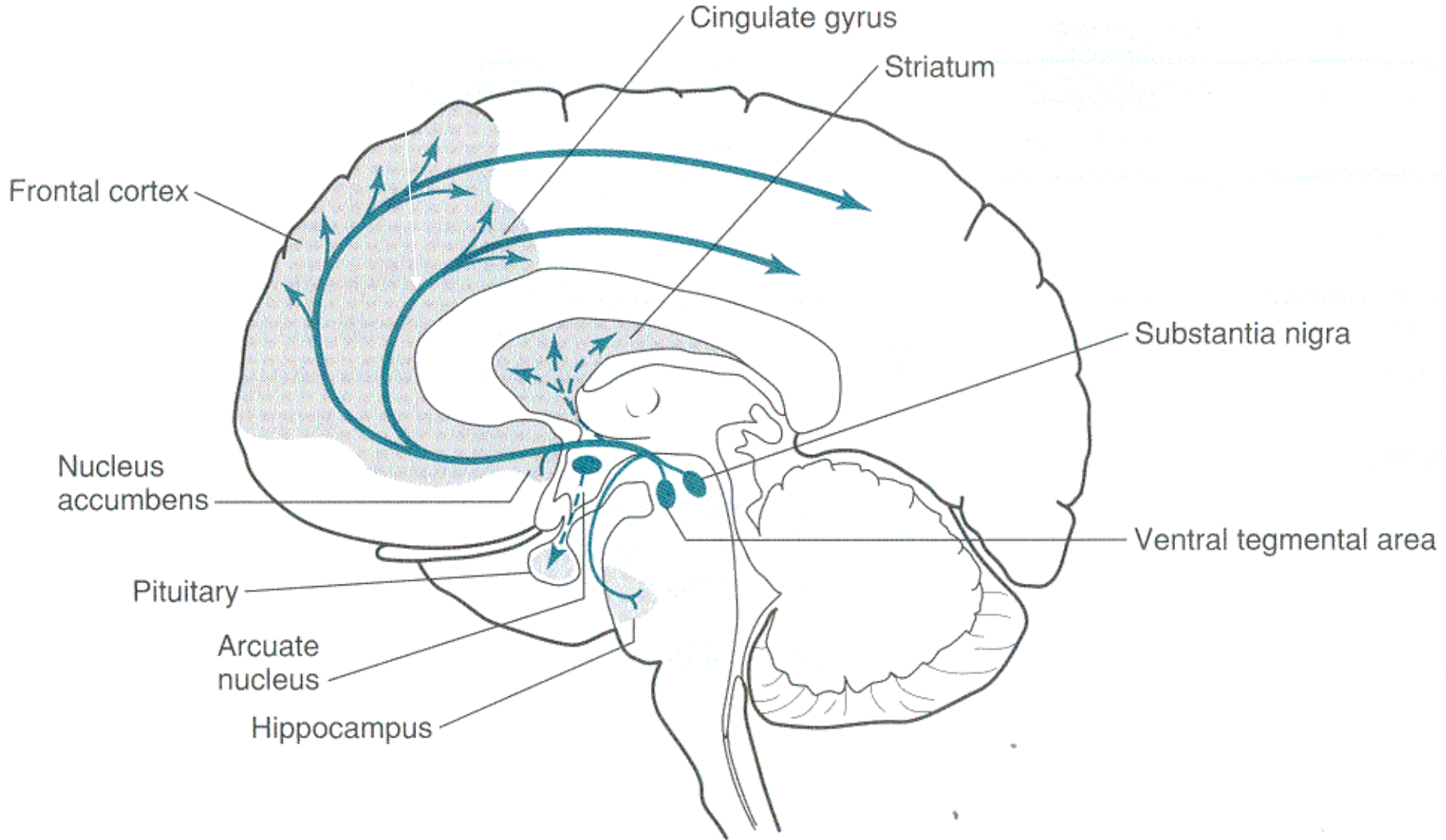
Antipsychotic drugs

- Drugs that block Dopamine receptors reduce schizophrenic symptoms
- Drugs that block dopamine consequently have side effects similar to Parkinson's disease

Tardive Dyskinesia results from prolonged use of typical antischizophrenic drugs.

Dyskinesia has some symptoms like Huntington's / Parkinson's Disease

Highlighted here are neurons that make dopamine;
Note their postsynaptic targets in the frontal cortex



Side Effects of Antipsychotic Drugs

- Wide range of side effects
 - tremor, postural rigidity, cramps,
 - Major problem is Tardive Dyskinesia
 - Repetitive involuntary movements, especially face mouth and lips
 - Irreversible
 - result of long term blockade of dopamine receptors leading to supersensitivity



Tremor: Parkinsonian symptoms

Symptoms of Schizophrenia

- Can be divided into two categories (Crow, 1991)
- Positive symptoms (seen as reflecting overactive brain function)
 - Hallucinations
 - Delusions
 - Disorganised speech
 - Disorganised behaviour
- More common in acute episodes
- Tend to respond to antipsychotics

Symptoms #2

Negative symptoms (under-aroused brain function)

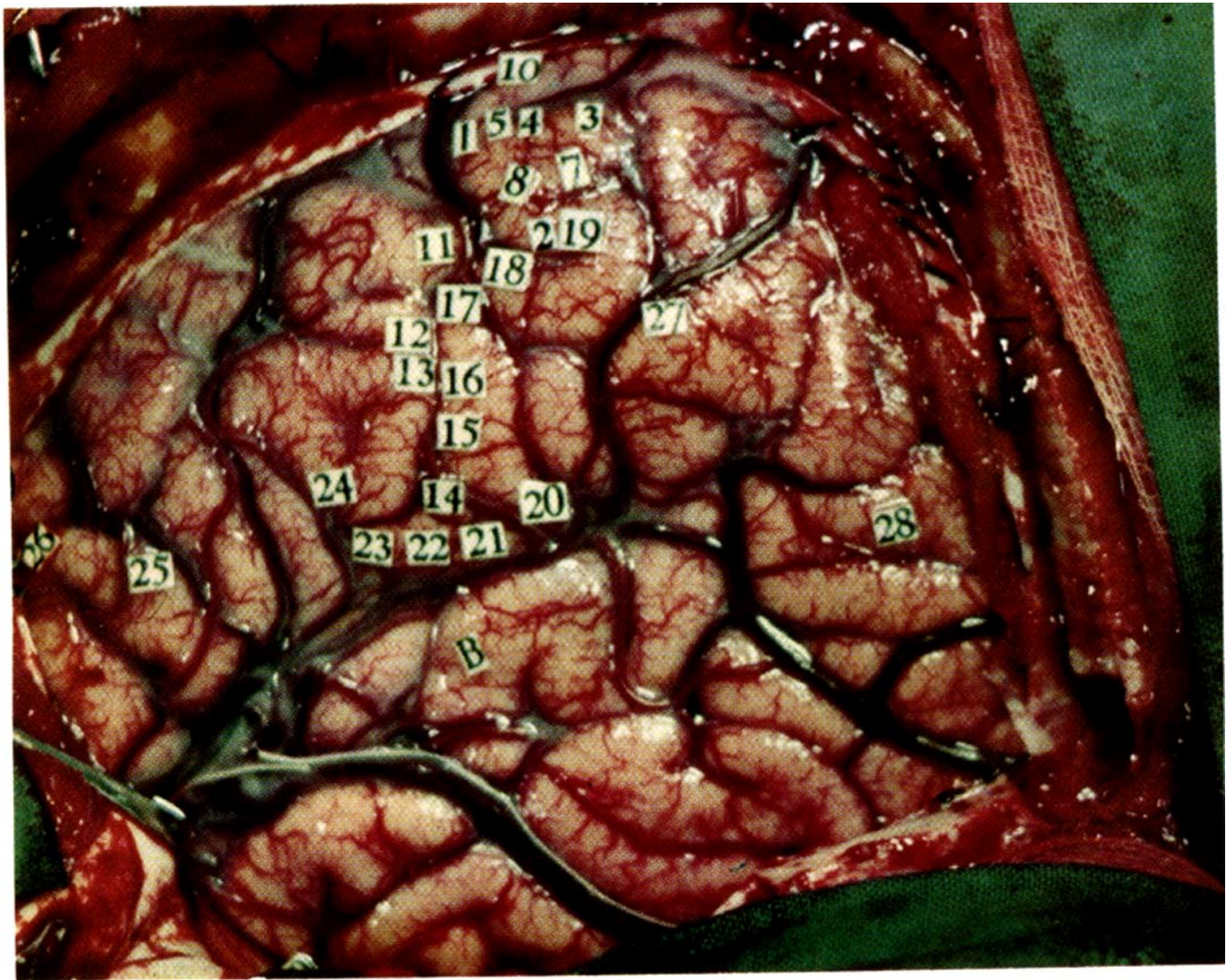
- Alogia (loss of fluency in thought & speech)
- Akathisia (inability to sit still)
- Affective blunting (Loss of fluency of emotional expression)
- Anhedonia (absence of pleasure or ability to feel it)
- Avolition (absence of drive)
- Catatonia (excessive immobility)

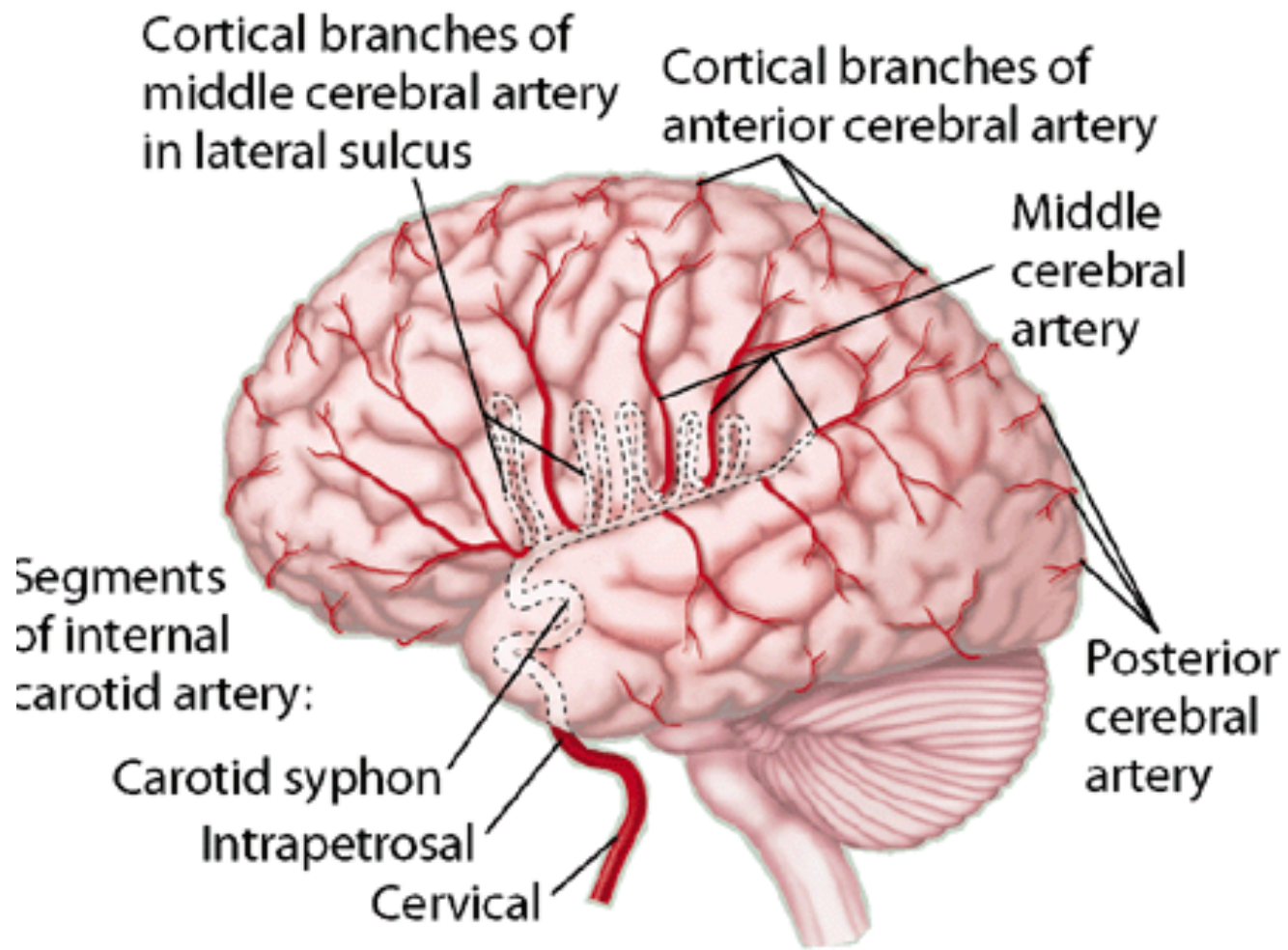


Akathisia (inability to sit still)

Back to Basic neurophysiology

- What are lesions?
- Why do people have strokes?
- How does the brain get damaged?
- Scope for recovery (Later half of the course).





Branches of anterior cerebral artery:

Callosomarginal

Pericallosal

Frontopolar and medial orbitofrontal

Anterior cerebral artery

Internal carotid artery

Basilar artery

Vertebral artery

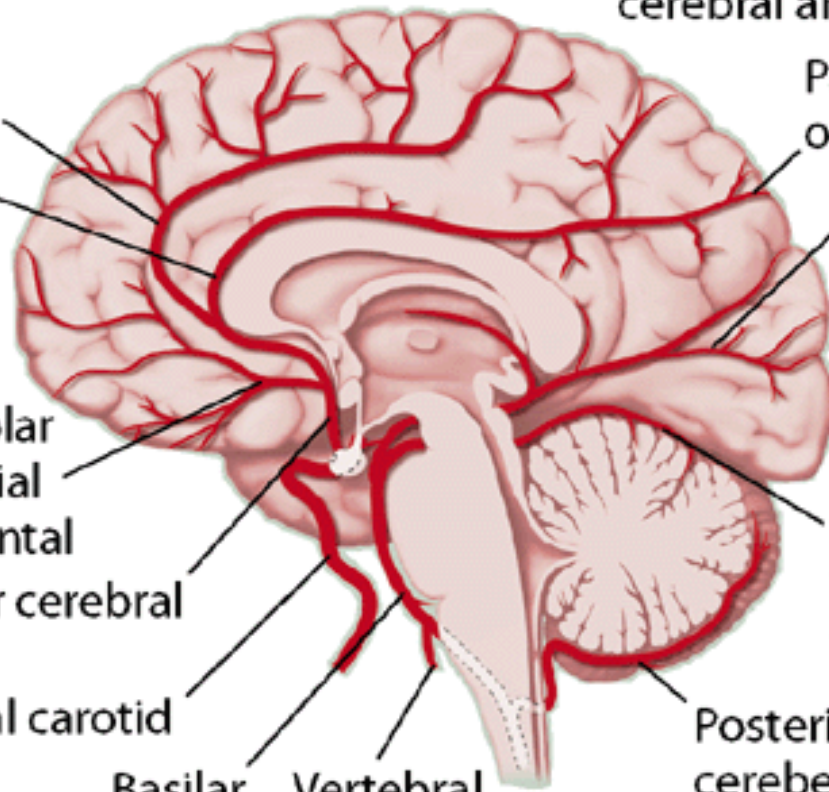
Branches of posterior cerebral artery:

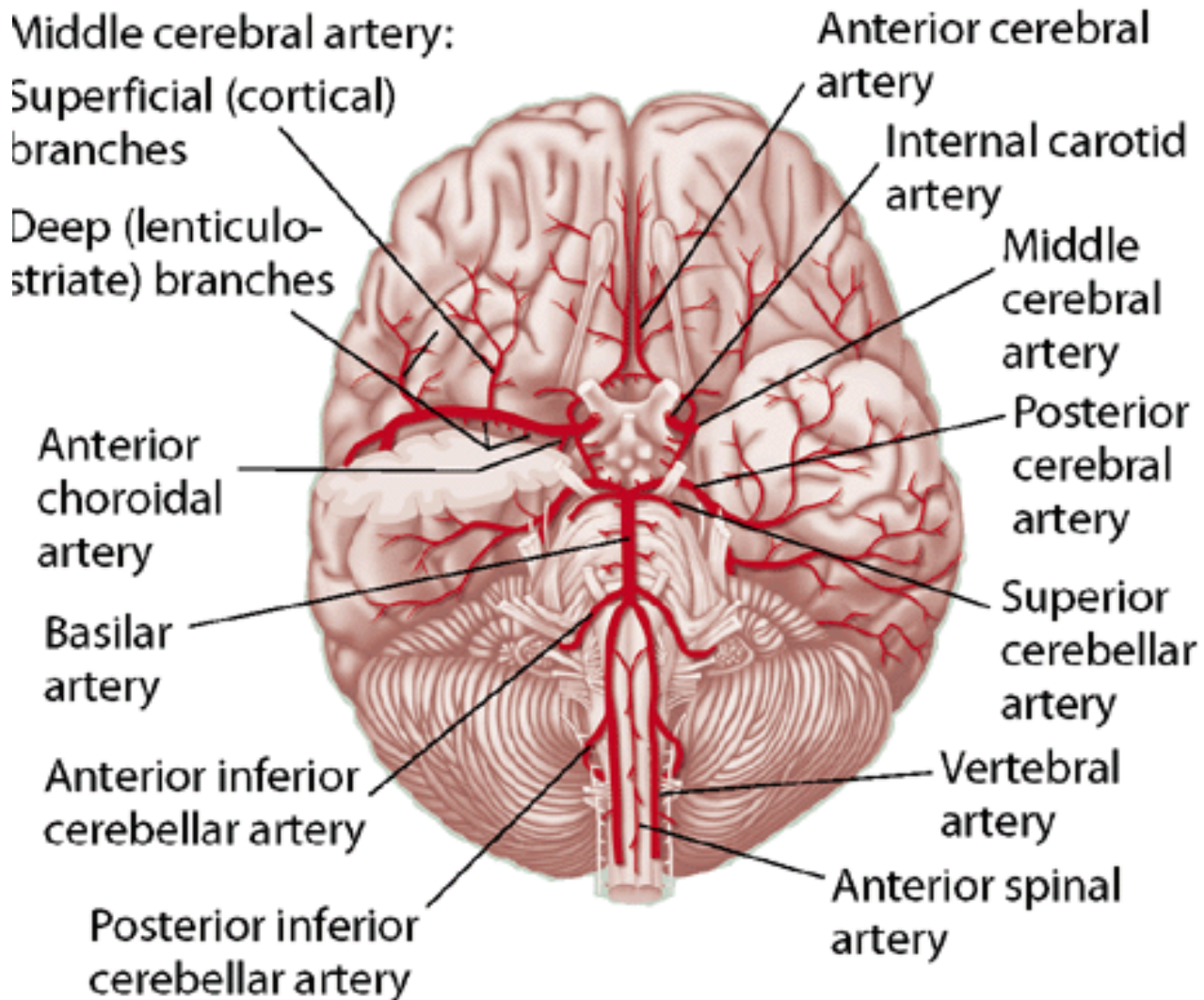
Parieto-occipital

Calcarine

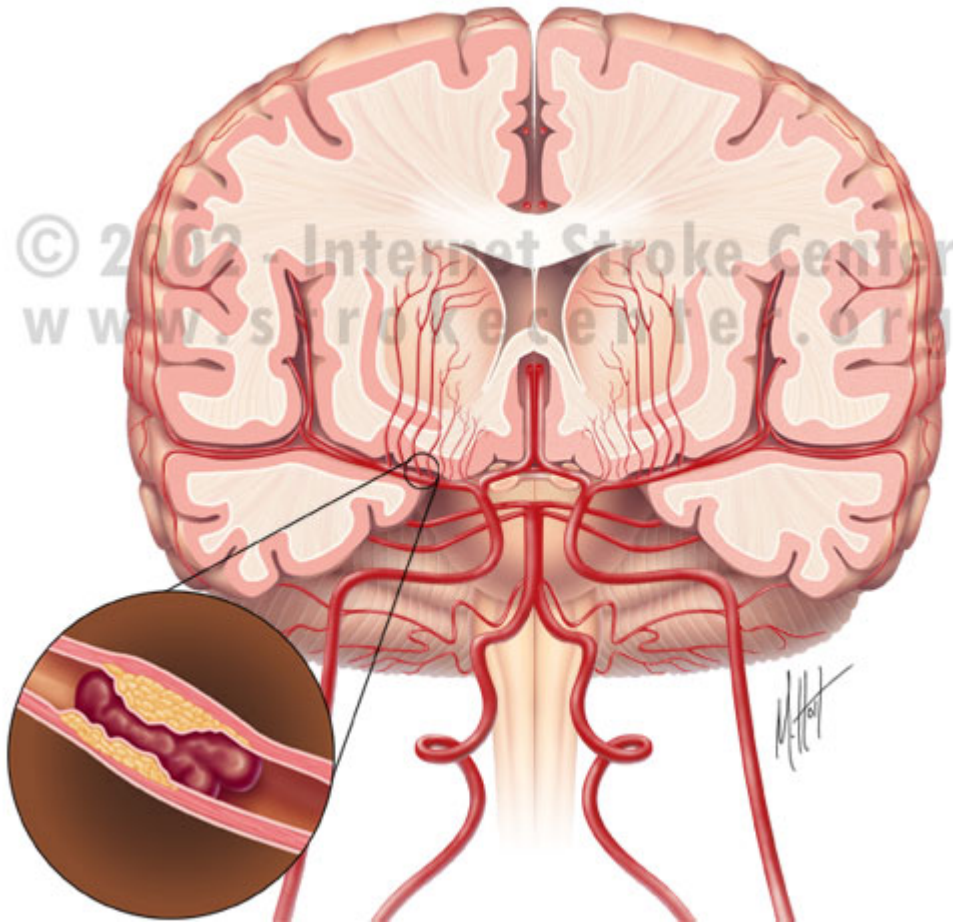
Superior cerebellar artery

Posterior inferior cerebellar artery





ISCHEMIC STROKE

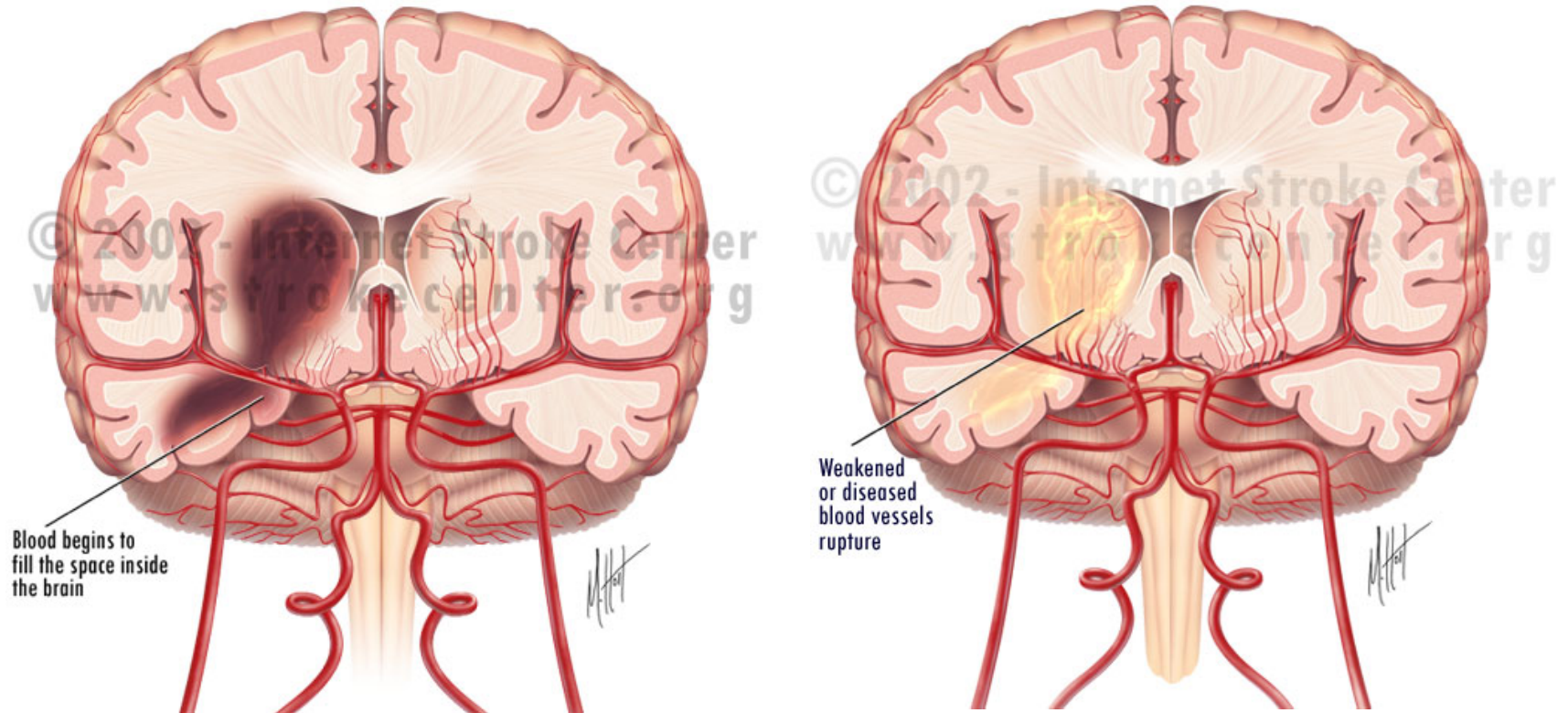


Who gets it?

Ischemic stroke is by far the most common kind of stroke, accounting for about 88% of all strokes. Stroke can affect people of all ages, including children. Many people with ischemic strokes are older (60 or more years old)

An ischemic stroke occurs when an artery in the brain becomes blocked.

INTRACEREBRAL HAEMORRHAGE



Intracerebral hemorrhage usually occurs in selected parts of the brain, including the *basal ganglia*, *cerebellum*, *brainstem*, or *cortex*. Occurs at all ages.

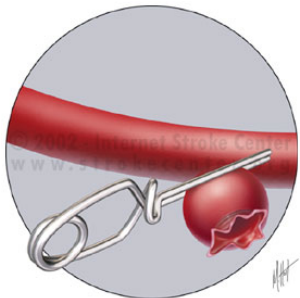
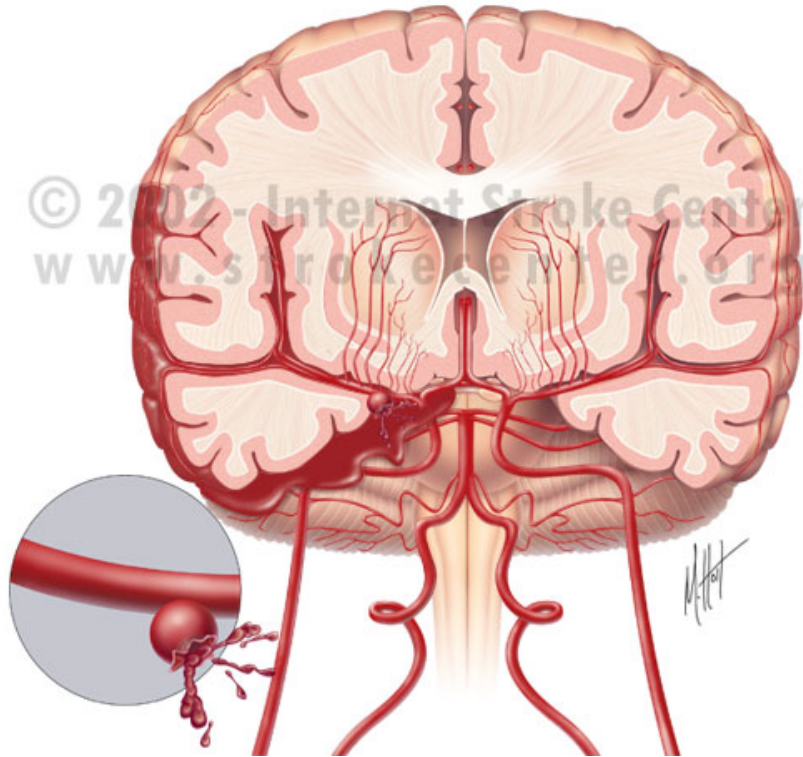
•A ruptured blood vessel will leak blood into the brain, eventually causing the brain to compress due to the added amount of fluid.

Subarachnoid Haemorrhage

Sub-arachnoid haemorrhage occurs when a blood vessel just outside the brain ruptures. The area of the skull surrounding the brain (the subarachnoid space) rapidly fills with blood.

Who gets it?

They may develop from birth or in childhood and grow very slowly. Some people have not one, but several aneurysms. Subarachnoid haemorrhage can occur at any age, including teenagers and young adults.



Surgical treatment of aneurysms involves placing clip on neck of aneurysm. .

Middle cerebral artery infarction

- The middle cerebral artery (MCA) is by far the largest of the cerebral arteries and is the vessel most commonly affected by cerebro-vascular accidents (CVA) or stroke.
- The MCA supplies most of the outer convex brain surface, nearly all the basal ganglia, and the posterior and anterior internal capsule.
- Infarctions that occur within the vast distribution of this vessel lead to diverse neurological problems. MCA stroke describes the sudden onset of focal neurological deficit resulting from brain infarction or ischemia in the territory supplied by the MCA.

One more time...

- Basal ganglia function: dopamine in excess produces schizophrenia
- Basic structure of a stroke (infarction of cerebral arteries)
- Lateralization and hemispheric differences
- Split brain patients.

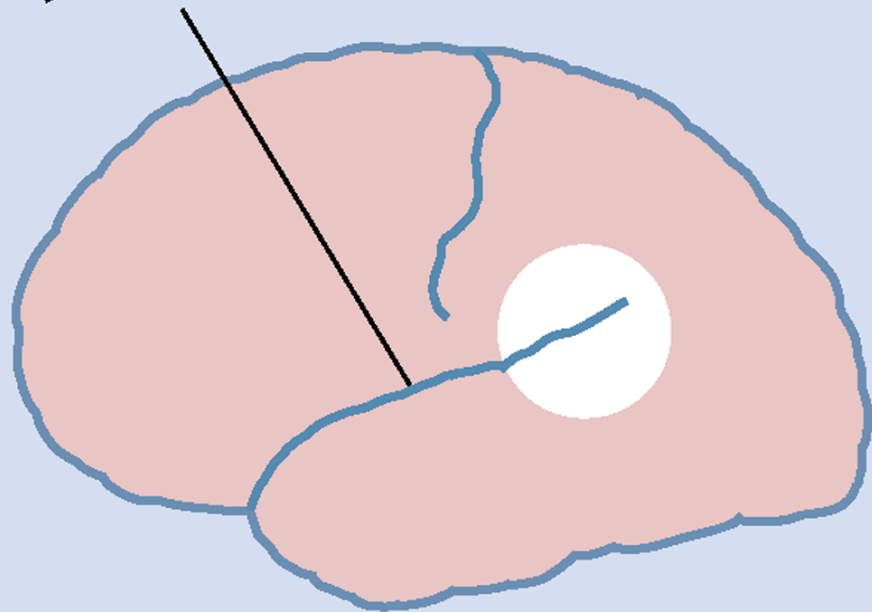
Recap

- Dopamine imbalances
- Antipsychotic drugs
- Structure of a stroke and lesions
- Today: hemispheric differences/cerebral lateralization.

Cerebral lateralization

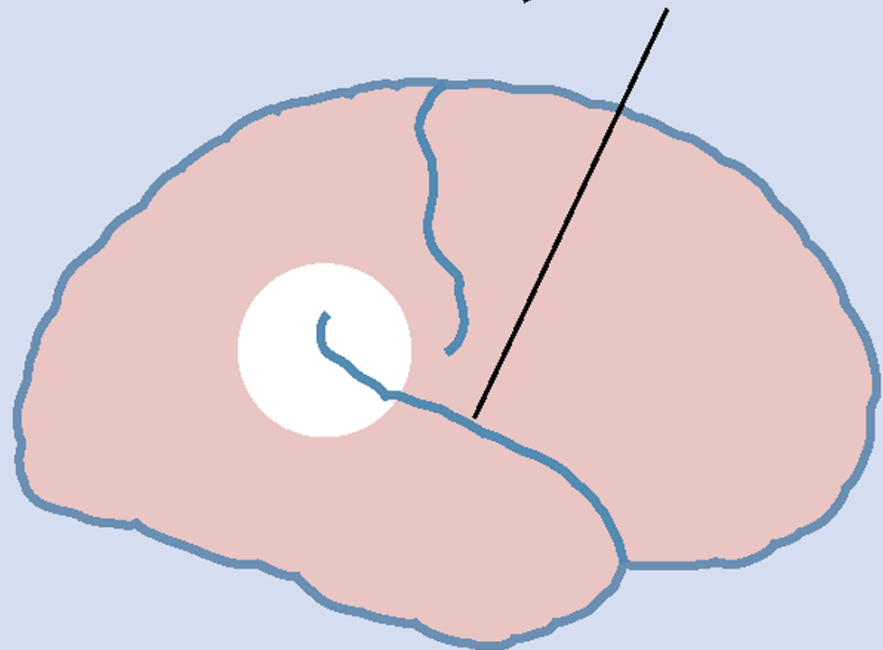
- We've seen the brain from the front to back (frontal to occipital)
- But what's happening in the two hemispheres?
- Are they different? Why so?

Sylvian fissure



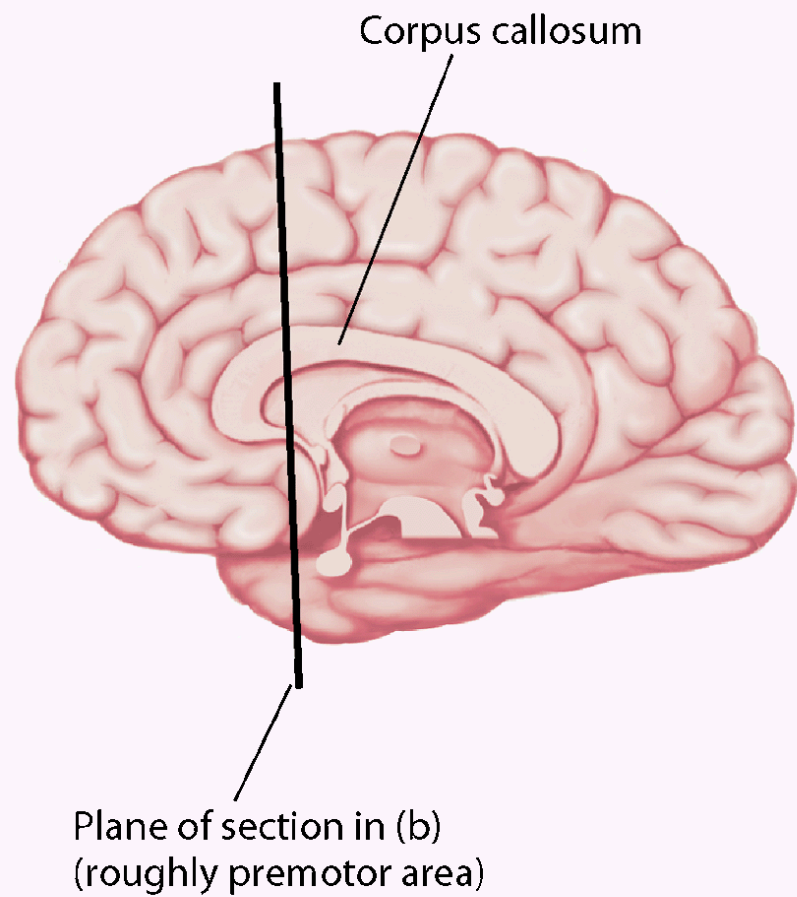
Left hemisphere

Sylvian fissure

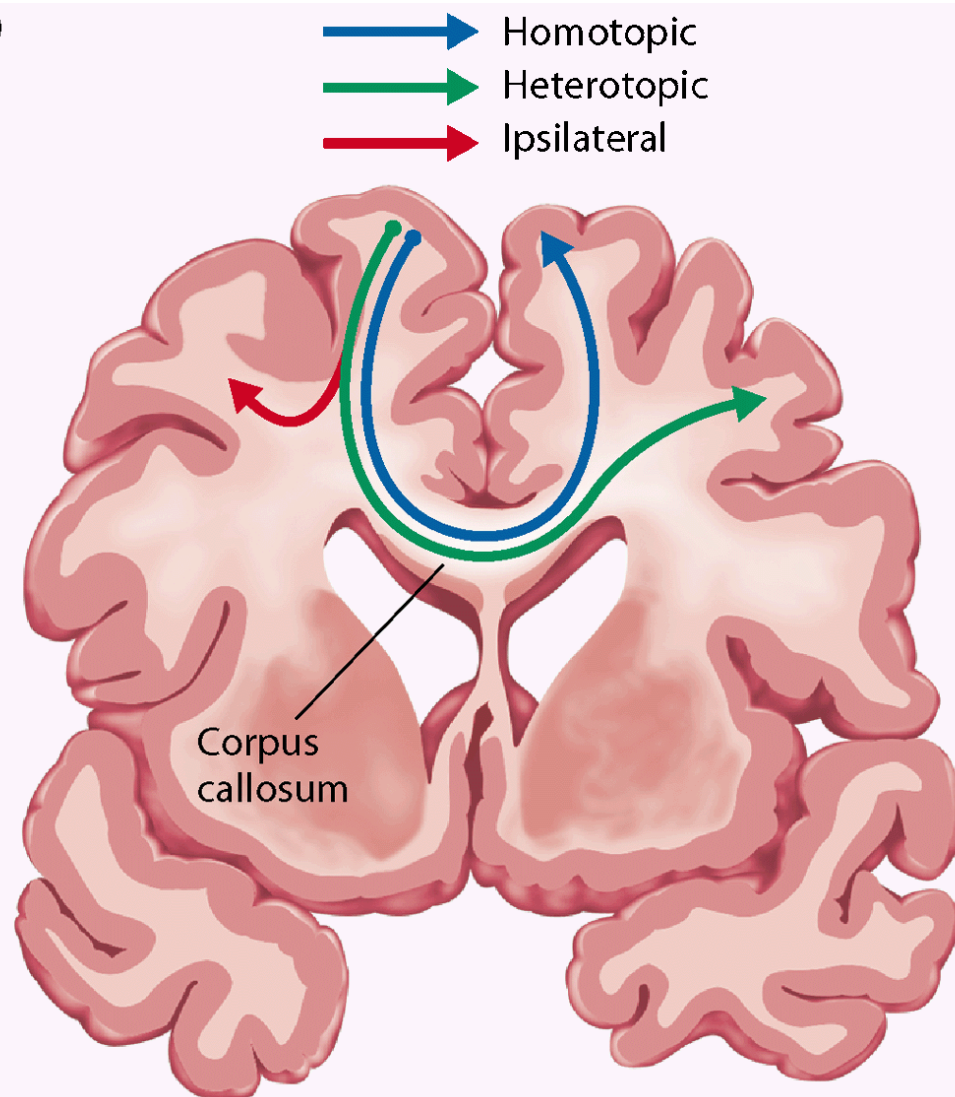


Right hemisphere

(a)



(b)



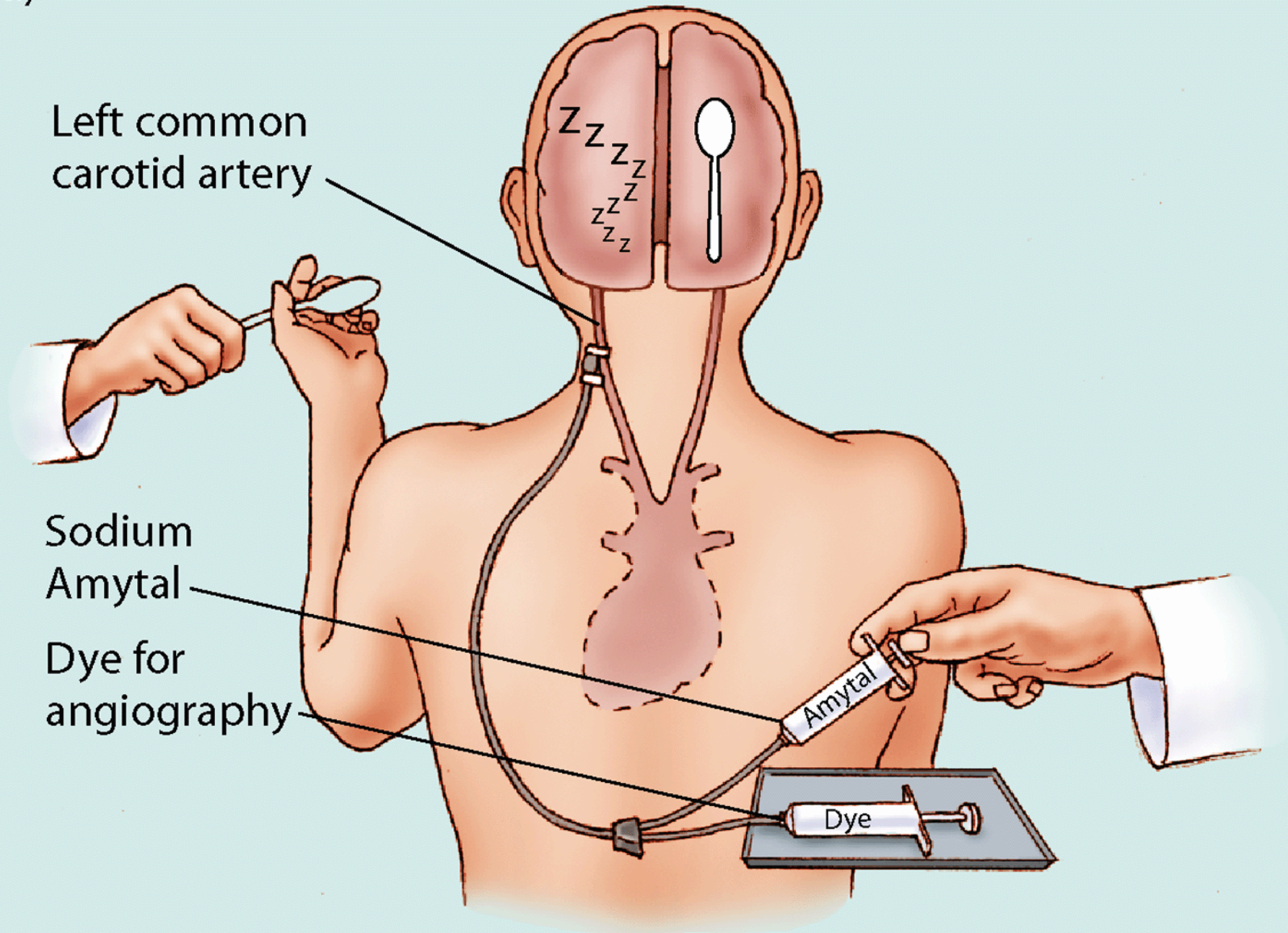
- Split-brain patients

- Sectioning of corpus callosum as a treatment for medically intractable epilepsy
- This procedure is called callosotomy.
- Can study the separate contributions of the left and right hemispheres to various abilities/tasks
- No inter-hemispheric inhibition.

- Split-brain patients

- Sectioning of corpus callosum as a treatment for medically intractable epilepsy
- This procedure is called callosotomy.
- Can study the separate contributions of the left and right hemispheres to various abilities/tasks
- “Split-brain” can be induced surgically by injecting Sodium Amytal (a barbiturate) into one carotid artery temporarily (5-10min) puts half the brain to sleep allowing neurologists to assess function in the awake hemisphere

(a)



Left common carotid artery

Sodium Amytal

Dye for angiography

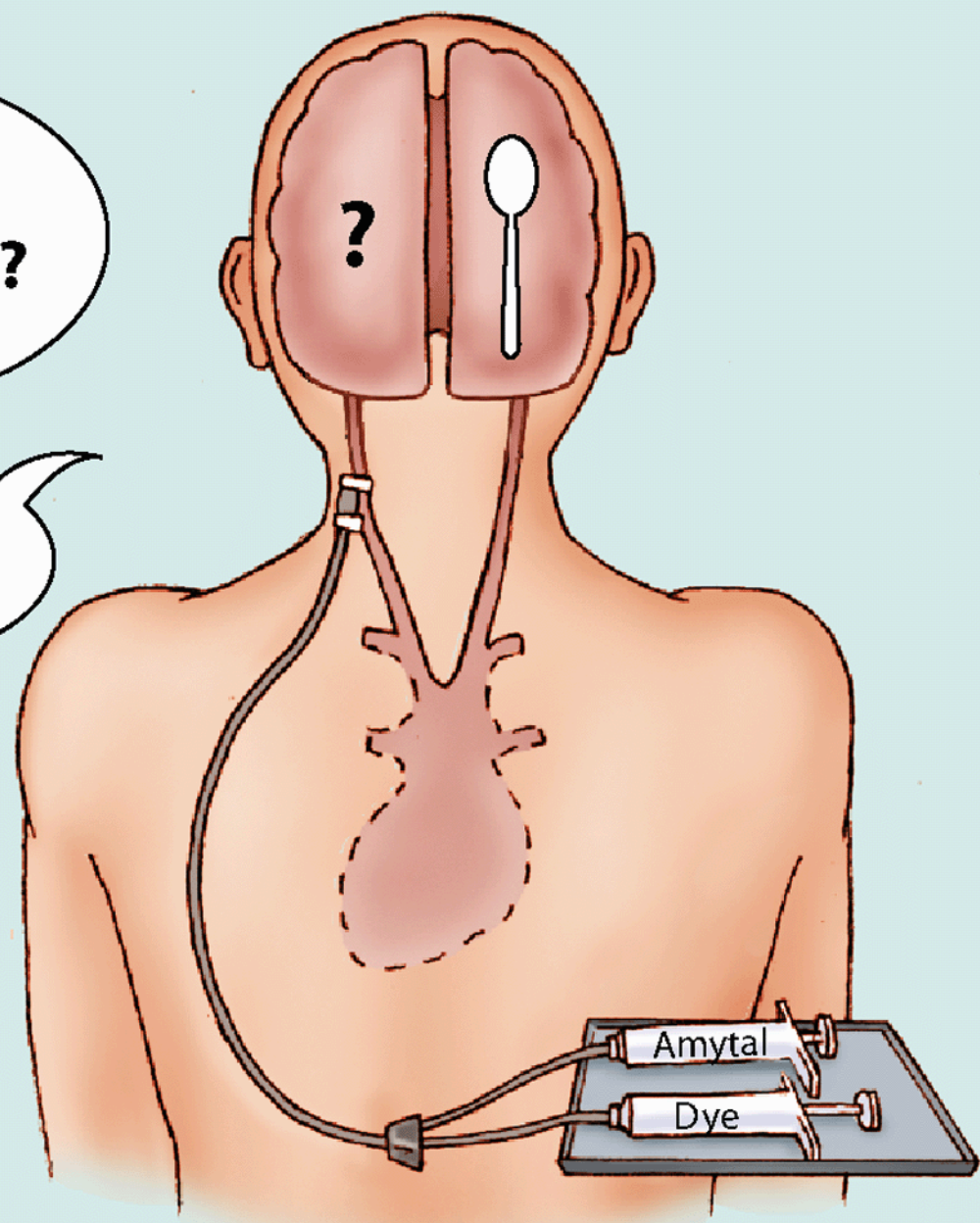
Amytal

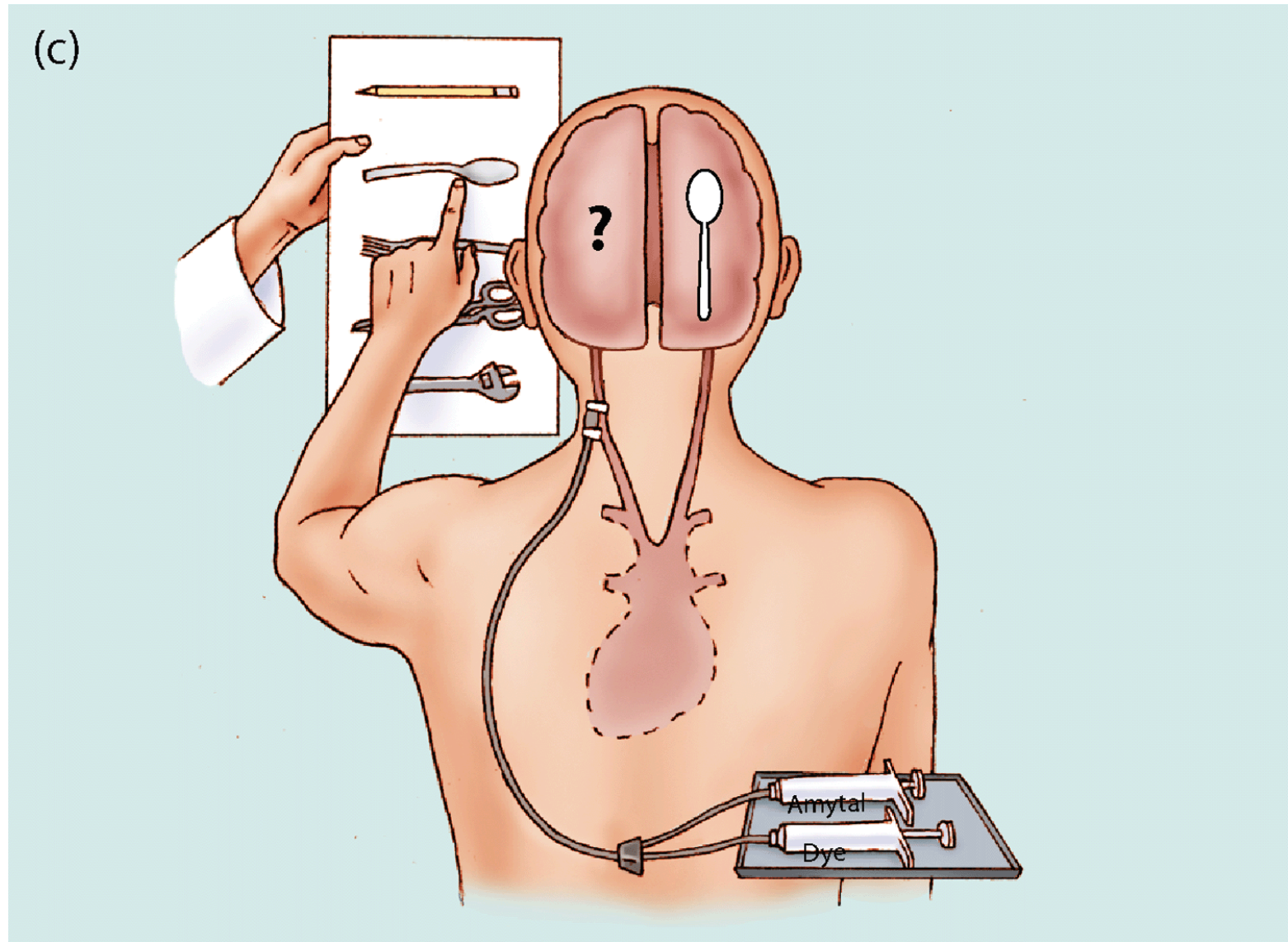
Dye

(b)

**What is it
I gave you?**

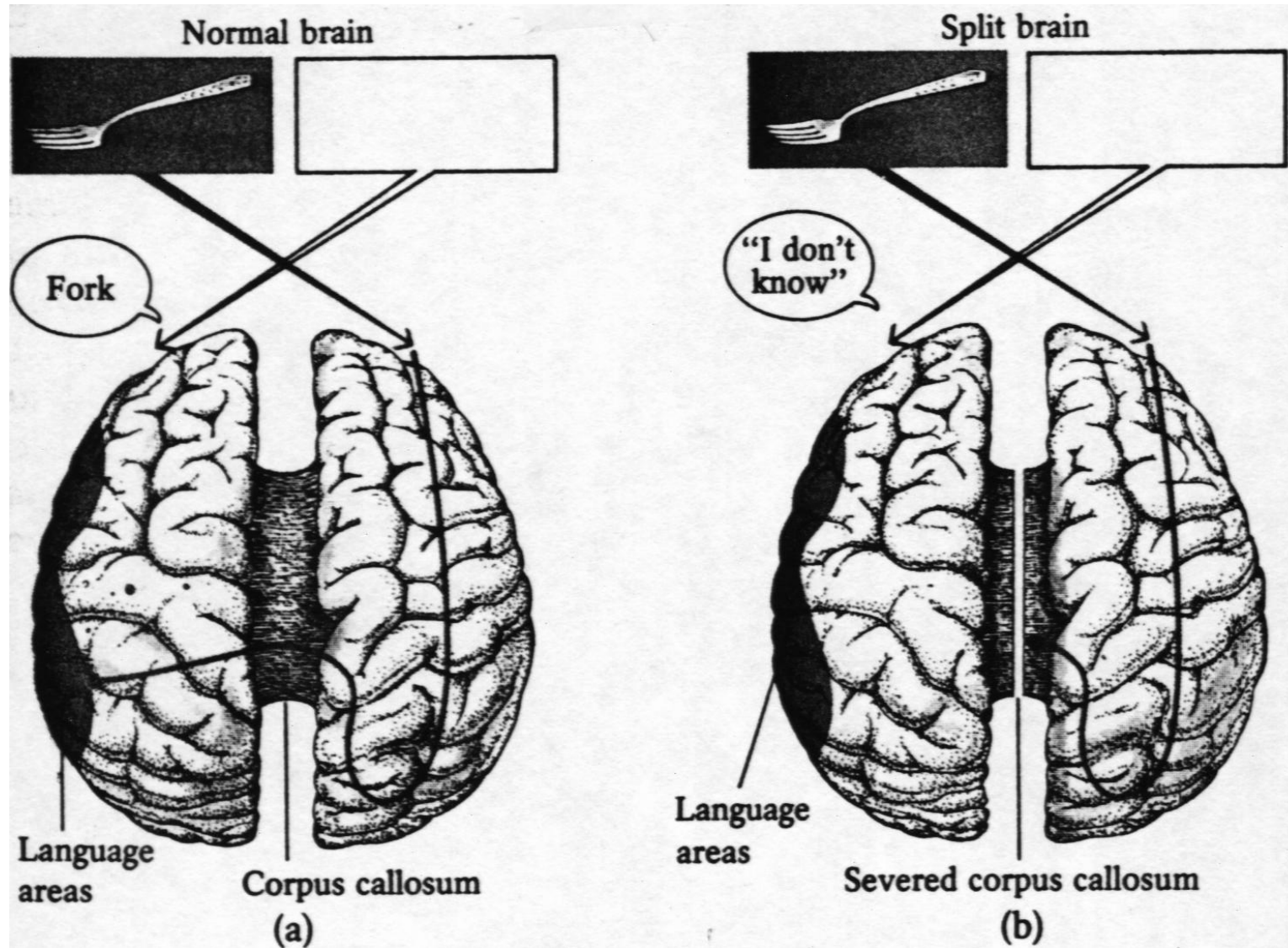
Nothing.





Result of the speech system being anaesthetized.
Patient cannot name the object but can point to it.

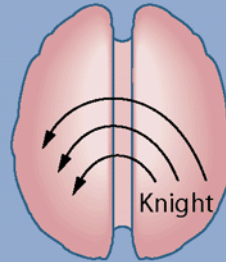
Split Brains



Right-hemisphere
stimulus

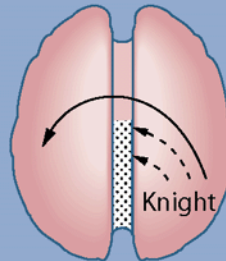
Left-hemisphere
verbal response

Normal brain



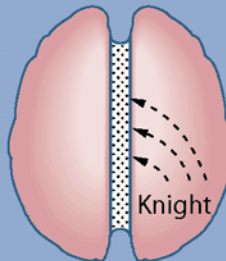
"Knight"

Partial split



"I have a picture in
mind but can't say
it. Two fighters in
a ring. Ancient and
wearing uniforms
and helmets...on
horses...trying to
knock each other
off...Knights?"

Complete split



"I didn't see
anything"

Cross hemispheric communication

- How does the brain control the movement of two limbs (each controlled by different hemispheres).
- Movement interference
- Consider patting your head and rubbing your belly.

Bimanual coordination

- Bringing two limbs together
- Unimanual movements: activation of primary motor cortex, cerebellum, basal ganglia.
- Bimanual movements are much more complex: involves neural crosstalk across the corpus callosum

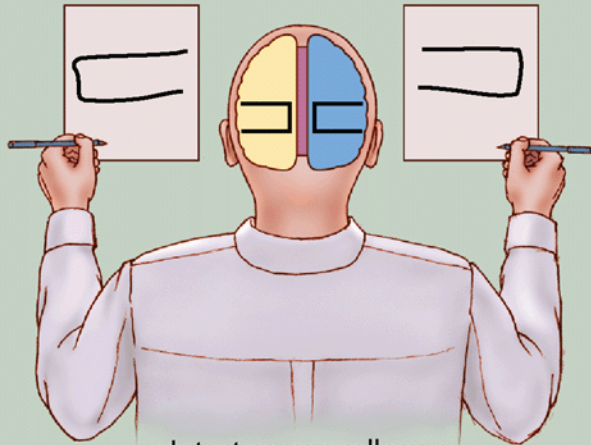
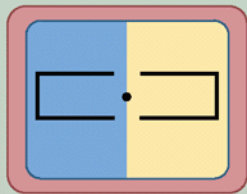
Bimanual coordination

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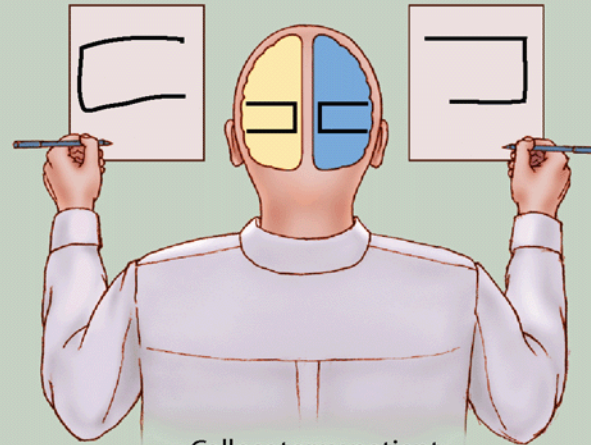
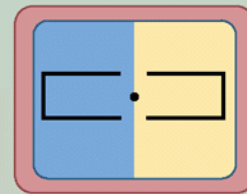
Experiment.

- While sitting at your desk, lift your right foot off the floor and make clockwise circles with it.
- Now, while doing this, draw the number "6" in the air with your right hand.
- Your foot will change direction!!!

Mirror symmetric

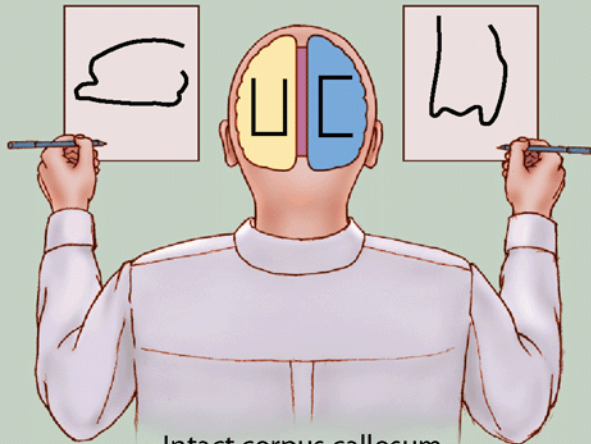
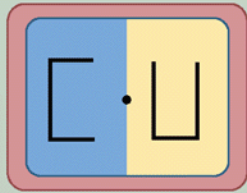


Intact corpus callosum

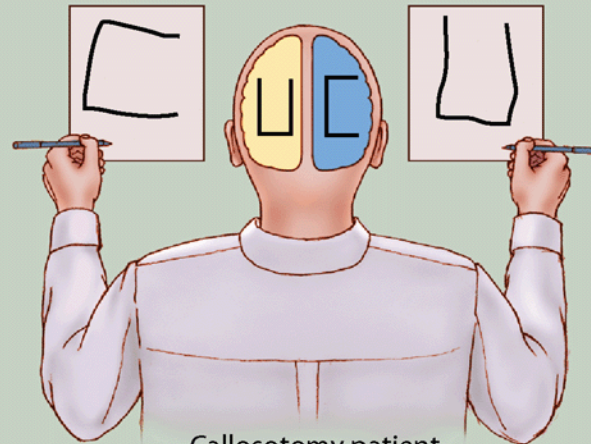
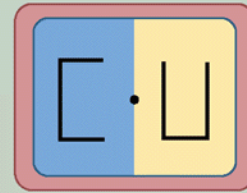


Callosotomy patient

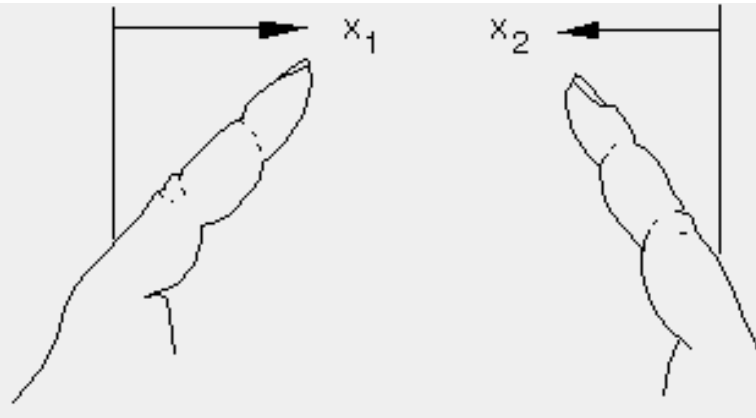
Non-symmetric



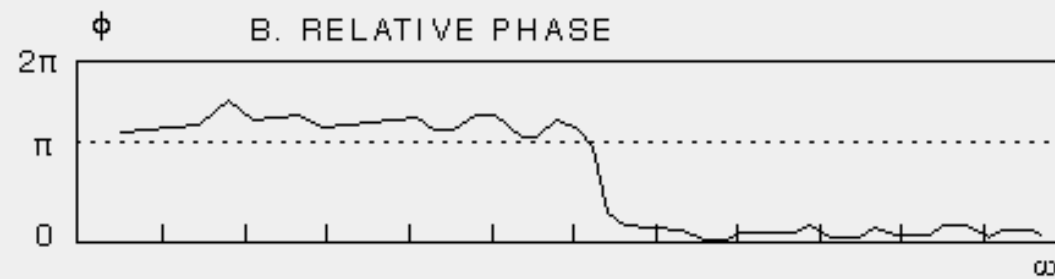
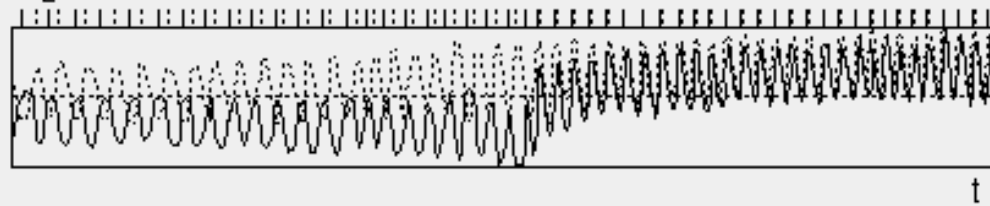
Intact corpus callosum



Callosotomy patient



x_1 ——— A. TIME SERIES
 x_2 - - - - -



Principles of bimanual coordination

- Inphase movements are much more stable
- Movements that involve homologous muscle groups are more stable
- Movement destabilizes at high speeds or switches to a new pattern
- Like Horses: walk, trot, gallop.

Frontal lobe lesions

- SMA/PMC lesions causes serious bimanual coordination problems.
- Actions are represented in many different ways in the frontal lobe (body-based, environment-based and task-based).

Anarchic hand *aka.* Dr. Strangelove syndrome

Caused by huge lesions in the frontal lobe.

- Hand seems to act with a mind of its own
- Patients do not feel that the hand is not part of their body (not controlled by aliens)
- Exhibits orderly goal-directed behavior when normal.

“One evening we took our patient, Mrs GP, to dinner with her family. We were discussing the implication of her medical condition for her and her relatives, when, out of the blue, much to her dismay we saw her left hand taking some left-over fish-bones and putting them into her mouth”.

“She was abashed by what she did, though a little later, while she was begging it not to embarrass her anymore, her mischievous hand grabbed the ice-cream that her brother was licking”.

“Her right hand immediately intervened to put things in place and as a result of the fighting the dessert dropped on the floor. She apologised profusely for this behaviour that she attributed to her hand’s disobedience. Indeed she claimed that her hand had a mind of its own and often did whatever “pleased it” ”.

“[the] left hand would tenaciously grope for and grasp any nearby object, pick and pull at her clothes, and even grasp her throat during sleep...

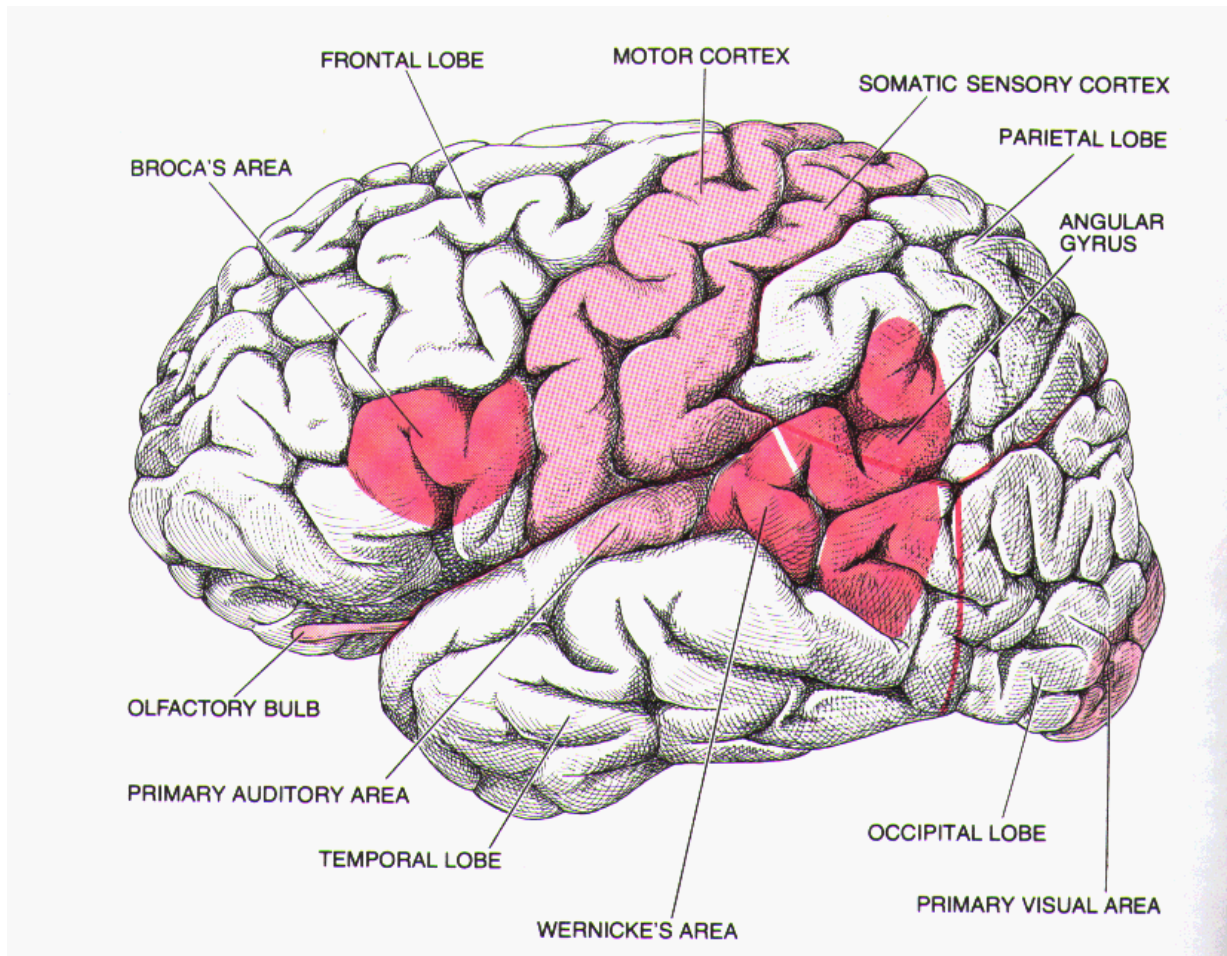
She slept with the arm tied to prevent nocturnal misbehavior. She never denied that her left hand and arm belonged to her, although she did refer to her limb as though it were an autonomous entity.”

One more time...

- Structure of a stroke/lesion
- Split brain experiments
- Cerebral lateralization and bimanual coordination
- Frontal lobe lesions and the alien hand syndrome

Language & Speech production

- Is a movement control issue
- Coordination and co-articulation (remember TULIP)
- Aphasia: due to damage to speech areas



Temporal parital
junction

Broca's aphasia: Frontal motor area
Serious lack of fluency and
grammatical problems

Wernicke's aphasia:
Severe Auditory Comprehension
Deficits
Speech Output Rapid (Fluent)
But Often Meaningless

Clinically classified varieties of aphasia.

Broca's & Wernicke's Aphasia (Non-Fluent vs. Fluent Speech)

Conduction Aphasia (Fluent, Good Comprehension Poor Repetition)

Anomia (Fluent, Good Comprehension/ Repetition, Poor Naming)

Damage To The Angular Gyrus & Inferior Parietal Lobe

Global Aphasia (Non-fluent, Poor Comprehension/ Repetition etc.)

Extensive Damage To Fronto-Temporal-Parietal Lobes

Finally, Foreign accent syndrome:

no ability to
communicate

[Play video](#)

http://news.bbc.co.uk/media/video/39522000/rm/_39522150_accent05_twigg_vi.ram

Cookie Theft - Non-fluent Speech



Broca's Aphasia -
"Red, red, water and
the plate and i got
there...."

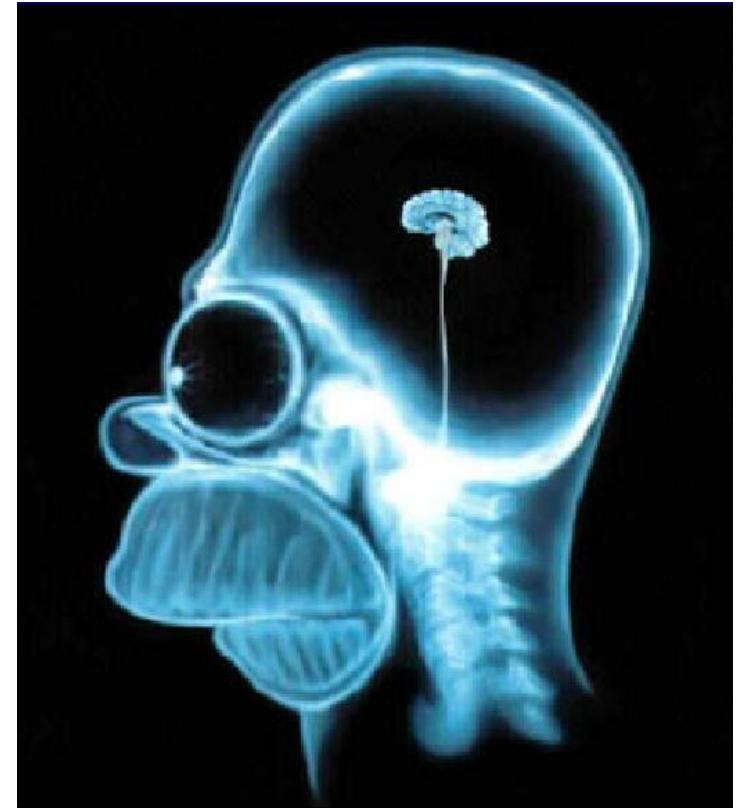
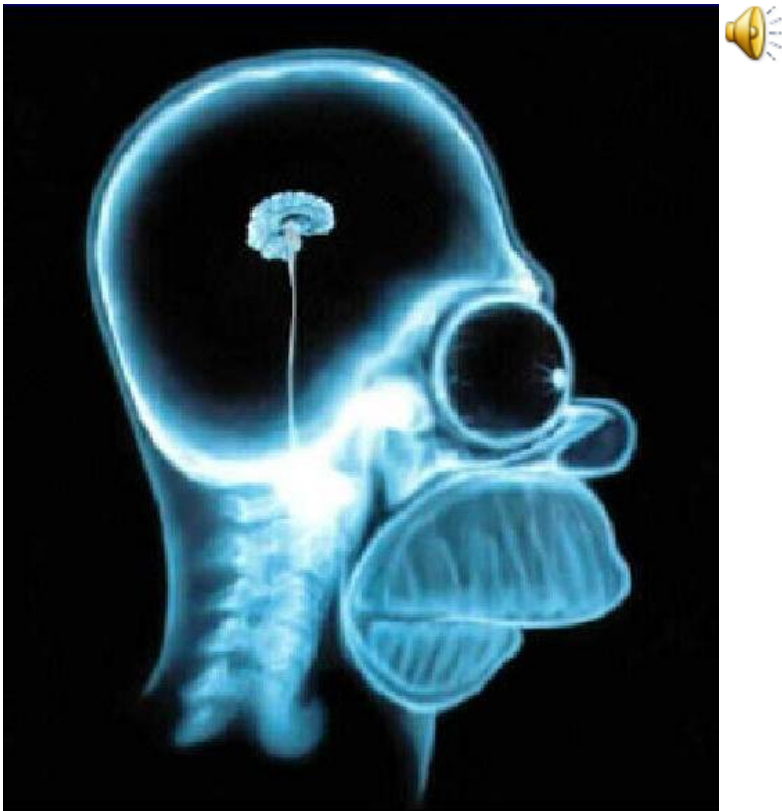
- Broca's Aph

Wash the plate and she wash it and she dry it and the pay...paylot....and that's the boy and there and he want and he want a stat the boy sig down here (points at stool) and he koot and he what there koot jar, and the girl the girl and the water" (JT: so what's happening with the boy then?) "Yes, she got the boy fall yes, on the floor and the water right in her in her in her in her.... (JT: what about the girl?) she laughter, laughter yes because the girl yes kooken yea" (PW laughs)

I got there and nnn.

Broca's Aphasia

- Severely Non-fluent
- (Responses: “Yes” “No” etc.)
- Production Reduced In Grammatical Complexity
- Poor Articulation (Dysarthria)
- Poor Melodic Line (Dysprosody)
- Poor Speech Volume (Hypophonia)



HOMER SEE HOMER DO:

Motor theory of speech perception.

Strong evidence for mirror neurons being active during speech perception

Shown by Iacoboni et al at UCLA.

Cookie Theft - Fluent Speech




- Wernicke's Aphasia -
 - “Well this is... mother is away here working her work out here to get her better, but when she's looking, the two boys looking in the other part. One their small tile into her time here. She's working another time because she's getting to. So two boys work together and one is sneakin' around here, making his work an' his further his time he had.”

Wernicke's aphasia

- Severe Auditory Comprehension Deficits
- Speech Output Rapid (Fluent) But Often Meaningless
- Phonemic (STOOL - “Pool”)
- Semantic (STOOL - “Chair”)
- Neologisms (STOOL - “Gwool”)

Universals of Language

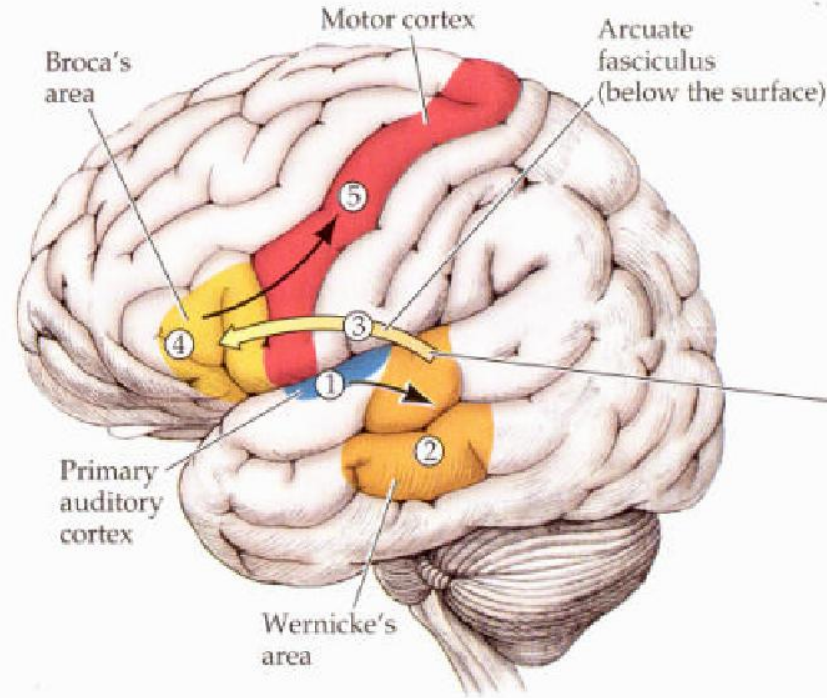
- Raise a Japanese baby in Mississippi and s/he' ll learn a Southern drawl and all other mannerisms from South
- **Semanticity**
 - Language conveys meaning
- **Arbitrariness**
 - No inherent connection between symbols/sounds and meaning in brain
 - e.g., origins of letter “A” or 

(a) Speaking a heard word

1. Information about the sound is analyzed by primary auditory cortex and transmitted to Wernicke's area.

2. Wernicke's area analyzes the sound information to determine the word that was said.

3. This information from Wernicke's area is transmitted through the arcuate fasciculus to Broca's area.



4. Broca's area forms a motor plan to repeat the word and sends that information to motor cortex.

5. Motor cortex implements the plan, manipulating the larynx and related structures to say the word.

Lesions of the arcuate fasciculus disrupt the transfer from Wernicke's area to Broca's area, so the patient has difficulty repeating spoken words, but may retain comprehension of spoken language (because of intact Wernicke's area) and may still be able to speak spontaneously (because of intact Broca's area).

Evidence reflecting pre-motor planning: speech errors

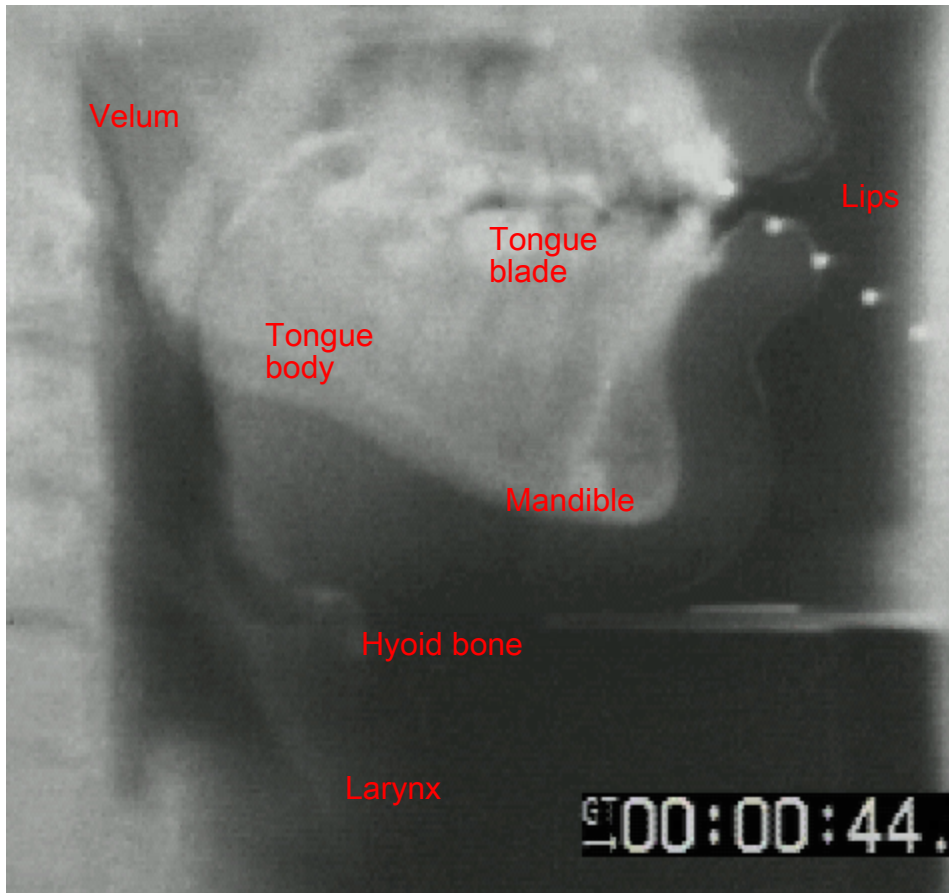
Common examples

- Substitution *Anymay* (Anyway)
- Exchange *emeny* (enemy)
- Shift highway driwing
- Addition the plublicity (publicity)
- Omission sonata _umber ten
(number)

■ Differences between speech and other movements

- In speech, there are very few clear-cut agonist-antagonist muscle groups
- Only one articulator, the mandible, has the kind of joint that plays a prominent role in other types of studied movements
- Tongue and facial muscles have relatively few spindles – proprioception has to be mediated by other kinds of sensory receptors
- Sensorimotor neural pathways are among the shortest in the body: fast conduction times and presumably short processing times for feedback control involving peripheral sensation
- Speech is a generative process, with an internally constructed plan and relatively little physical interaction with the environment

What is the number of degrees of freedom to be controlled?



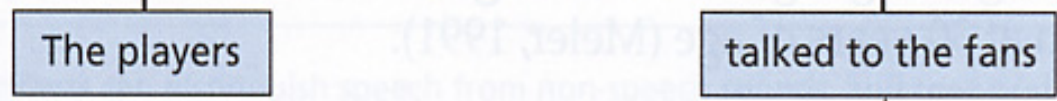
- Consider the movements of each of these structures
- Approximate number of muscle pairs that move the
 - Tongue: 9
 - Velum: 3
 - Lips: 12
 - Mandible: 7
 - Hyoid bone: 10
 - Larynx: 8
 - Pharynx: 4
- There are also:
 - muscles of the respiratory system

- Implication: The number of degrees of freedom that have to be controlled in speech is large and the control problem seems immensely complicated

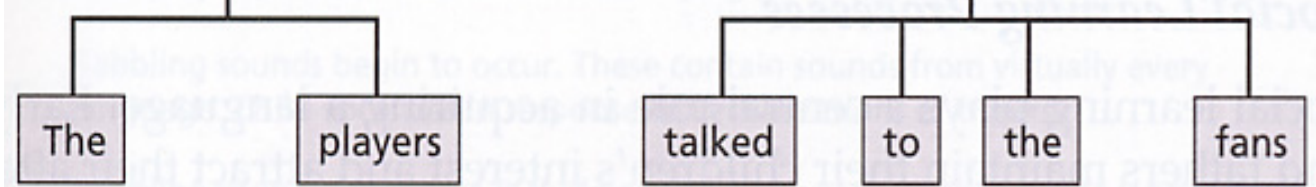
Sentences

The players talked to the fans.

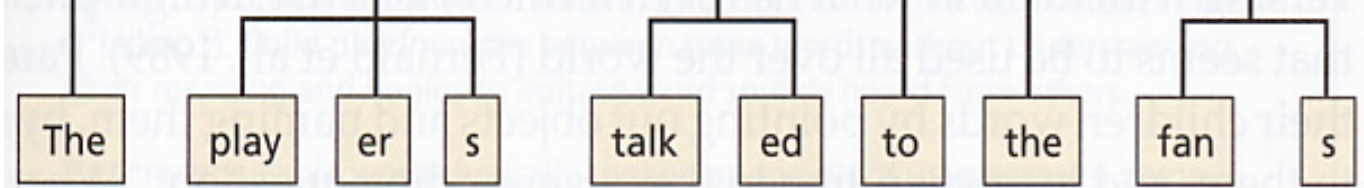
Phrases



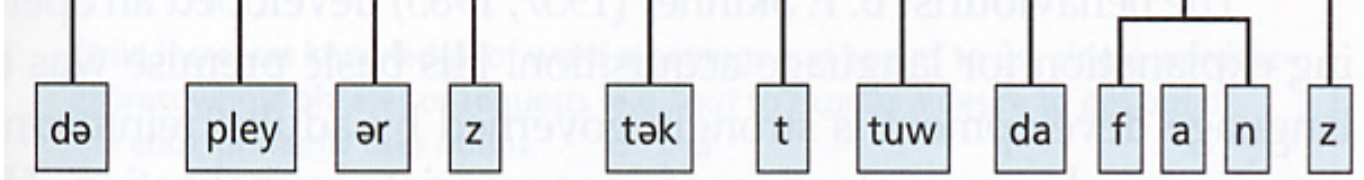
Words



Morphemes

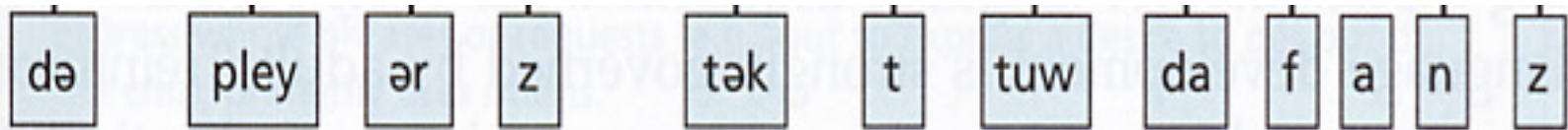


Phonemes

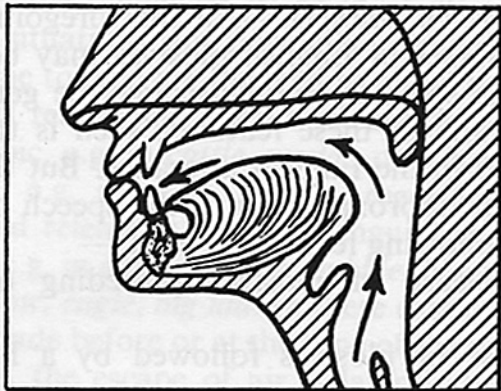


Phonemes

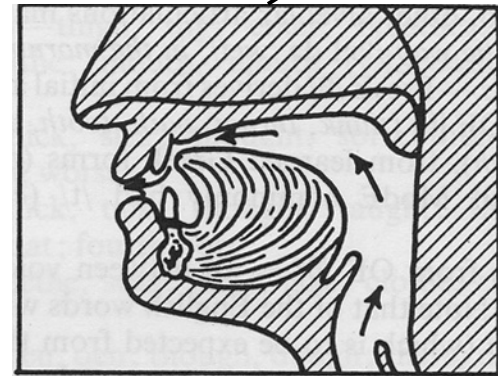
Phonemes are the smallest significant units of sound in a language.



What's involved is changing the column of moving air.

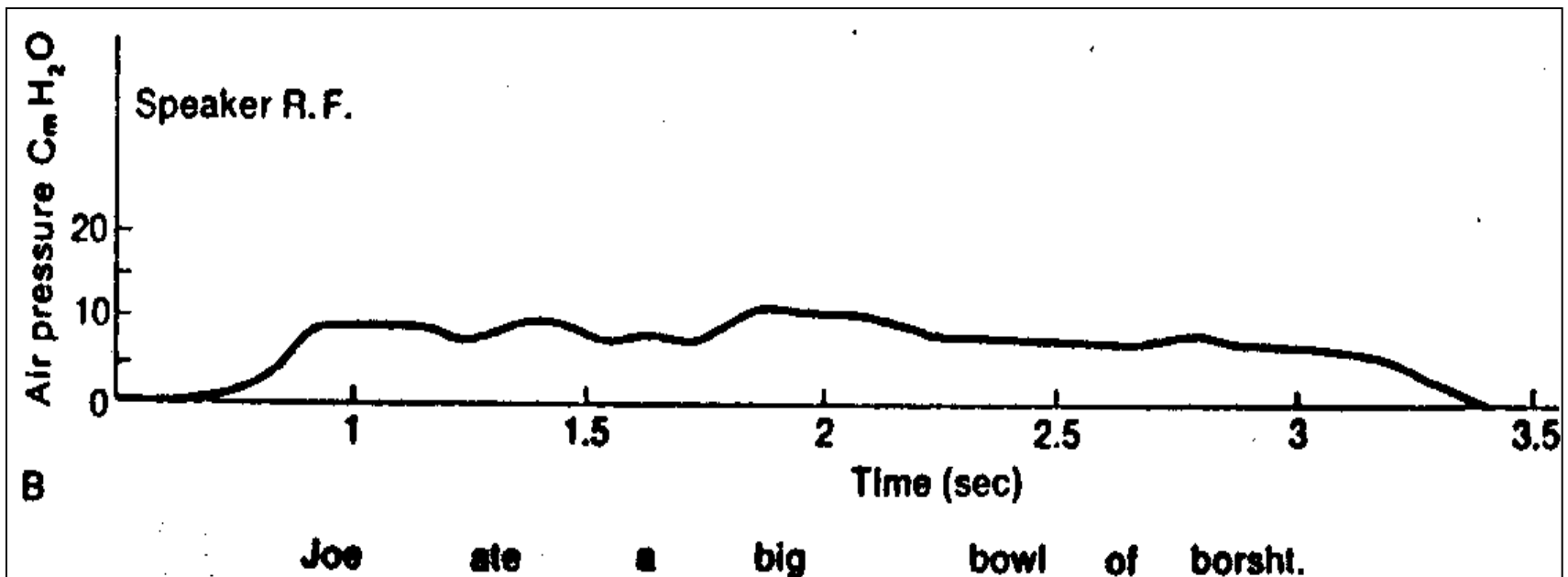


/p, b/ Bilabial Plosives (explosive sound)



/s, z/ Fricatives (based on friction)

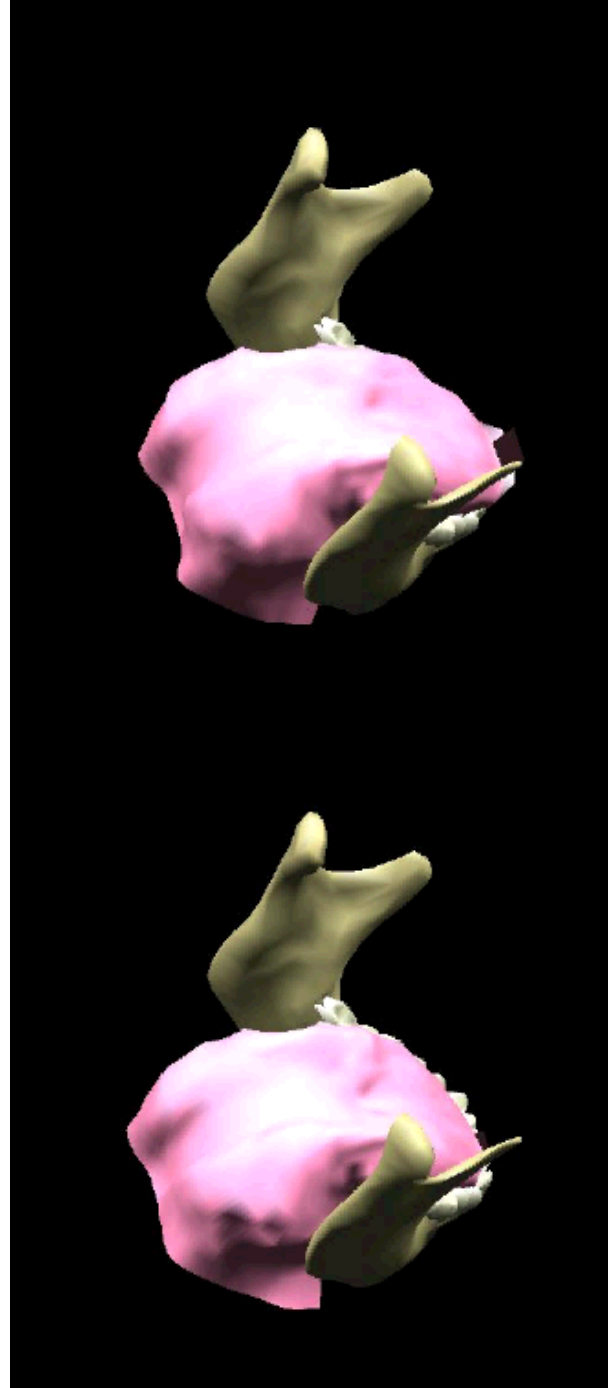
Difference between p and b as well as between s and z is voicing (vibration of vocal cords). Onset of voicing is responsible for difference between pa and ba.



The respiratory system

- most massive (slowly-moving structures)
 - Provides energy for sound production
 - Fluctuations to help emphasis
 - Different patterns of respiration: breathing, reading aloud, spontaneous, counting
 - Different muscles are active at different phases of the respiratory cycle – a complex, low-level motor program

- **Consonants**
 - Place of articulation: where disruption of airflow takes place
 - Manner of articulation: how disruption takes place
 - Voicing: When vocal chords begin to vibrate
- **Vowels**
 - Placement in mouth: front, center, back
 - Tongue position: high, middle, low



Other speech control systems

- Larynx
 - Smallest structures, most rapidly contracting muscles
 - Voicing, turned on and off segment-by-segment
- Vocal tract
 - Intermediate-sized, slowly moving structures: tongue, lips, velum, mandible
 - Can produce sounds at rates up to 15/sec
 - To do so, the movements are coarticulated (TULIP)
 - Controlled by high-level motor programming (frontal areas).

What kind of information is used by the brain to regulate speech?

Auditory

probably not used very much.

Processing times would be too long
Some of the movement toward vowel targets occurs during consonants, when little or no sound is generated

Orosensory (somatosensory) feedback:

Muscle tension (tendon organs) and length (spindles), joint (TMJ) position receptors, surface contact pressure

Could be particularly useful for achieving consonant targets

Is Language uniquely human?

- Yes. At least syntax generation is.
- Ability to arrange the symbols in a structured way.
- Generate an infinite number of combinations of symbols from a few
- The problem of projective predication.
- Even Sign language has this “generative” property (every SL is different).



MANUELA HARTLING/REUTERS

Border collie Rico, who can fetch at least 200 objects by name, retrieves a Pokémon toy in Berlin yesterday. His retrieval rate is comparable to that of a toddler, according to German researchers.

Meet Nim Chimpsky



Nim Chimpsky with psychologist Laura Ann Petitto. Petitto was his caretaker and sign language tutor.

At Columbia University, Herbert Terrace designed the program to teach Nim sign language.

After years of work and videotape analysis of Nim's conversations, Terrace found that when Nim combined symbols into longer sequences, he was either imitating his trainer's previous signs, or "running on" with his hands until he got what he wanted (e.g., "eat Nim eat" or "play me Nim play"). Moreover, Nim signed spontaneously only when he wanted something whereas humans use language in a more diverse way.

That animals use symbolic communication is probably true.

But there is no evidence that their language is Structured or Generative.

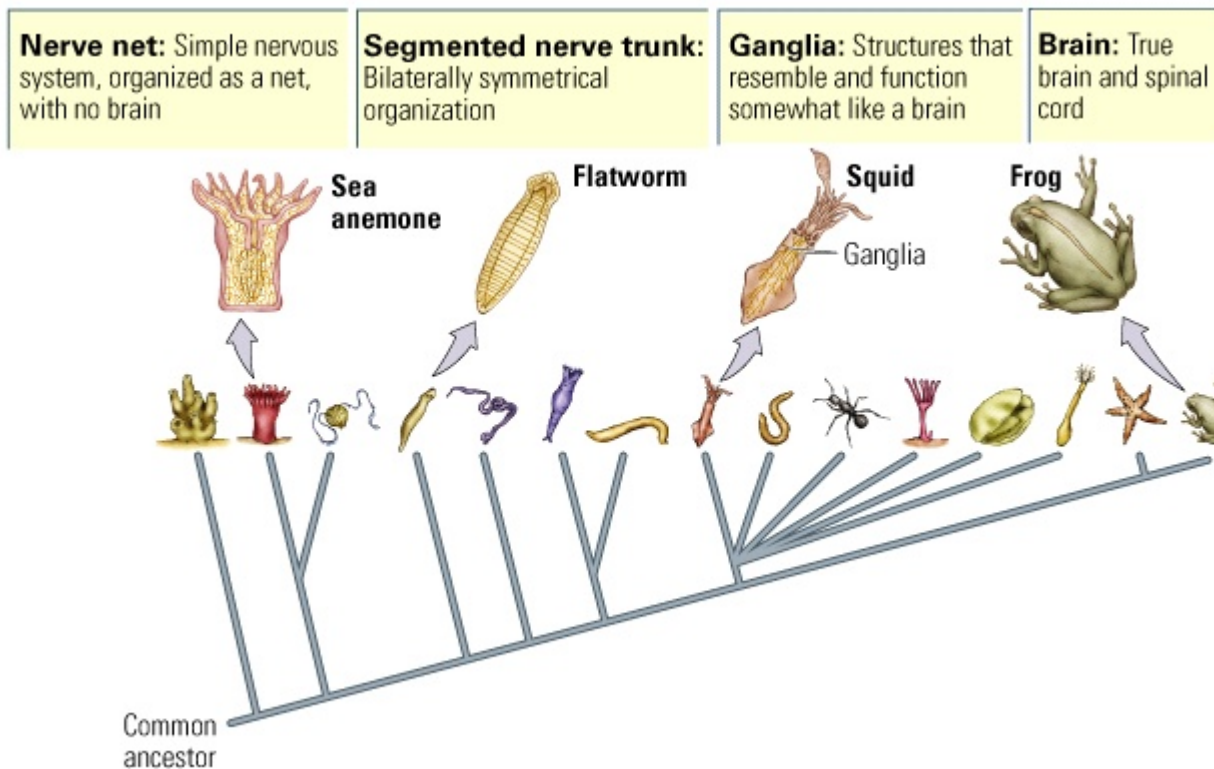
Evolutionary Reasons?

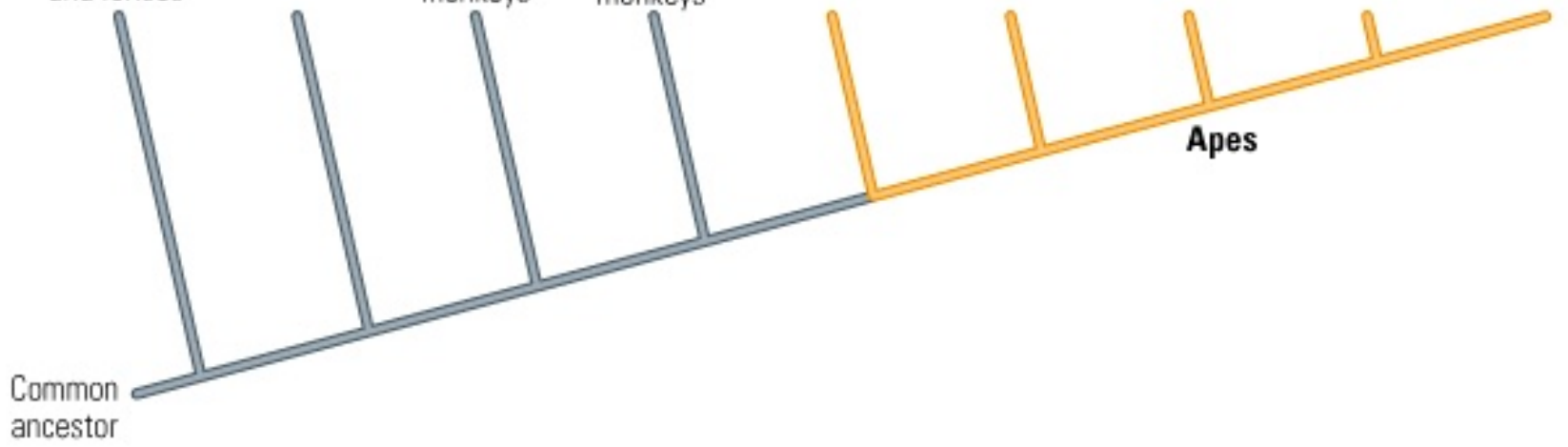
Horse, sheep, human and dog



Evolution

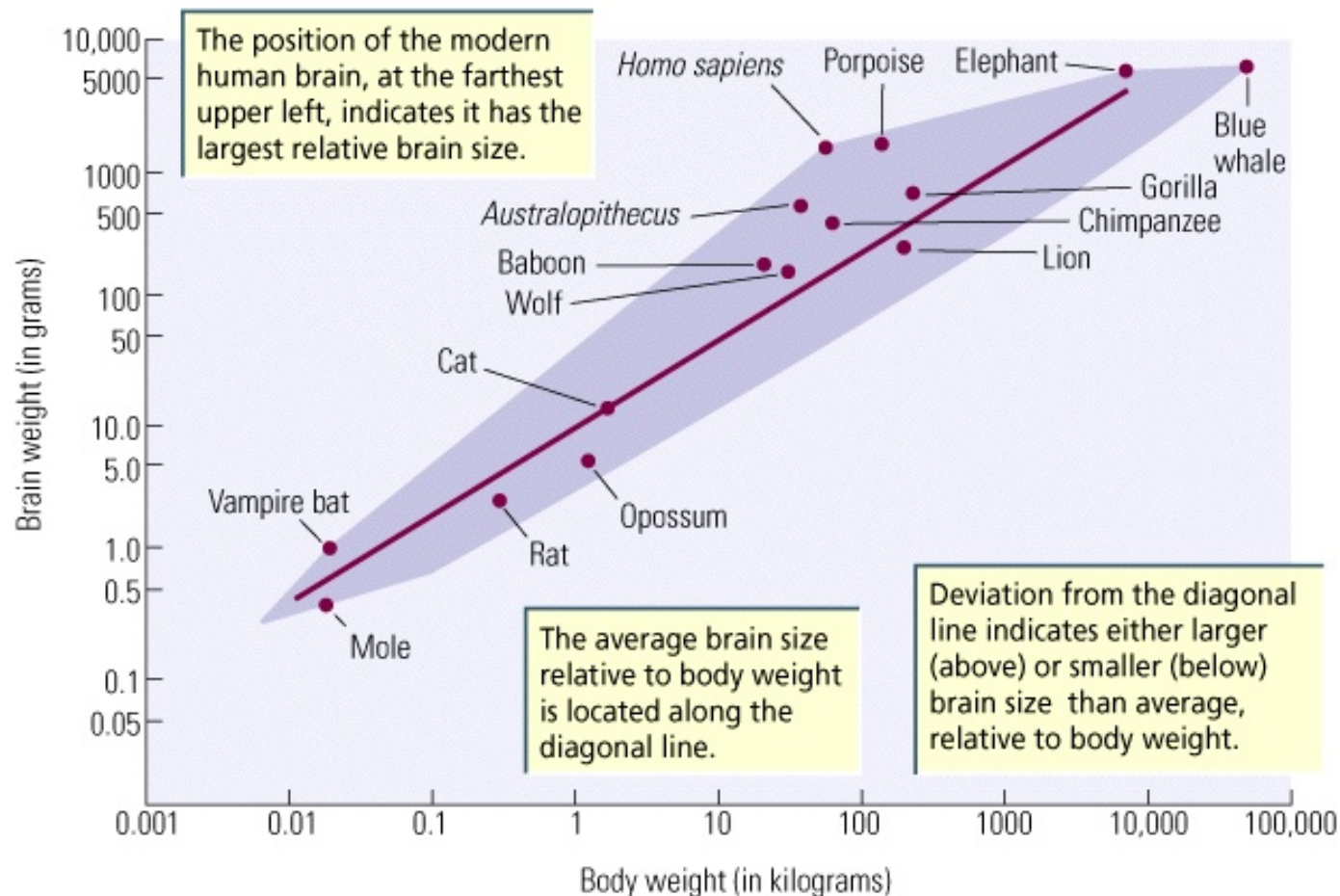
- Animal phyla





Human evolution

- Increase in brain size
- Encephalization quotient



One more time...

- Language disorders: Aphasias
- Frontal lobe and speech motor planning
- Mechanisms of speech production

Midterm Readings

News Items - links to site - sendspace.com - pdf (readings)
sections 3 and 4

Section in text with people drawing "U" and "C" with
different hands

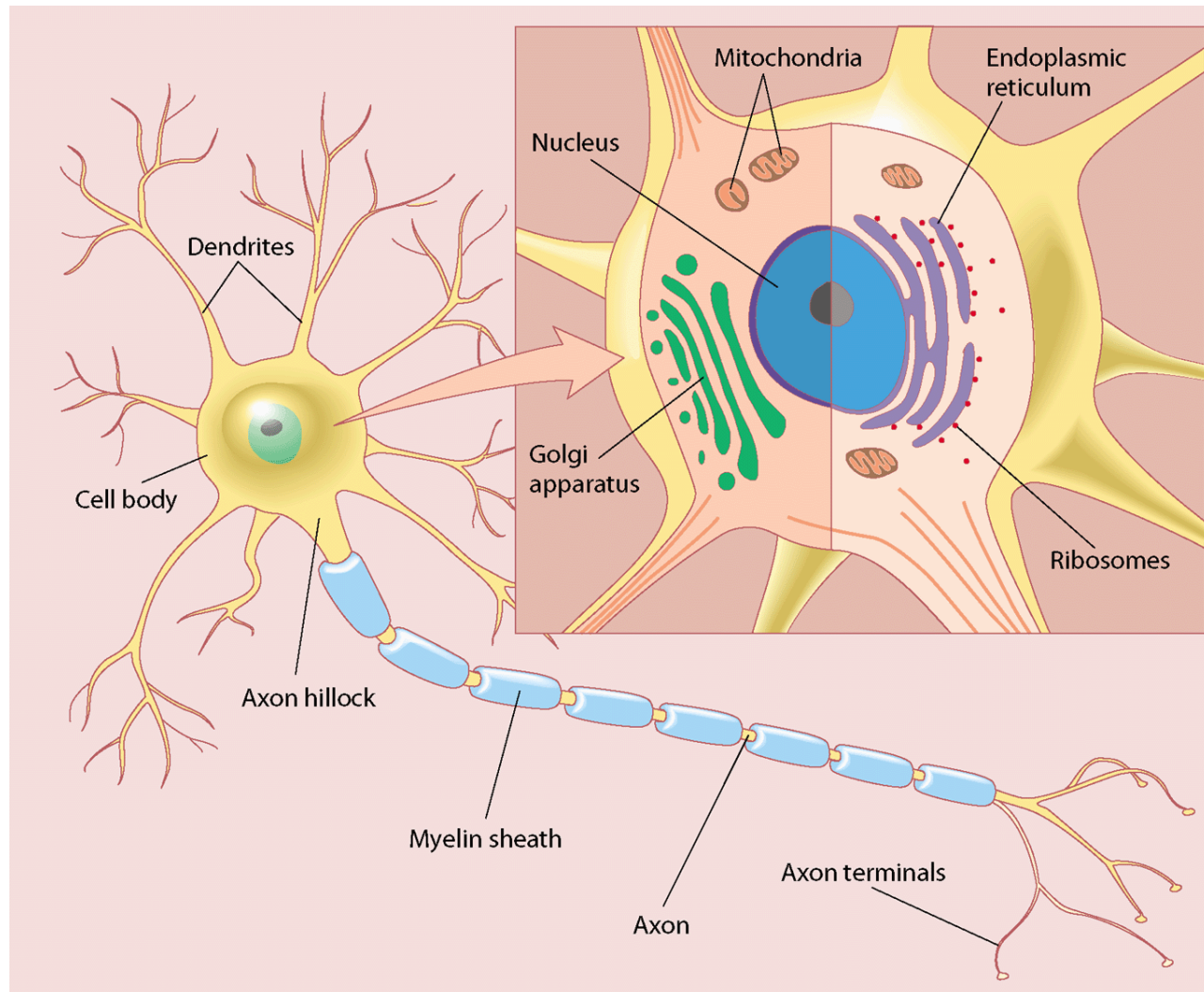
How to record from da brain

Some basics about neuronal functioning

- 1) Neuron structure
- 2) Neural communication: neural transmitters
- 3) Ensemble neural activity.

The Anatomy of a Neuron

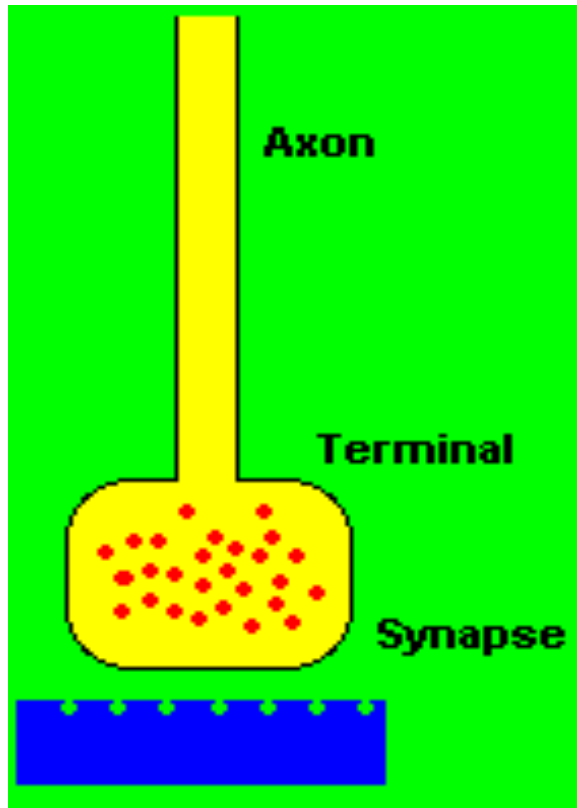
- cell body (or soma),
- dendrites,
- axon



Neuron Physiology

- neurons perform computations, they transform information.
- the functional components of a neuron.
 - an input component (dendrites)
 - an integration component (axon hillock)
 - a transmission component (axon)
 - an output component (synapse)
- passive vs. active conductance
- electrical vs. chemical transmission

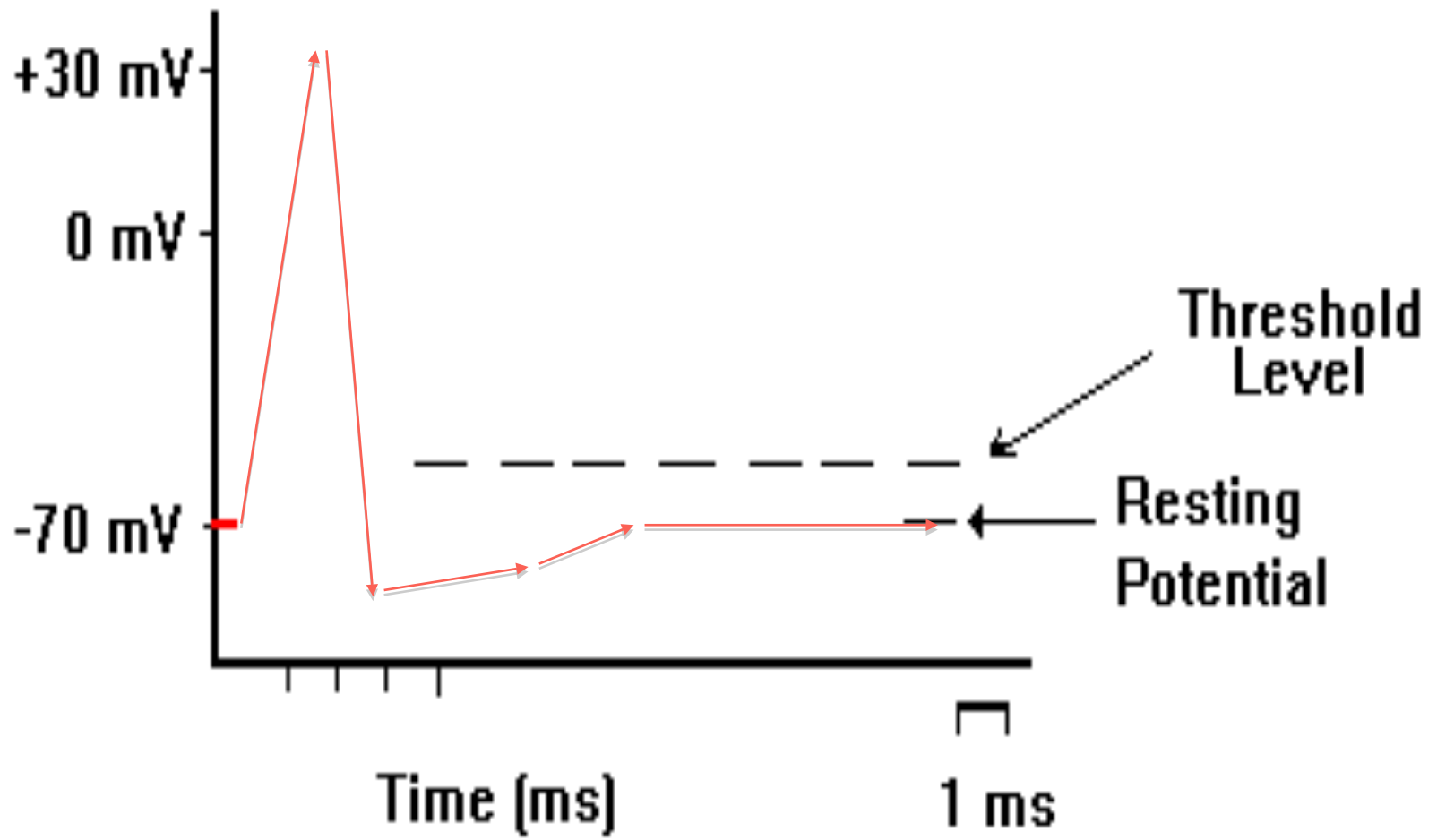
The Synapse



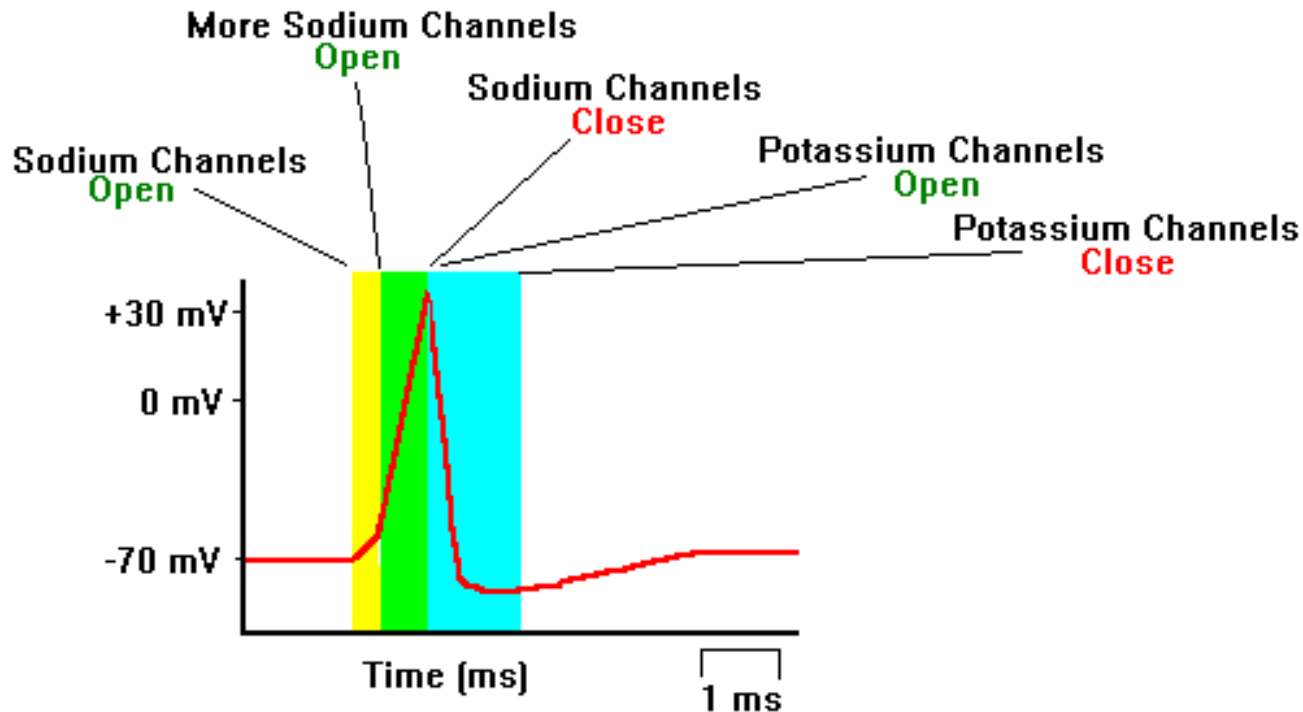
- Axon terminal releases neurotransmitters
- Neurotransmitters cross the synapse and bind to receptors on another neuron
- Neurotransmitters released, taken up again by first neuron

Neural Communication

- Neural messages reflect membrane potential changes
- A cell excited (stimulated) from its resting potential state fires an **ACTION POTENTIAL** → release neural message
- The neural message => Neurotransmission from one neuron to another neuron across a synapse.



Action Potential



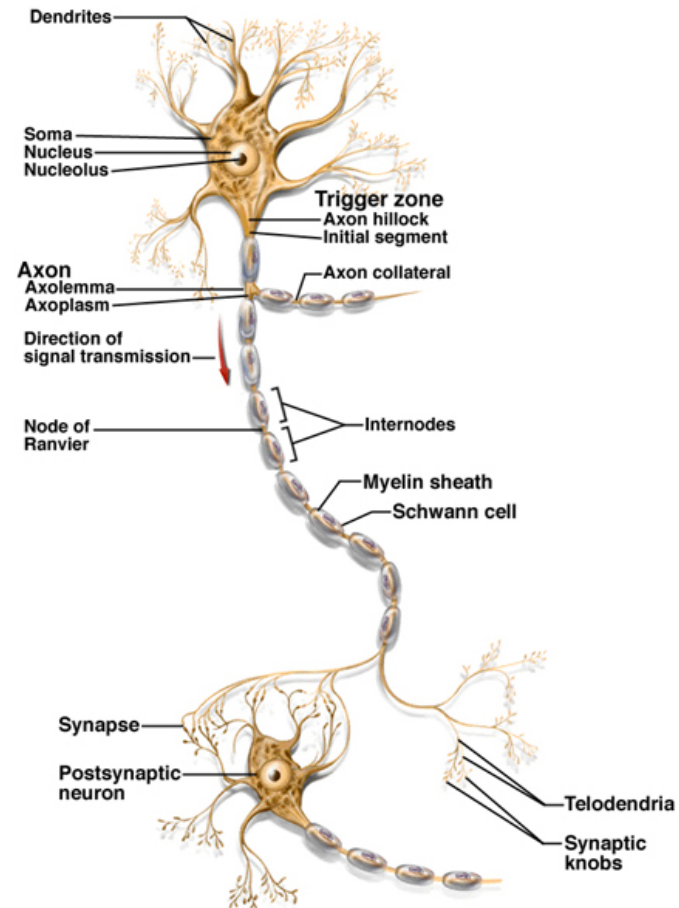
- Involves the action of voltage-gated channels
- Massive, rapid exchanges of ions in and out of the cell

Action Potentials

- How neurons transfer information
- Changes neuron's membrane potential
- Rising phase – membrane depolarizes
- Overshoot
- Falling phase – membrane repolarizes
- Undershoot
- Restoration of resting potential

The Propagation of Action Potential

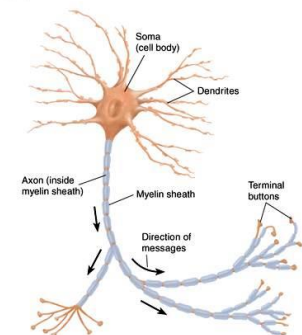
- Long-distance traveling:
Eg. from the motor cortex to the spinal cord of giraffe.
- Loss-free and Fast
- The natural solution:
 - myelination
 - regeneration



Synaptic Transmission

- When an action potential reaches the terminal button, synaptic vesicles release neurotransmitter (NT) into the synaptic cleft
- NT diffuses over the cleft
- At least three possible scenarios after this:
 - NT molecules do not attach to a postsynaptic receptor
 - NT released in an area with no immediate receptors
 - NT “keys into” a receptor site
- The latter scenario leads to change in the ionic permeability of the postsynaptic membrane
 - Excitatory postsynaptic potential (EPSP)
 - Inhibitory postsynaptic potential (IPSP)

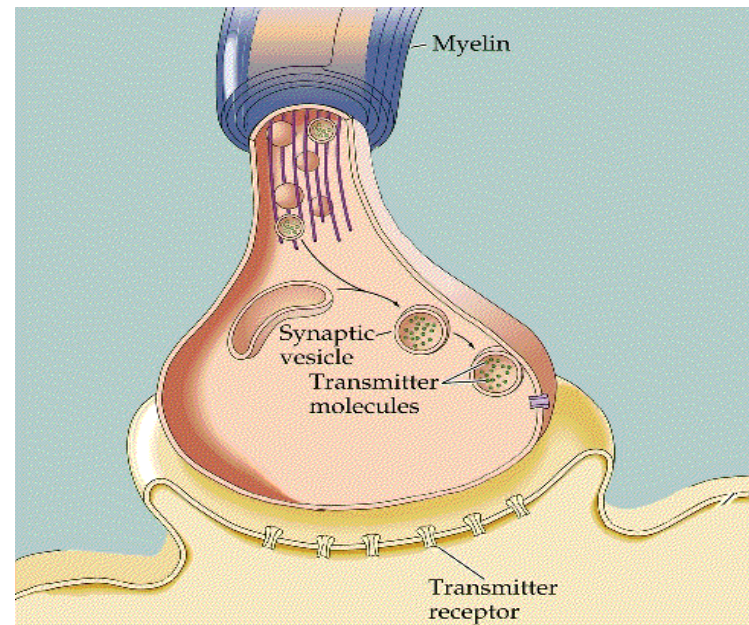
► Multipolar Neuron



Neuronal Interaction

- Chemical synapses and neurotransmitters

- Synapses: the contact sites between neurons
- Pre- and post- synaptic neurons
- Action potential triggers the release of neurotransmitter
- Neurotransmitters drift across the synaptic cleft
- Neurotransmitter-gated channels open, generating electrical current (or postsynaptic potential (PSP))
- Dependent on the sign of PSP, synapses are clarified as excitatory and inhibitory ones.



Neurotransmitters (NT)

Probably 100' s

**Neurons often classified
by the NT it releases**

**Effect of NT depends on
nature of receptor site**

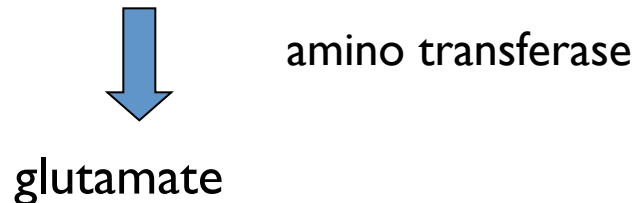
<i>Class</i>	<i>Examples</i>
Amino Acids	Glutamate GABA
Acetylcholine	Acetylcholine
Monoamines	Serotonin Dopamine Norepinephrine Epinephrine
Purines	Adenosine
Gases	Nitric Oxide (NO)
Peptides	Endorphins

Neurotransmitters ... Basic Concepts

- **Biosynthesis:** All NT - synthesized in the cell
- **General role of NT:**
 - Different NT seem to be important for different aspects of behaviour
 - Many drugs that affect behaviour and experience do so by their effects on synaptic transmitters or on receptors

Glutamate

- Possibly, among the first NT type to have evolved
- Principal excitatory NT in the brain
- Produced in abundance in cells
- Biosynthesis: α ketoglutarate

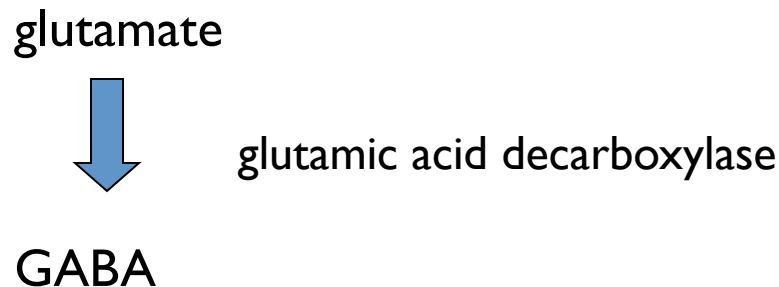


- Stored in synaptic vesicles released at terminal buttons

Gamma Amino-Butyric acid (GABA)

Principal inhibitory NT in the brain

- Produced in cells that contain glutamic acid decarboxylase
- Biosynthesis:



- Stored in synaptic vesicles released at terminal buttons
- Responsible for most of inhibitory information transmitted
 - Most neurons receive GABA types of input
- Alcohol facilitates (agonist) GABA receptors

Acetylcholine (ACh)

- First neurotransmitter discovered
 - Generally Facilitative Effects
 - Biosynthesis in the cell
-
- ***Functions in muscular contractions***
 - Secreted by efferent axons at muscular junctions - Initiates all voluntary actions



The Black widow spider (Latrodectus) and Cottonmouth are so toxic because they trigger massive release of acetylcholine from neurons.

ACh

ACh acts on two different types of post synaptic receptors:

- Nicotinic receptors

- found at [neuromuscular junction](#) of skeletal (only) muscles,
- on post-ganglion neurons of the [parasympathetic nervous system](#), and
- on many neurons in the brain (e.g. in the [hippocampus](#)).
- nicotine is an [agonist](#) of ACh activity
- curare is an antagonist (hence its ability to paralyze skeletal muscles)

- Muscle receptors

- found at neuromuscular junctions of [cardiac](#) and [smooth muscle](#) and on
- glands,
- On post-ganglion neurons of the [sympathetic nervous system](#).
- muscarine (a toxin of certain [mushrooms](#)) is an agonist.
- atropine is an antagonist (its use in [acetylcholinesterase poisoning](#))

Agonist - increases activity

Antagonist - decreases activity

Catecholamines

- Two important catecholamines:
 - Dopamine (DA)
 - Norepinephrine (NE)

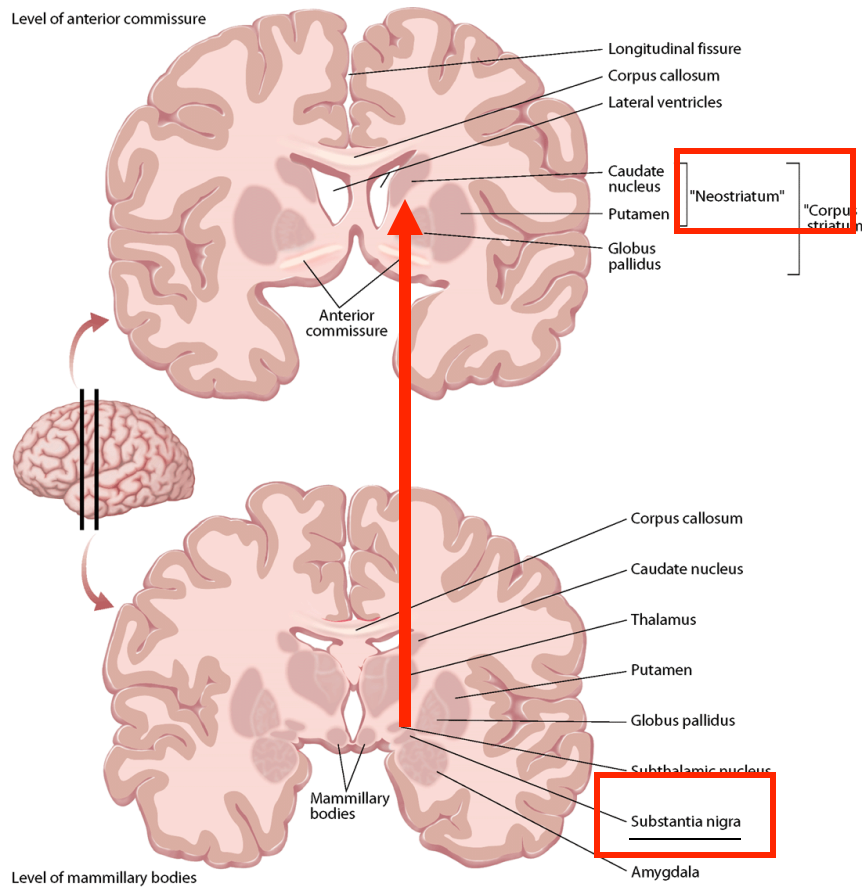
Produce both inhibitory and excitatory post synaptic potentials depending on the receptor

Essential function of catecholamines is to mobilize

- Stored in synaptic vesicles released at terminal buttons

DA

- *Involved in the control of movements*



Major DA Circuits & Nuclei

- The nigrostriatal system
- DA nuclei in the substantia nigra (SN).

SN -> striatum of the basal ganglia

Cocaine- a strong reuptake inhibitor of dopamine

- 1. chronic use=lose receptors in the postsynaptic membrane
- 2. block reuptake of dopamine= down regulation occurs and less receptors are available.
- 3. mood elevation is due to dopamine effects.

Addictive drugs

- Nicotine, morphine, etc. Produce their effect by causing dopamine to be released.
- And dopamine can cause release of endocannabinoids (present in all neural systems). Gives you the "high" effect
- Glutamate and acetylcholine also initiate endocannabinoid synthesis and release.

Norepinephrine

- *Involved in attention and readiness to act; involved in the alarm reaction (a-k-a adrenalin)*
 - Transmitted to almost every brain region
 - Major cell bodies located in locus coeruleus of the pons, medulla, and thalamus **release norepinephrine also release by the endocrine system**

Indoleamine: Serotonin

Functions: regulation of mood and pain; involved in eating, dreaming, and arousal

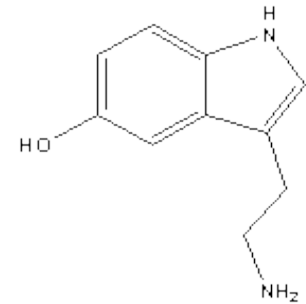
- Major Cell nuclei located in the raphe nucleus
- Raphe nucleus -> cerebral cortex, basal ganglia, dentate gyrus of hippocampus

5HT = serotonin

LSD interacts with the 5HT transmission; LSD alters visual perceptions

Overview of Serotonin

- Serotonin (5-hydroxytryptamine, or 5-HT) is a monoamine neurotransmitter synthesized in serotonergic neurons in the central nervous system.
- The functions of serotonin are numerous and appear to involve control of appetite, sleep, memory and learning, temperature regulation, mood, behavior (including sexual), cardiovascular function, muscle contraction, endocrine regulation, and depression



Serotonin (5HT) Biosynthesis

Tryptophan (an dietary amino acid)



tyrosine hydroxylase

5-hydroxytryptophan (5-HTP)

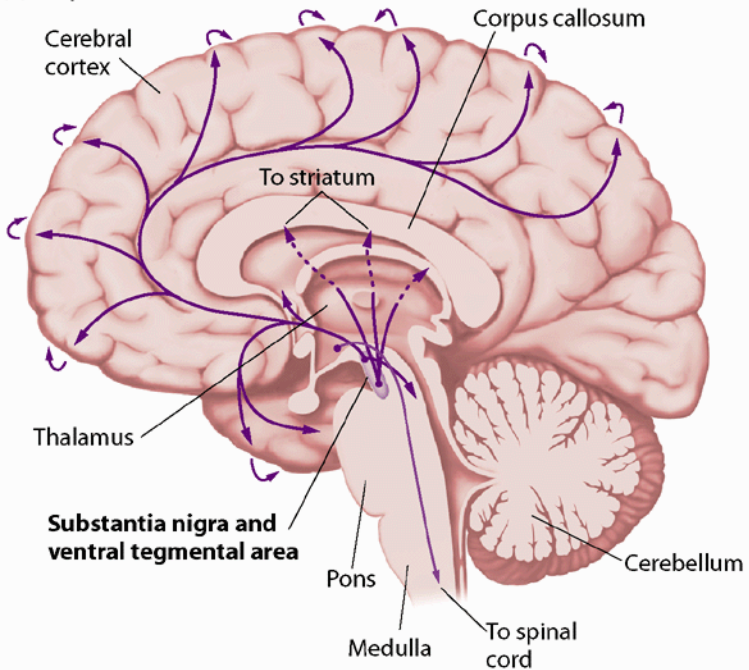


5HT decarboxylase

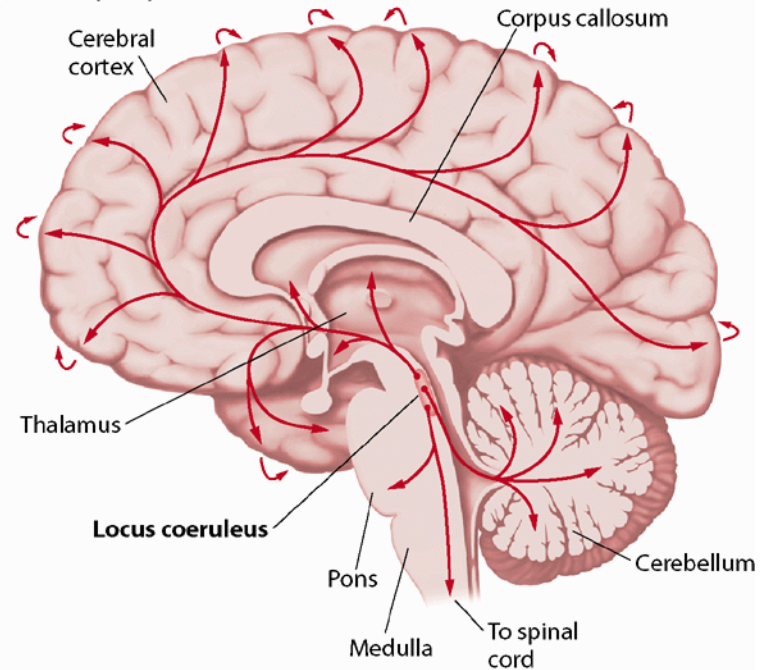
5-HT (5-hydroxytryptamine)

Tryptophan (an dietary amino acid) -> obtained from bananas, corn, meats (turkey),
Meals can alter synthesis of 5HT: chocolate and sugars boost up synthesis of 5HT

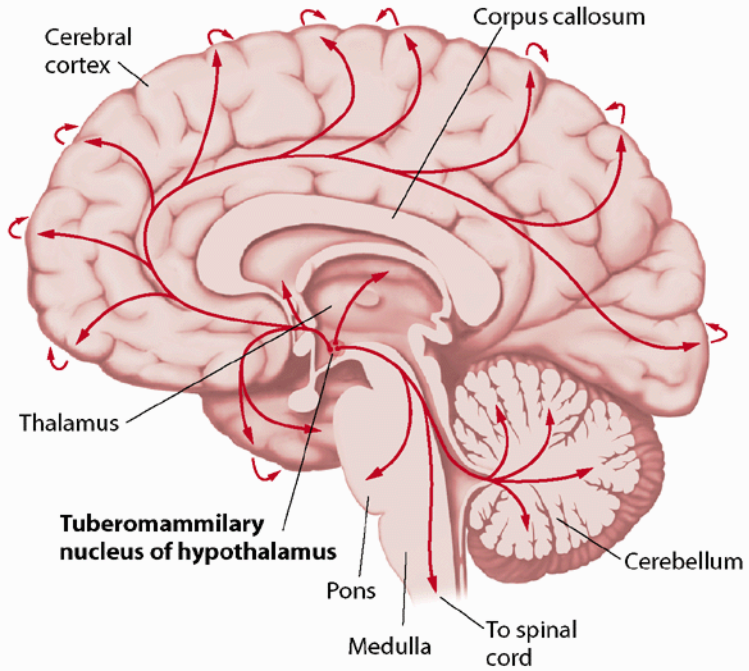
(a) Dopamine



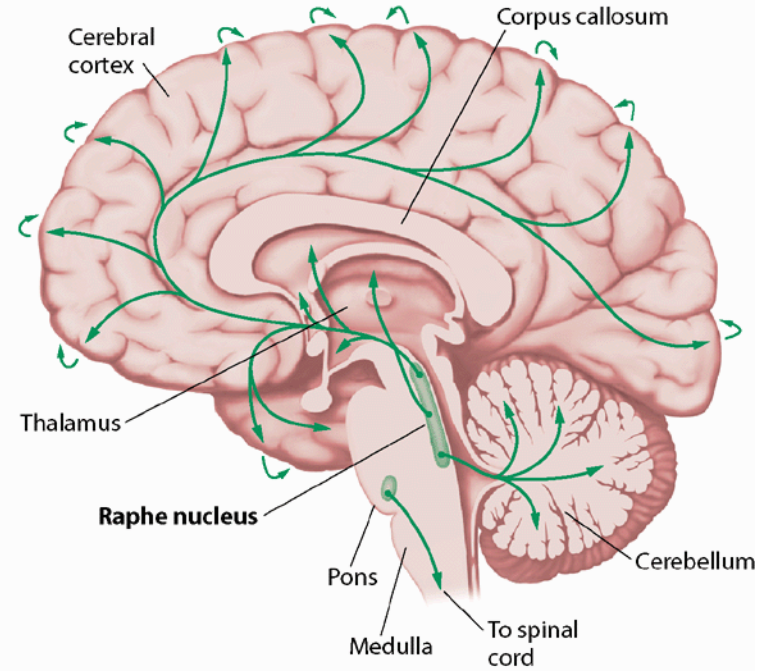
(b) Norepinephrine



(c) Histamine



(d) Serotonin

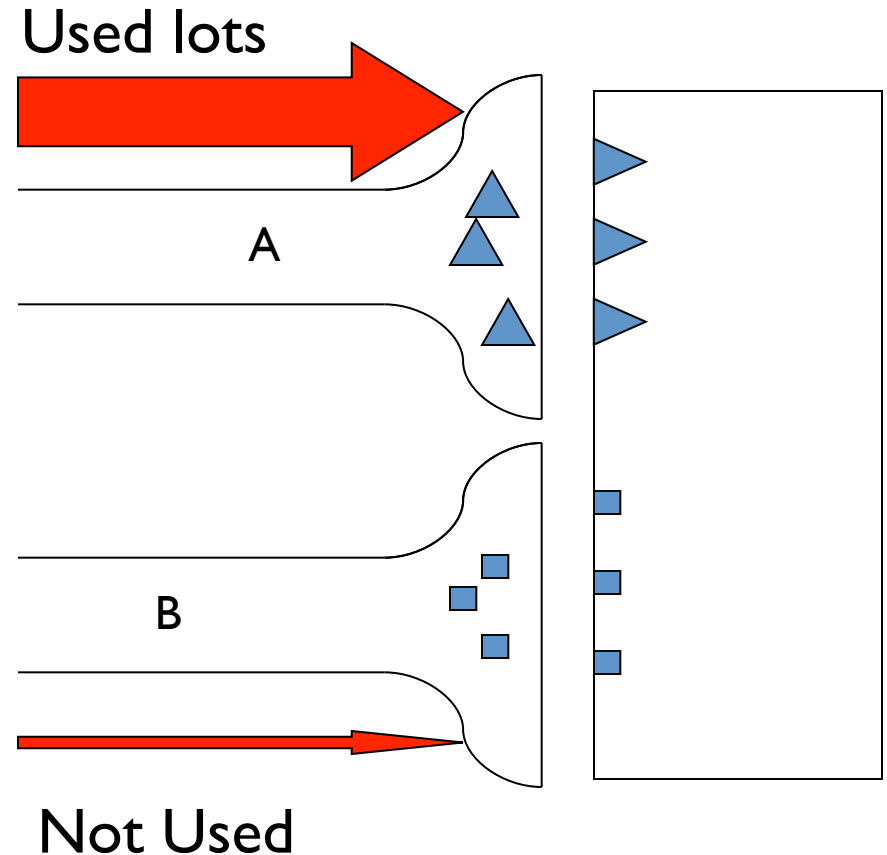


How do Neurons compute?

- By changing conduction and ion potentials.
- Made possible by Neurotransmitters.
- Strengthening and weakening of synapses (Hebbian learning rule).

Strengthening synapses

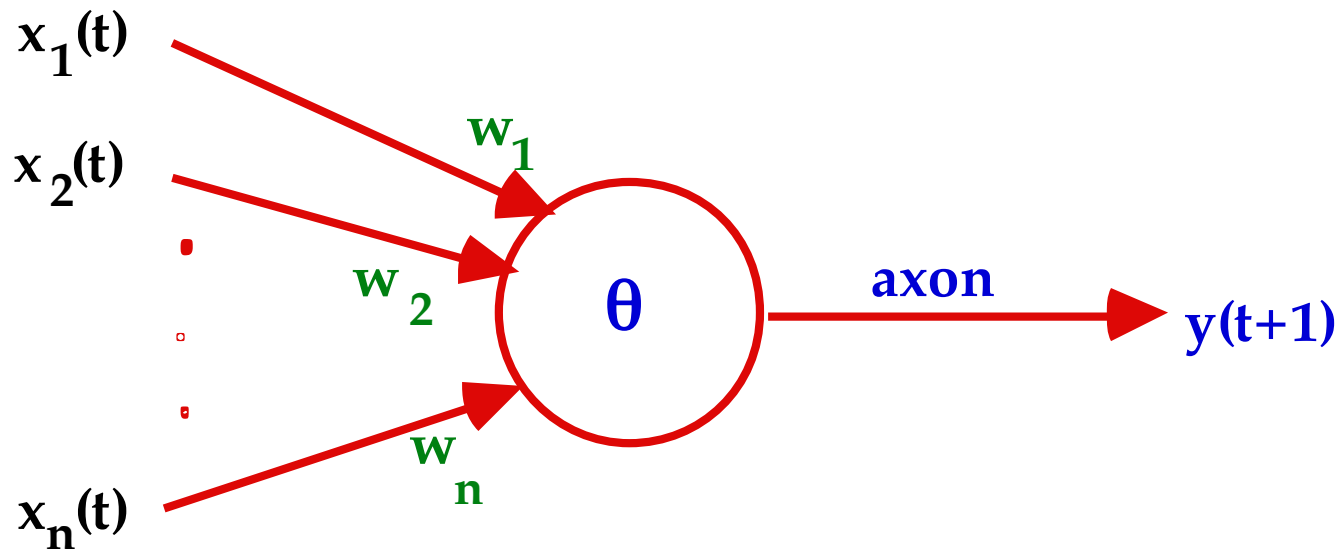
- Synapses used often are strengthened (A)
- Those not used are weakened and can become ineffective (B)



Neurons that fire together, wire together

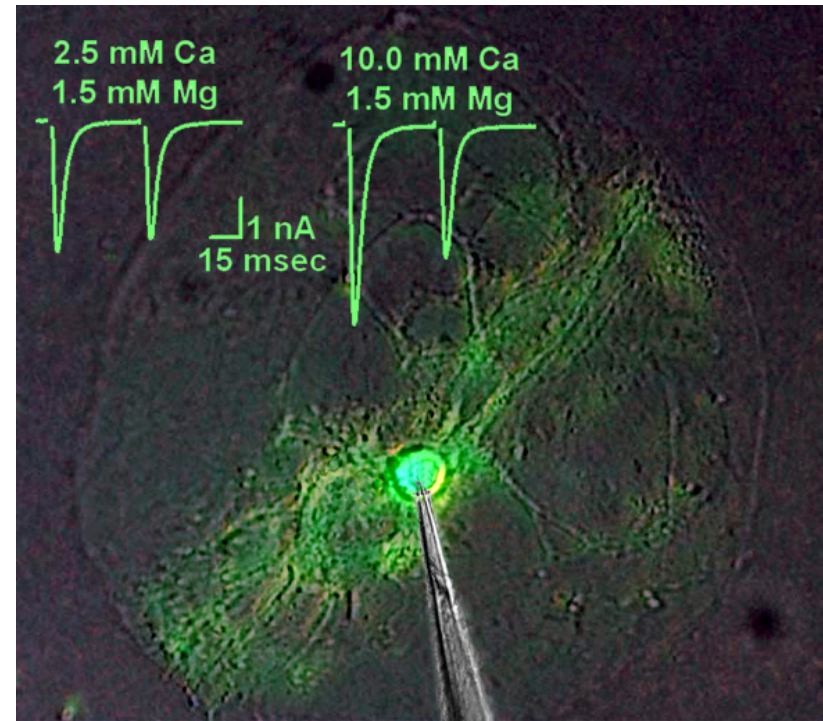
Learning Rule:

When two connected neurons are both excited, the connection between them is strengthened



Single-Cell Recording

- Electrical activity of a neuron is recorded via electrode implanted near the cell (sometimes inside the cell – see fig).
- Only feasible in animals or special cases where human brain surgery is involved.
- Multi-cell recording is possible via array of microelectrodes. Computer programs separate signals from different neurons.
- Rate coding: the *number* of action potentials is important (e.g. 40 spikes/sec). Spike coding: the *timing* of each action potentials is important (e.g. spike #1 occurred at 0.52 msec).
- Excellent temporal resolution, but limited to a few neurons.



Midterm

This is the last slide that will be on the midterm

No class on Monday

Check readings on Avenue

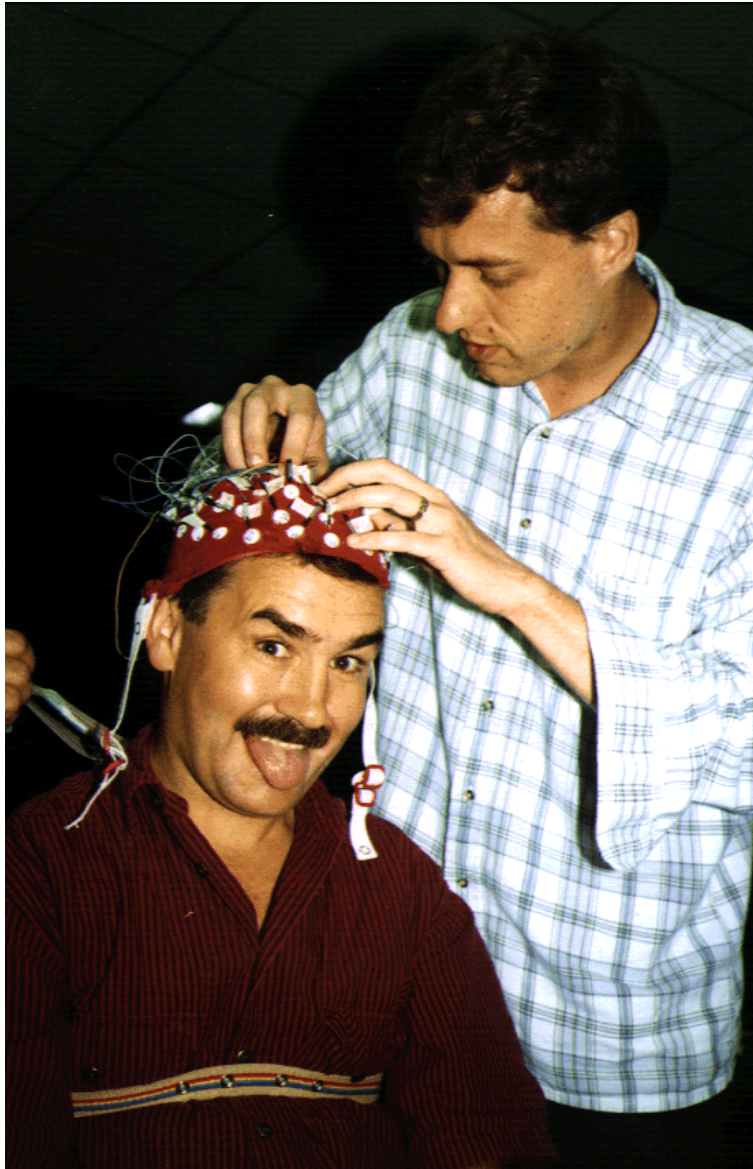
Important non-invasive techniques

- EEG: electroencephalography
- MEG: magnetoencephalography
- MRI: magnetic resonance imaging (structural and functional *aka* fMRI).

Positron emission tomography (PET)

Transcranial magnetic stimulation (TMS)

Electroencephalography by EEG



Quantity measured: electric potential on the scalp surface

Order of magnitude: 20 μ V

Temporal Resolution: ms

Spatial Resolution: cm

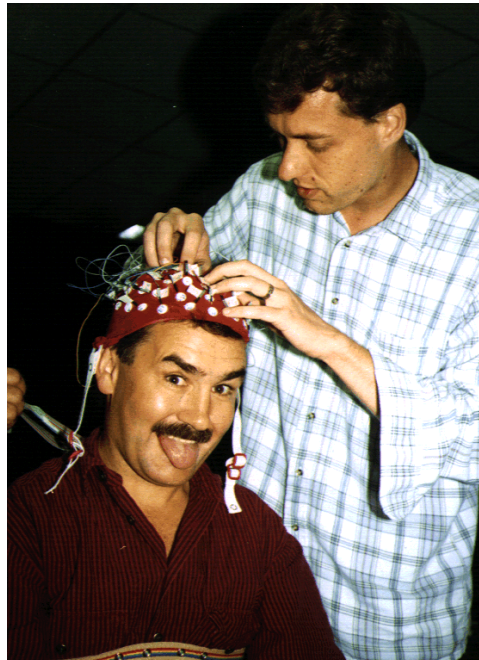
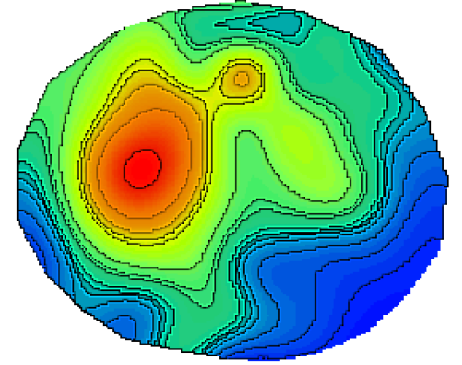
Cost: cheap

Advantage: easy to record

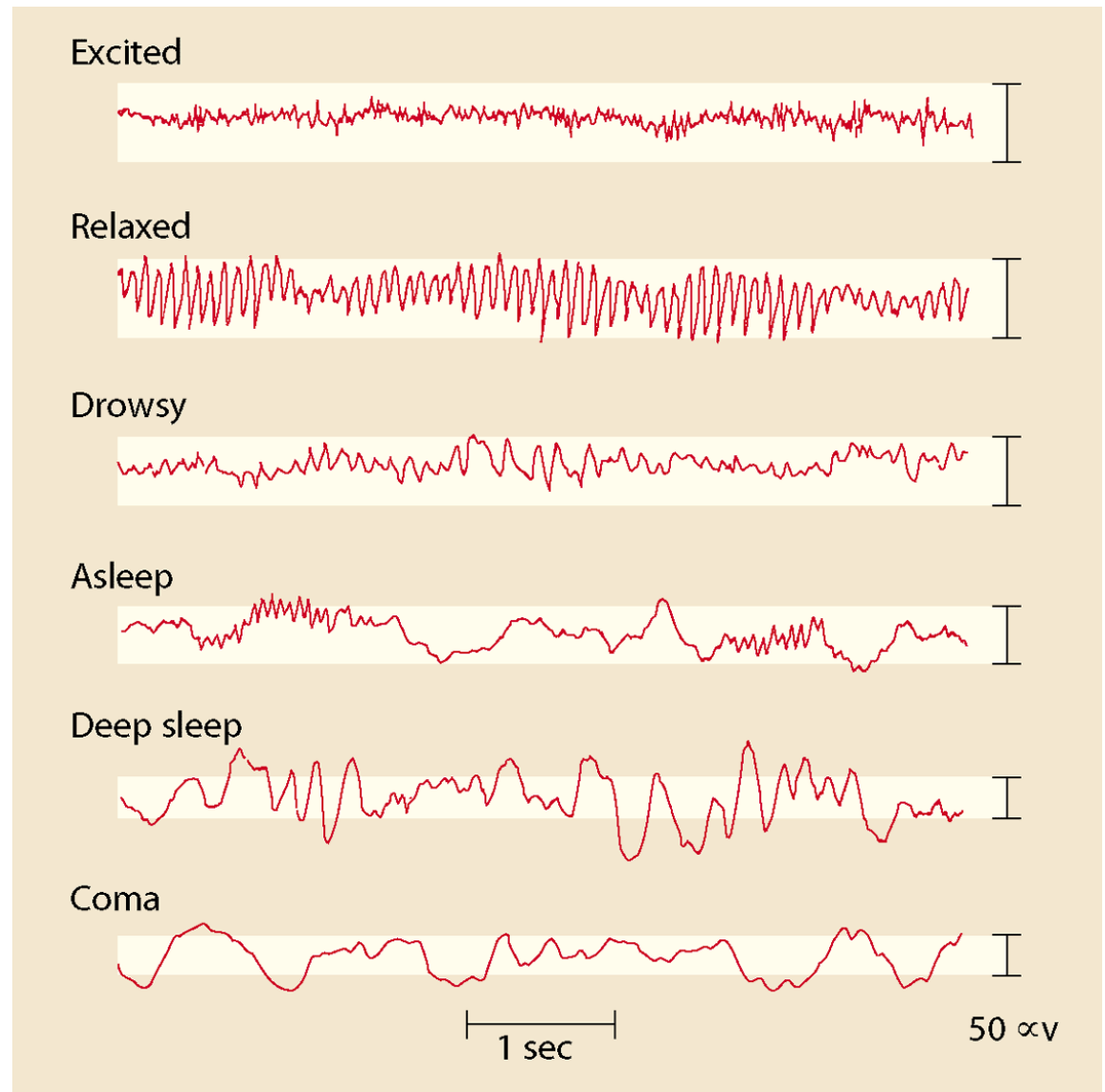
Disadvantage: signals get smeared before they reach the scalp



EEG Technology

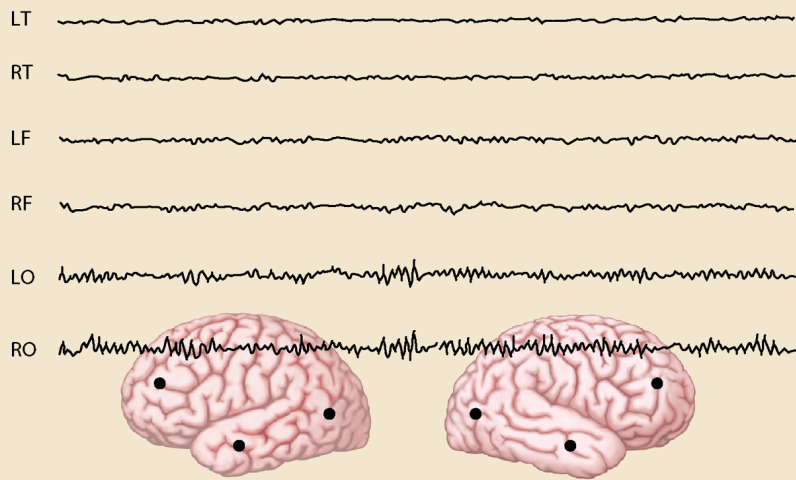


EEG



- Clinically useful as distinct brain states show characteristic EEG signal

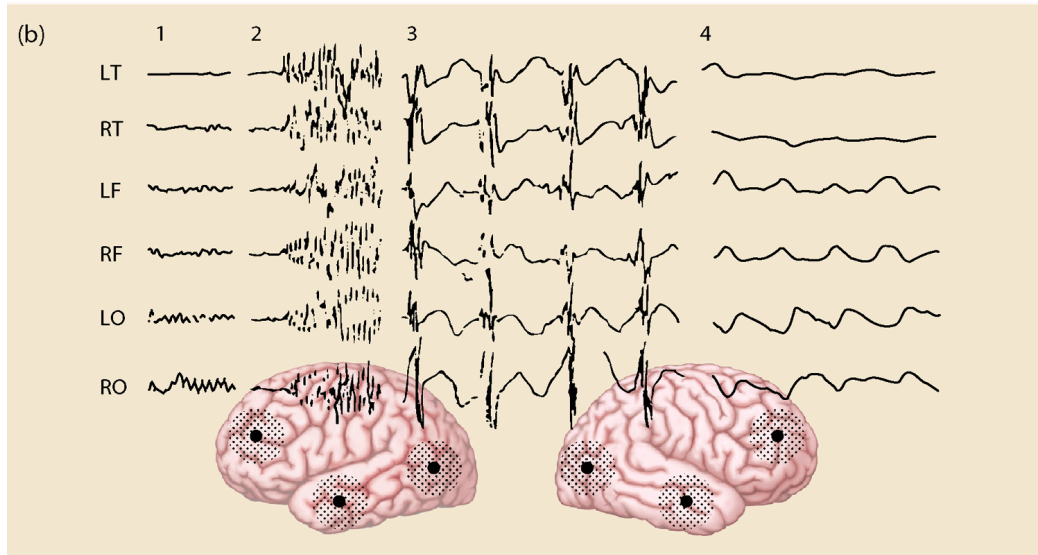
(a)



EEG

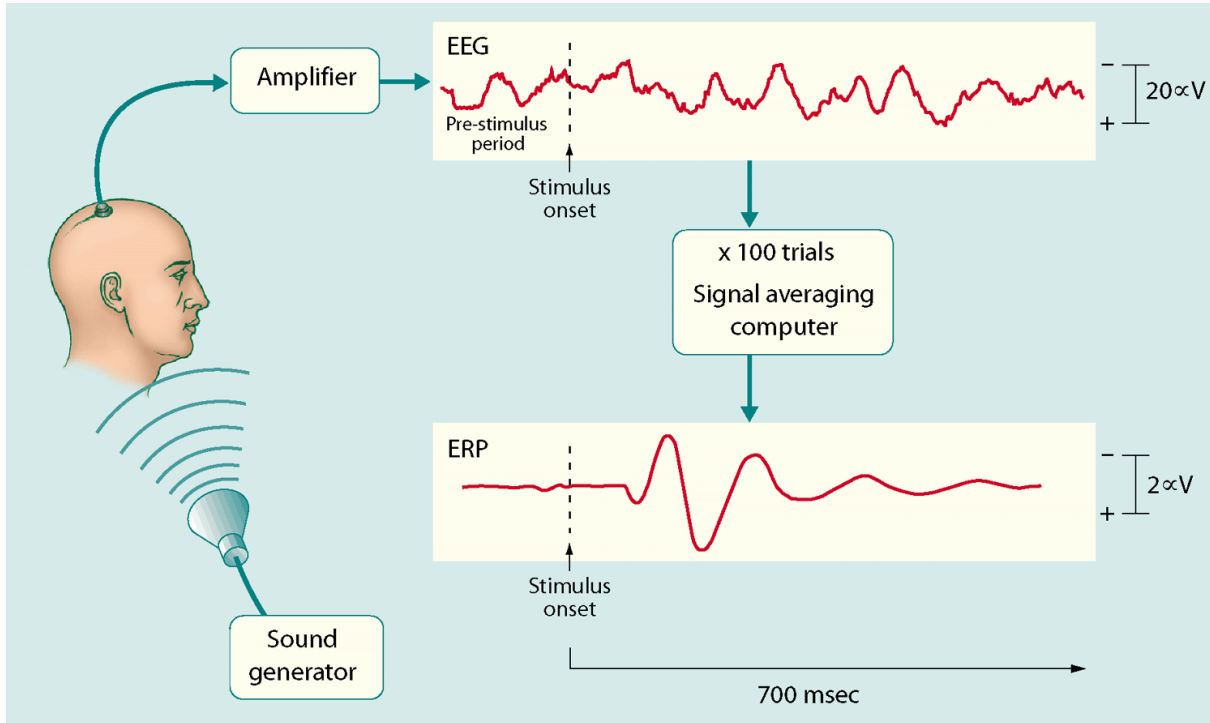
Normal Activity

Seizure Activity



- Clinically useful in determining the focus of epileptic seizure

EEG

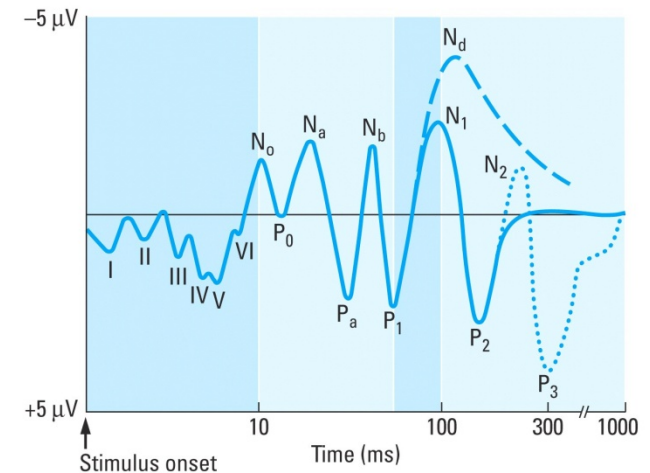
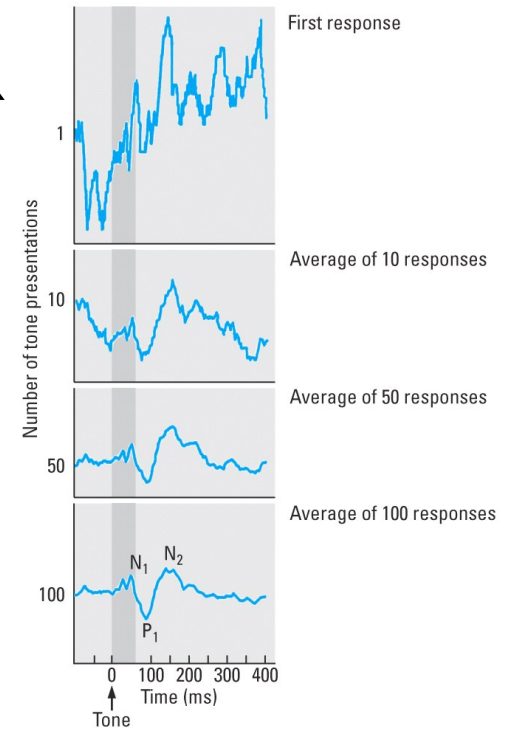


“Event-related Potentials”

- Background EEG signal can be removed by trial-averaging revealing the response of a brain region to stimuli

Event-Related Potentials (ERP)

- Changes in the EEG signal that are correlated with a discrete sensory stimulus (e.g. a light turning on).
- ERPs difficult to detect because they are weak and embedded in noise -> averaging needed.
- Peaks and troughs in the ERP waveform associated with different stages of processing (e.g. early sensory stages vs. later cognitive stages).
- Evolution of the ERP wave through the brain over space and time shows processing pathways.



Magnetoencephalography y MEG



Quantity measured:
components of the magnetic
field

Order of magnitude: 100fT

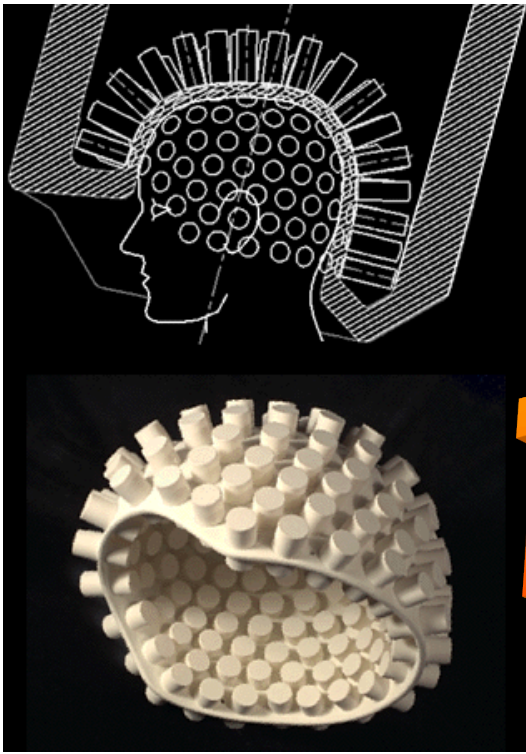
Temporal Resolution: ms

Spatial Resolution: cm

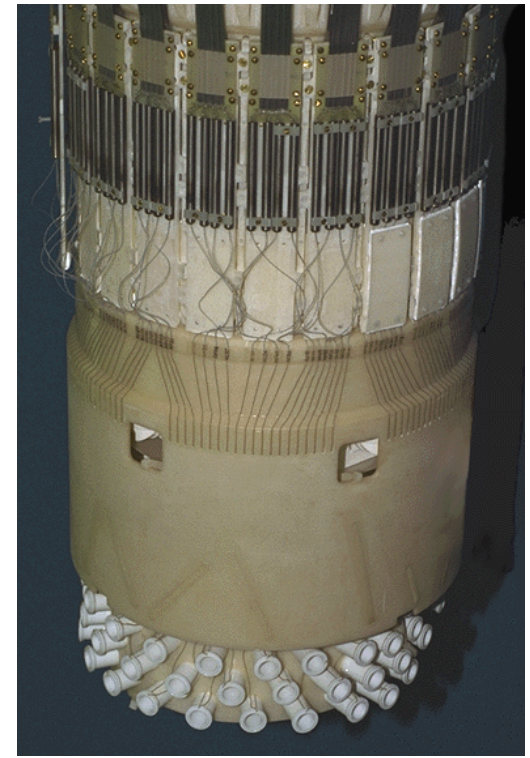
Cost: expensive

Advantage: Clean signals

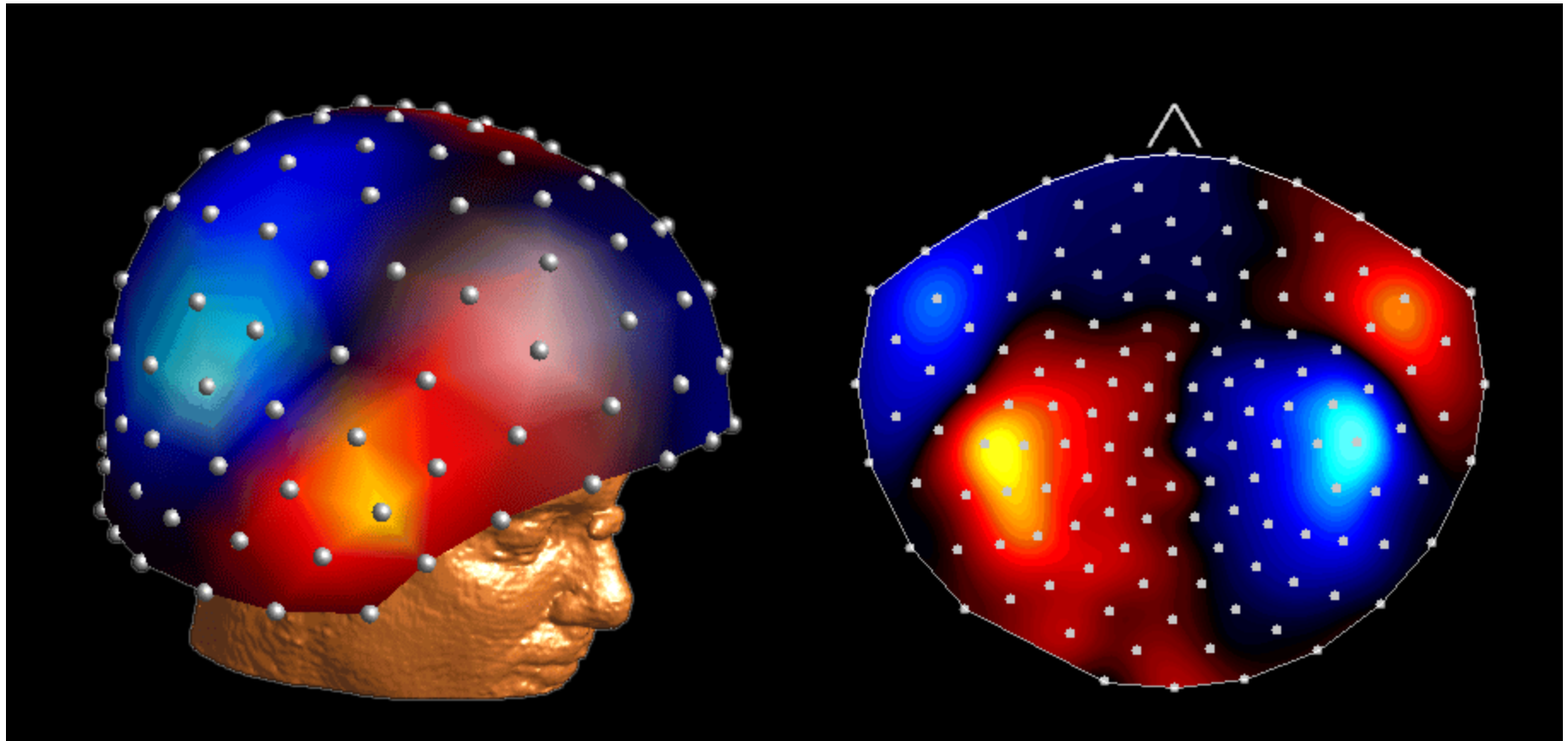
Disadvantage: Insensitive to
radial currents



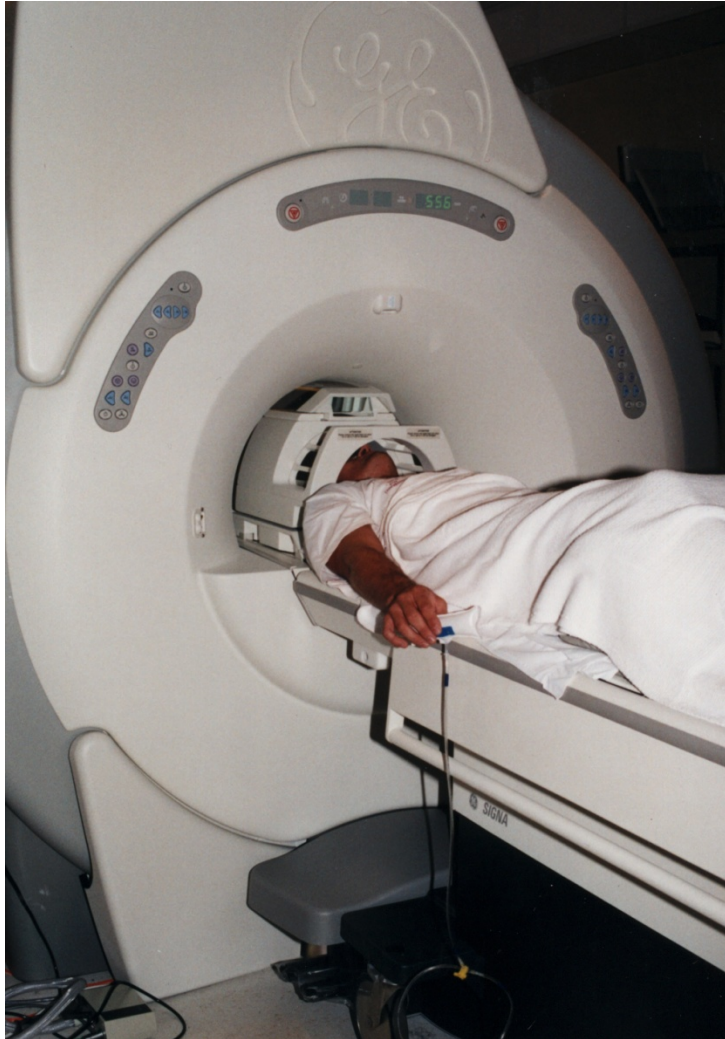
MEG Technology



Magnetic field on subject's head and in polar projection



Magnetic Resonance Imaging: MRI



Quantity measured: 'water content' of the brain tissue

Knowledge gained: brain structure

Temporal Resolution: min

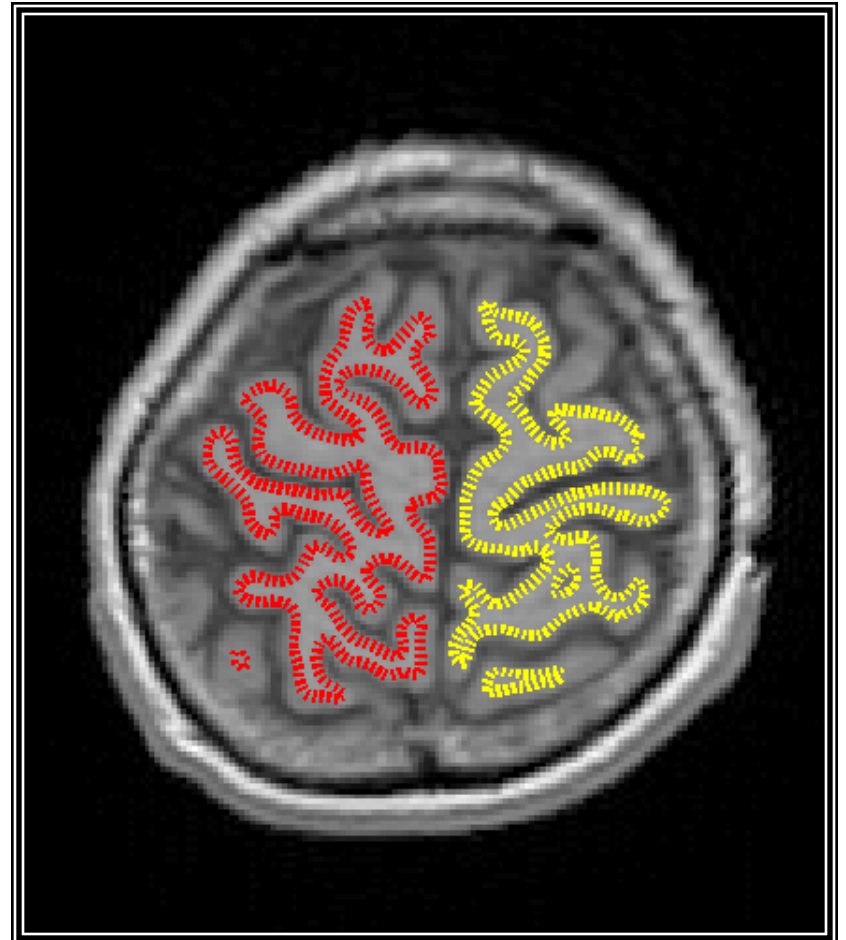
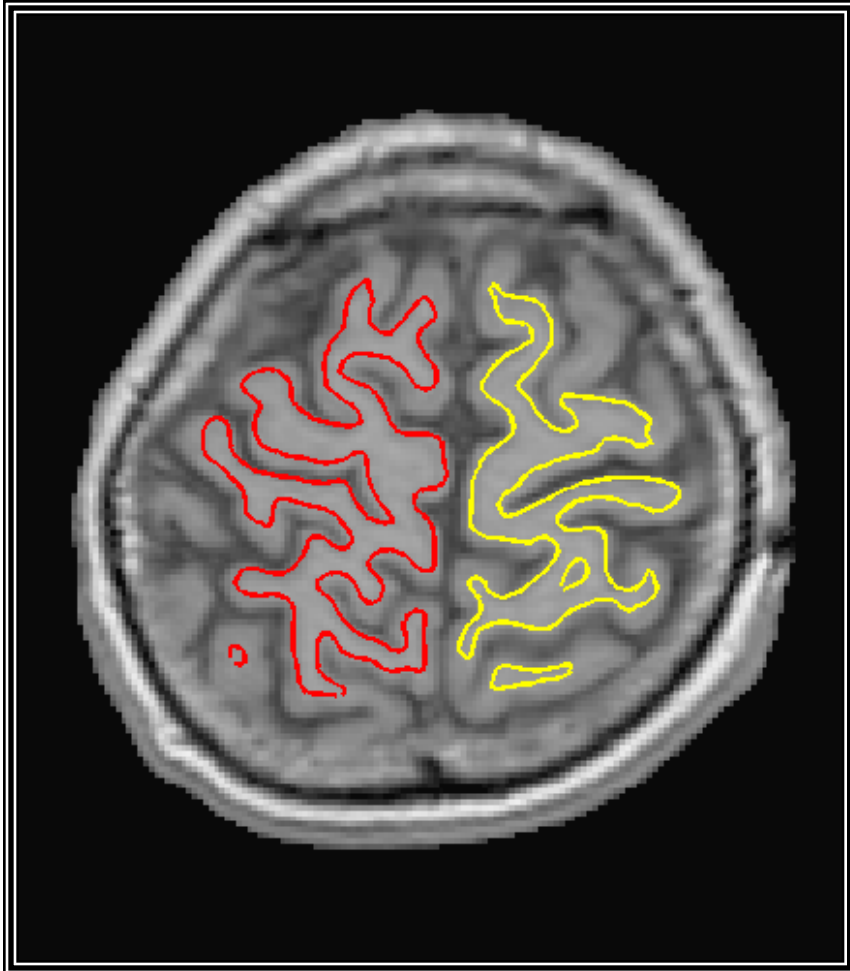
Spatial Resolution: mm

Cost: expensive

Advantage: 3D-volume resolution

Disadvantage: no functional or temporal information

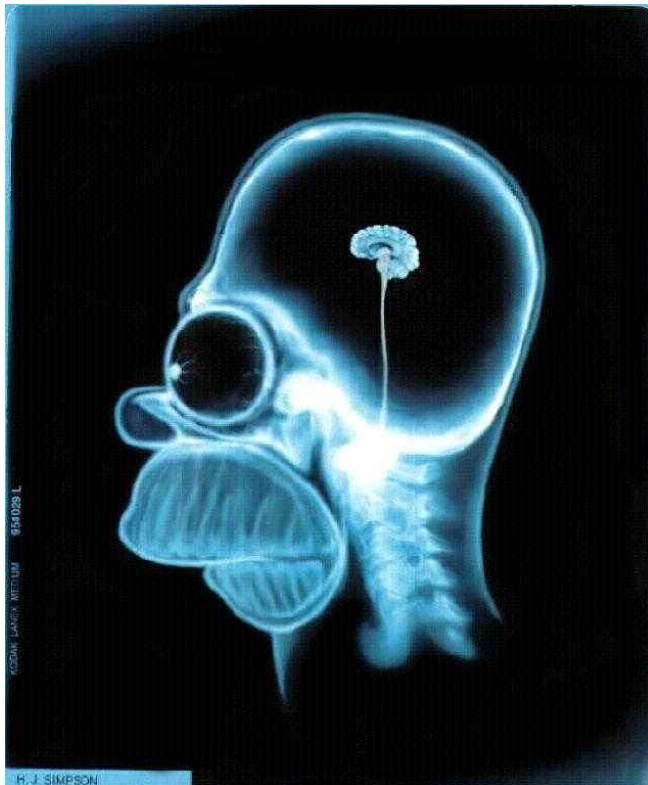
Using the gray-white matter boundary as an anatomical constraint



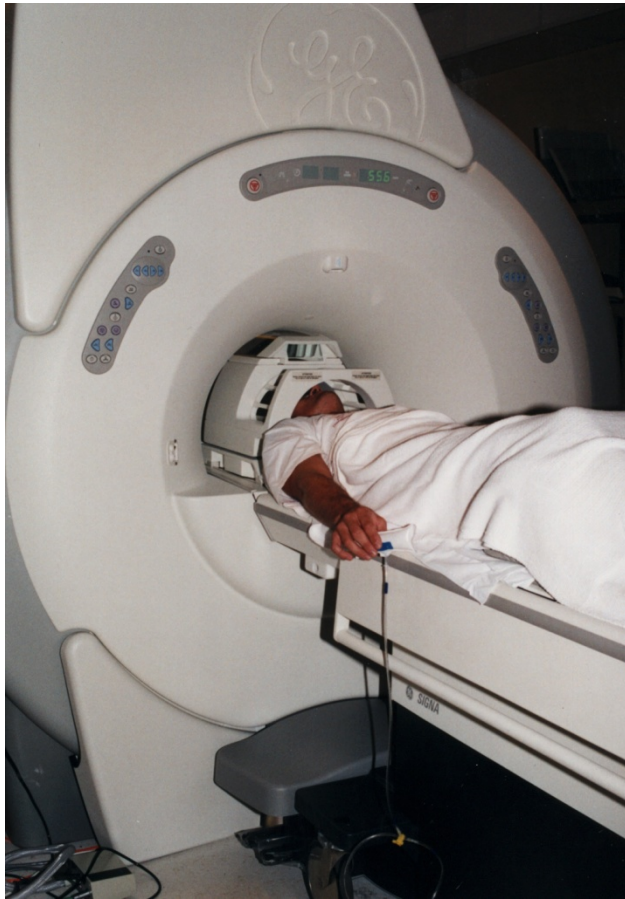
MRI vs. fMRI

MRI studies brain anatomy.

Functional MRI (fMRI) studies brain function.



Functional Magnetic Resonance Imaging: fMRI



Quantity measured: ratio between oxy- and deoxyhemoglobin

Knowledge gained: activated areas

Temporal Resolution: sec

Spatial Resolution: mm

Cost: expensive

Advantage: 3D-volume resolution

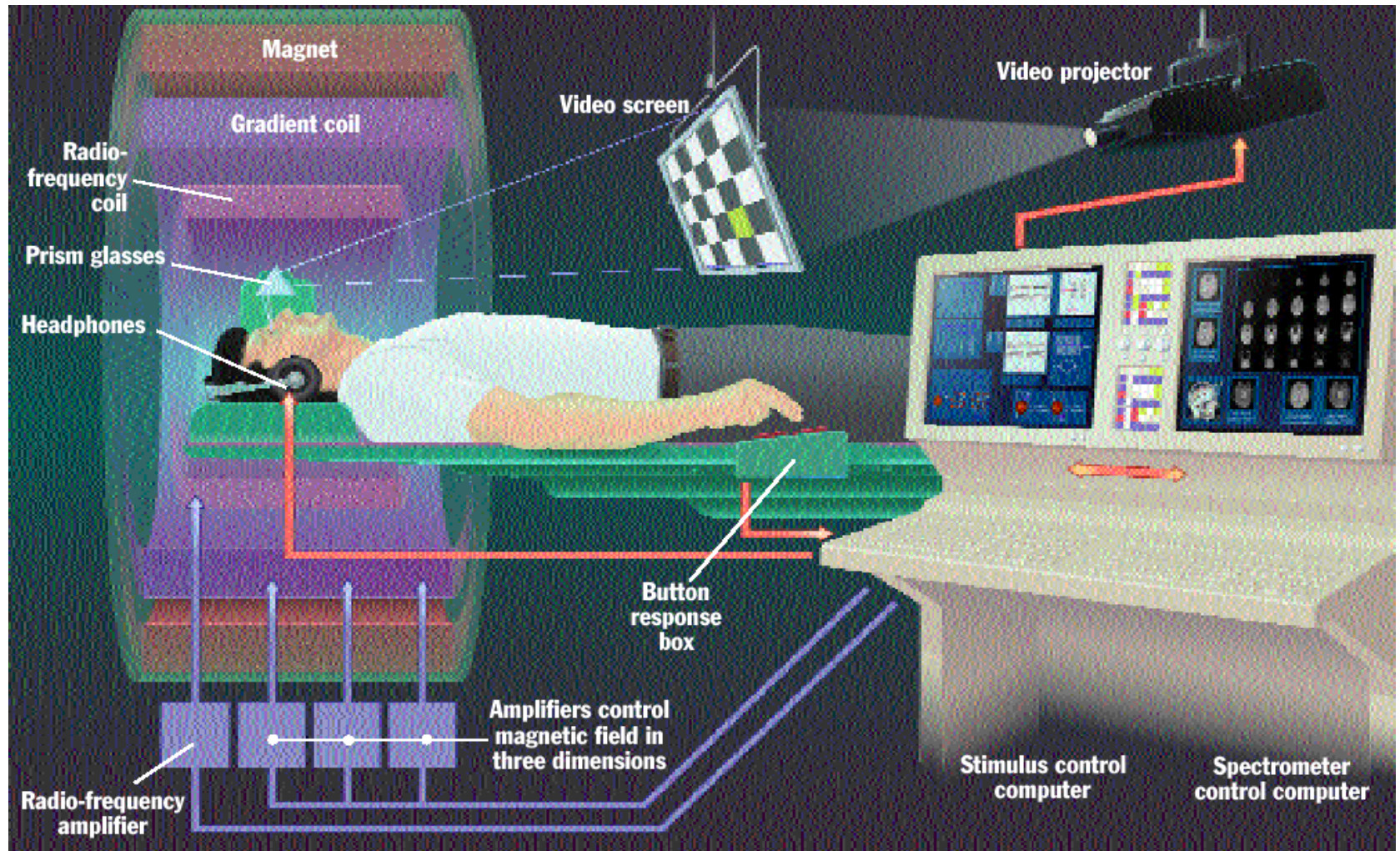
Disadvantage: low temporal resolution, no straight forward analysis

How powerful is this magnet

- About 250,000 more powerful than the earth's magnetic field.



fMRI Setup



fMRI Experiment Stages: Prep

1) Prepare subject

- Consent form
- Safety screening
- Instructions

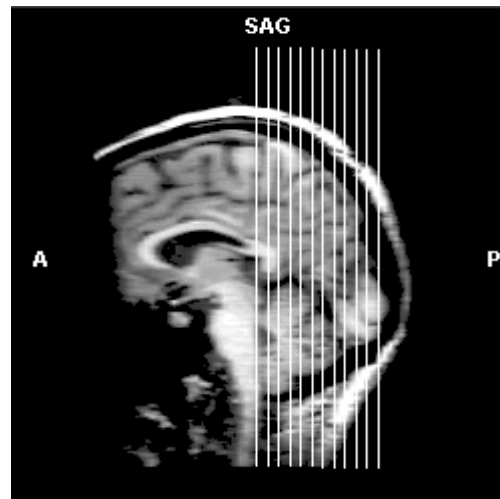
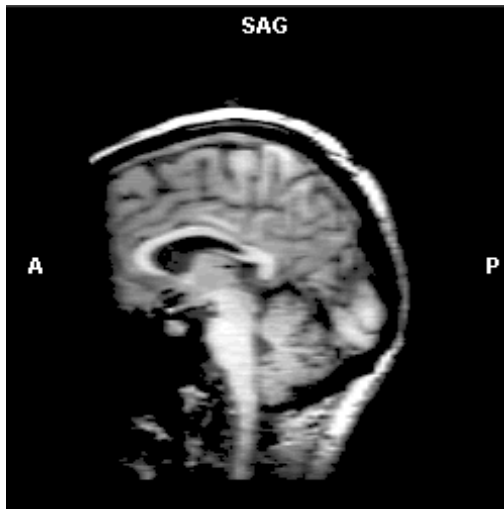
2) Shimming

- putting body in magnetic field makes it non-uniform
- adjust 3 orthogonal weak magnets to make magnetic field as homogenous as possible

3) Sagittals

Take images along the midline to use to plan slices

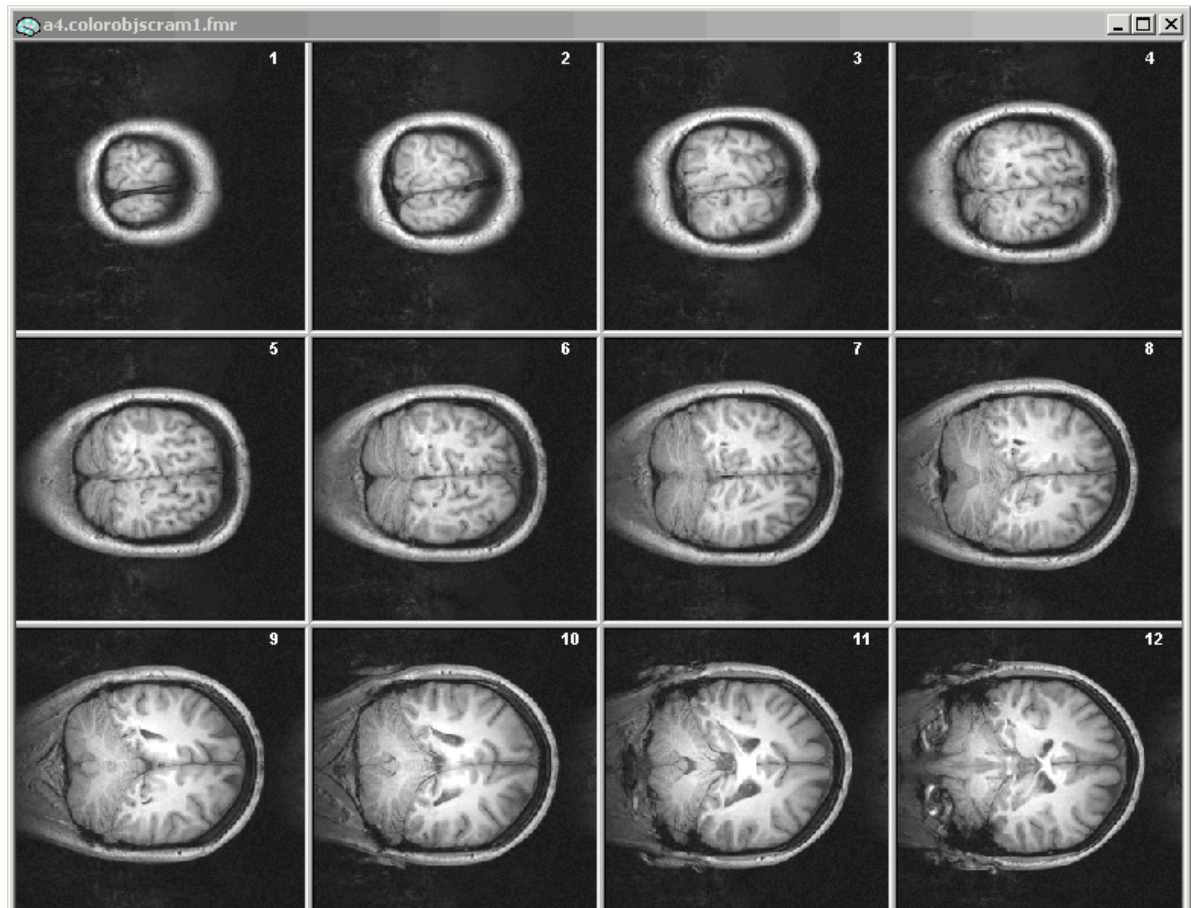
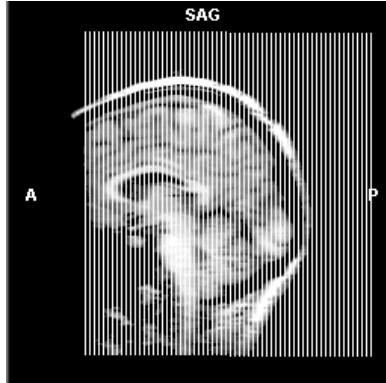
Note: That's one g, two f's



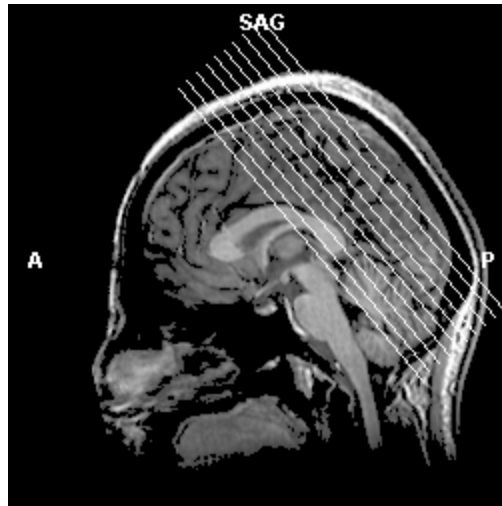
fMRI Experiment Stages: Anatomicals

4) Take anatomical (T1) images

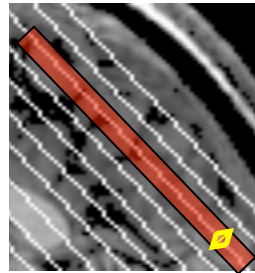
- high-resolution images (e.g., 1x1x2.5 mm)
- **3D data**: 3 spatial dimensions, sampled at one point in time
- 64 anatomical slices takes ~5 minutes



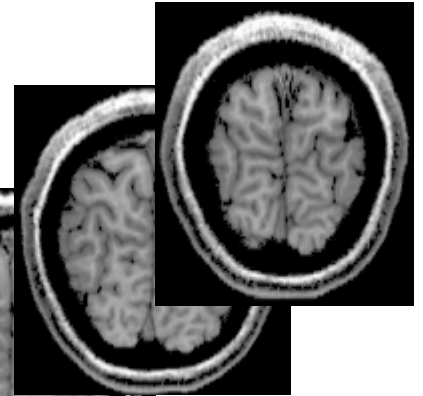
Slice Terminology



SAGITTAL SLICE

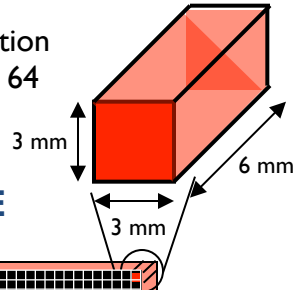


Slice Thickness
e.g., 6 mm



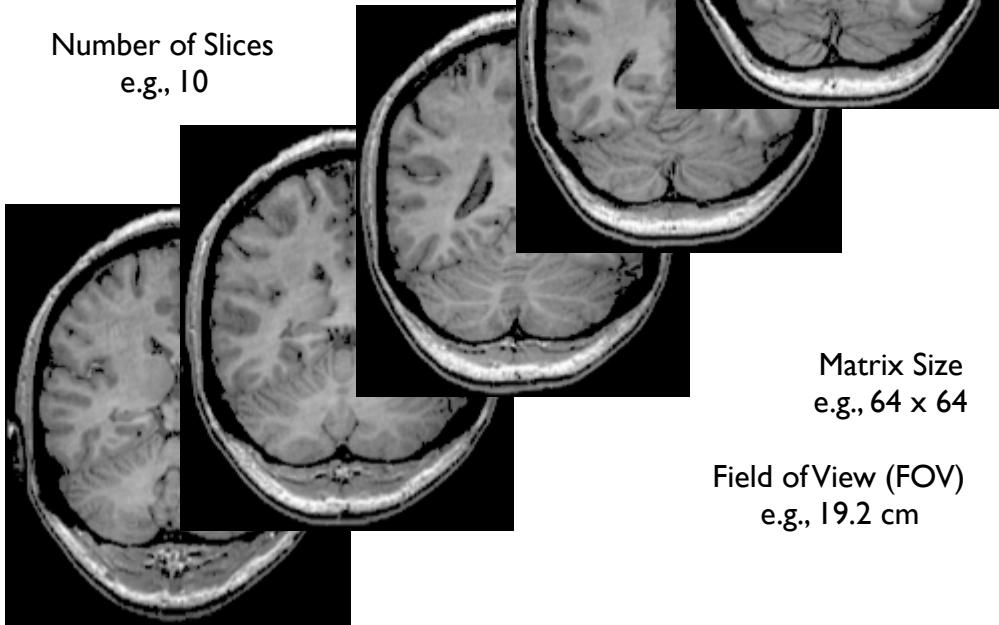
VOXEL
(Volumetric Pixel)

In-plane resolution
e.g., $192 \text{ mm} / 64$
 $= 3 \text{ mm}$



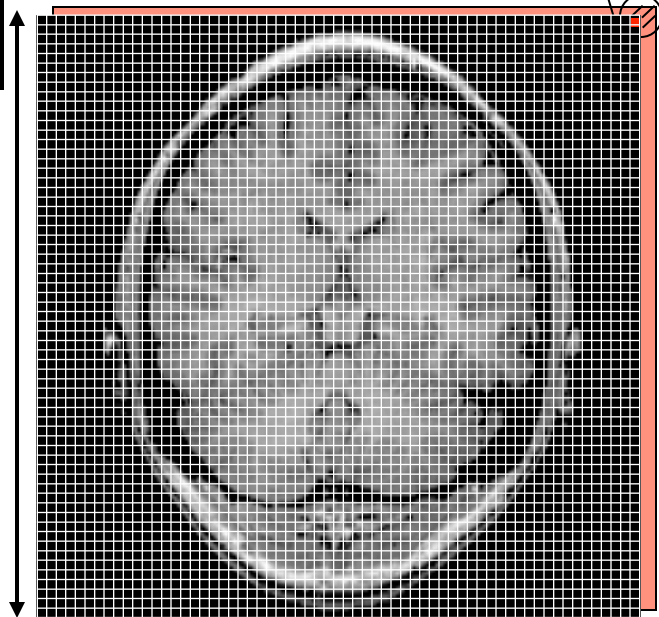
IN-PLANE SLICE

Number of Slices
e.g., 10

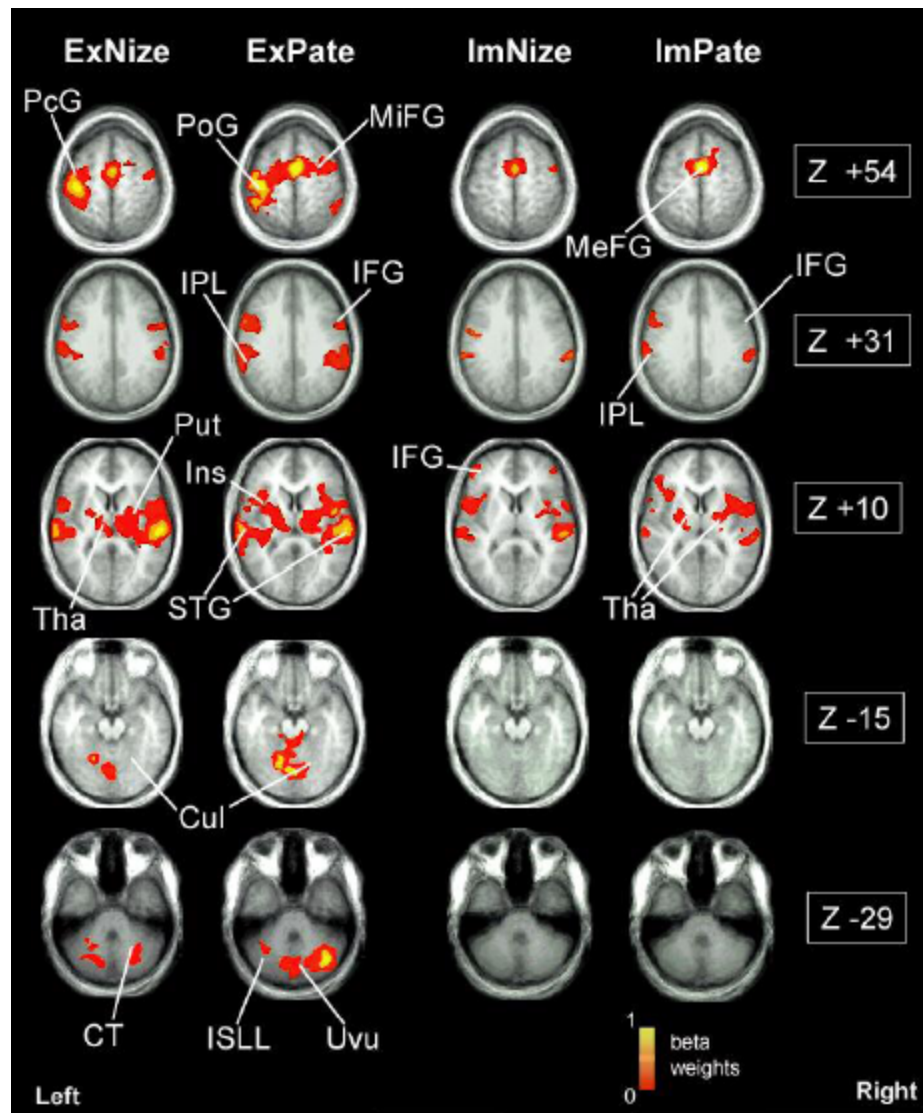


Matrix Size
e.g., 64×64

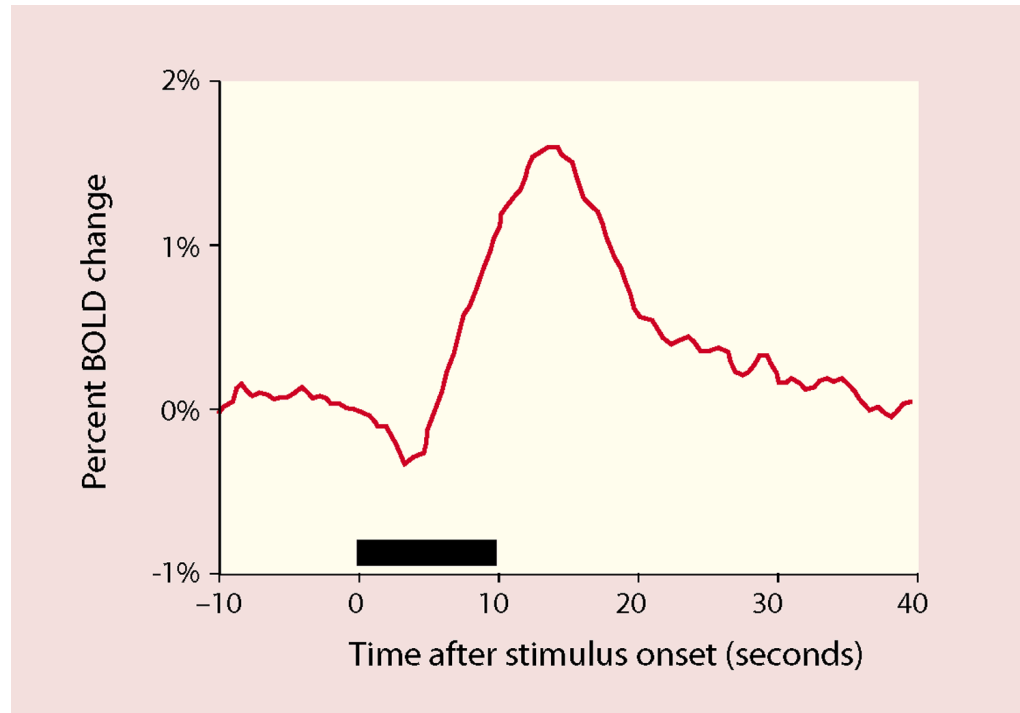
Field of View (FOV)
e.g., 19.2 cm



IMAGINATION vs EXECUTION OF MOVEMENTS



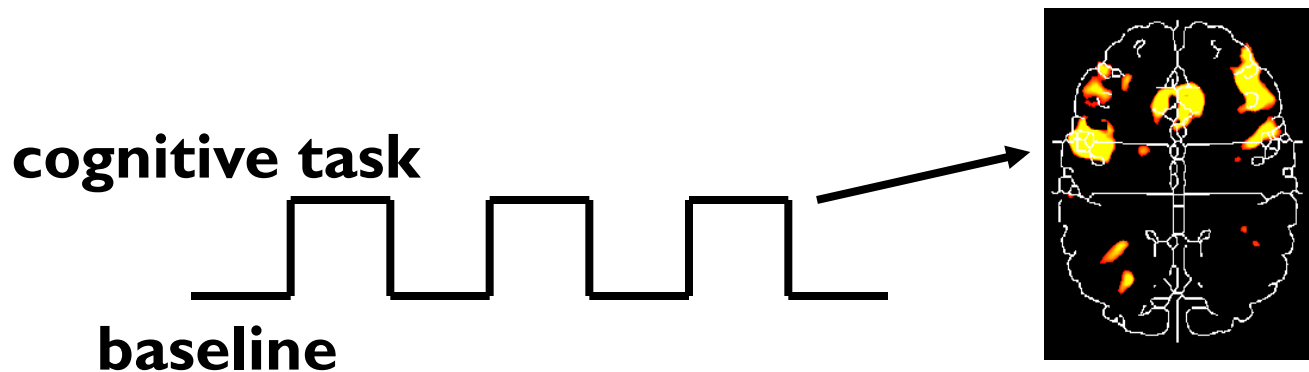
Functional MRI



- Takes advantage of the fact that neural activity is followed by blood flow in a highly predictable manner
- Altered blood flow alters RF signal from active brain regions

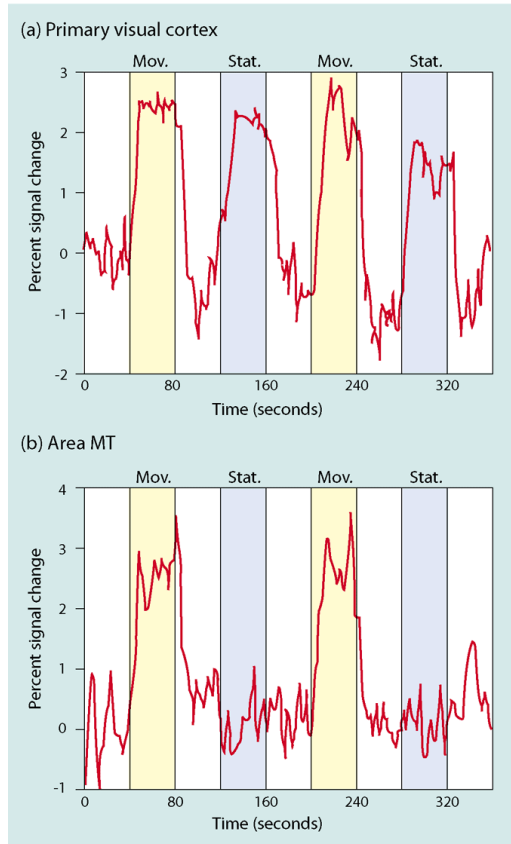
Functional MRI

- Permits examination of brain regions that become active during cognitive performance



Facilitates comparison of brain activity in different population

Functional MRI

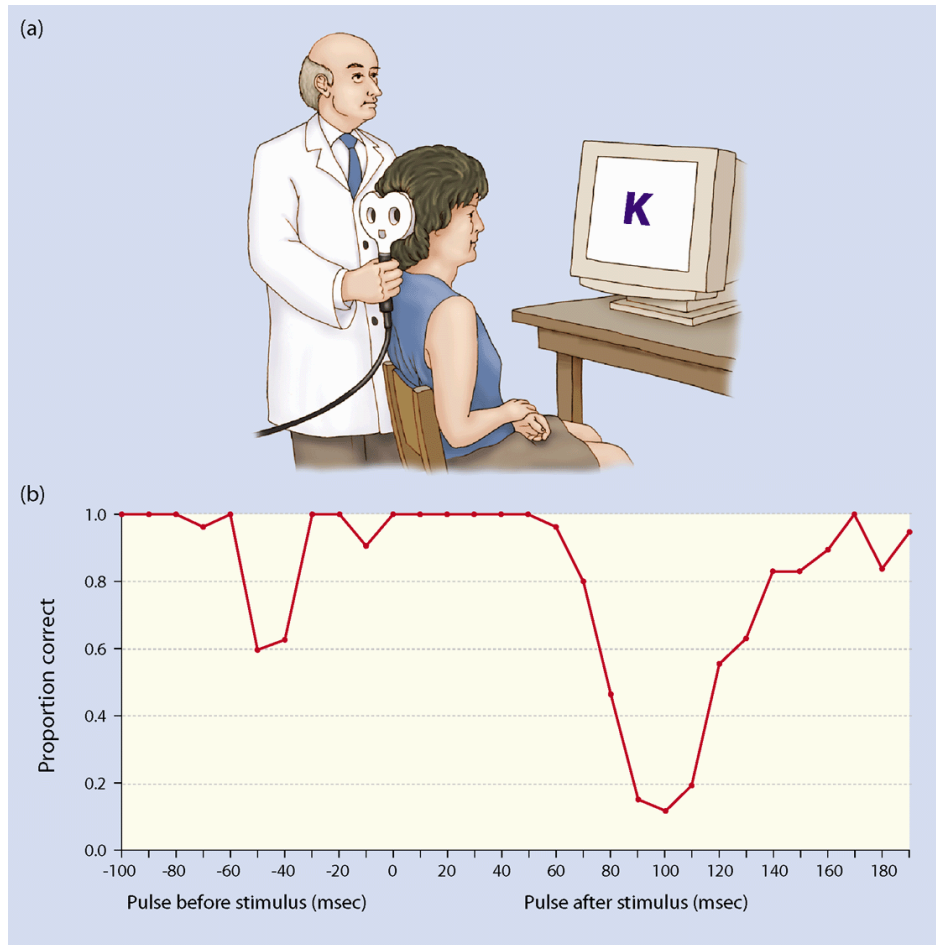


- Analysis methods take advantage of known hemodynamic properties of the brain

Magnetic Resonance Spectroscopy (MRS)

- Standard fMRI is tuned to the resonance frequency of hydrogen (component of water).
- MRI can be tuned to the resonance frequency of other chemicals (e.g. creatin -> label for neuron -> diagnosis of cell loss; choline -> precursor of ACh).

Transcranial Magnetic Stimulation

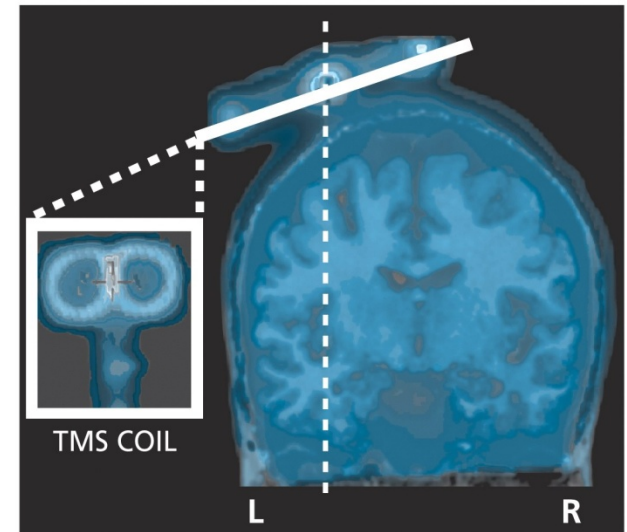
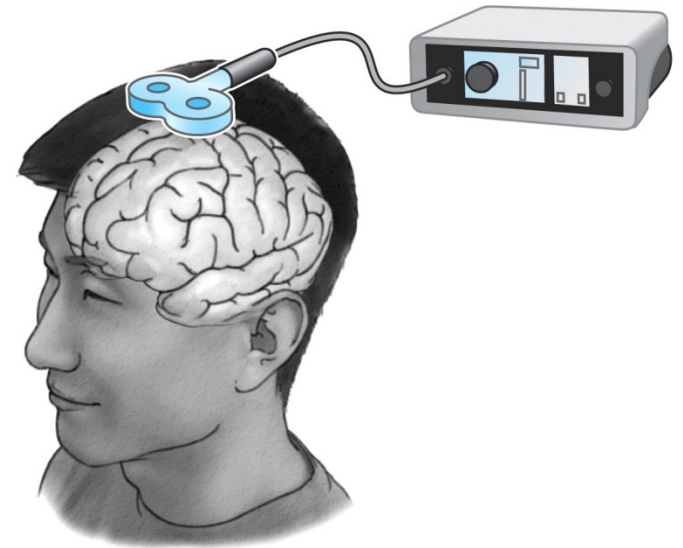


- Coil placed over target brain region
- Cognitive failures recorded



Transcranial Magnetic Stimulation (TMS)

- Focused oscillating magnetic fields can activate or suppress neural activity across the skull.
- Pluses and minuses:
 - Noninvasive.
 - Allows direct manipulation of neural activity.
 - Used as therapy for depression.
 - Single pulses affect brain activity for only a few seconds.
 - Repeated pulses can change brain activity for weeks.
 - Really scary.

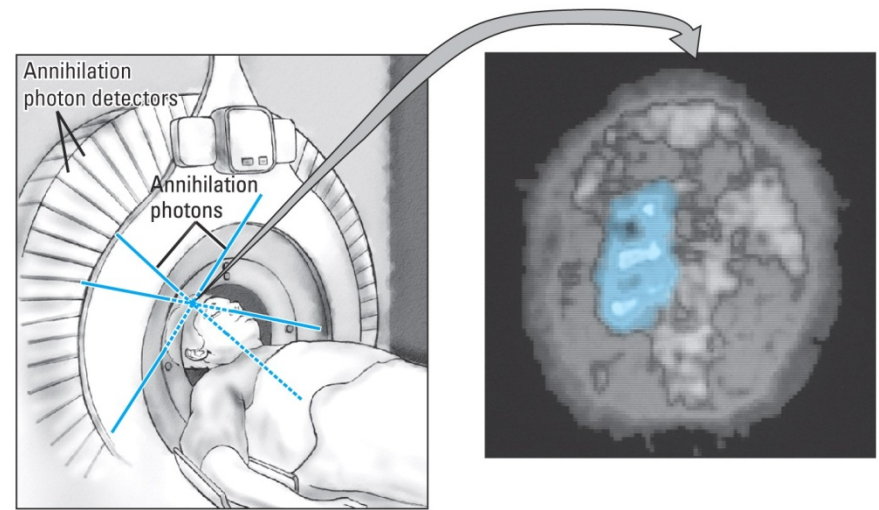


Positron Emission Tomography

- Type of tracer determines type of activity detected
 - ^{15}O radioactive oxygen, is injected into bloodstream with water
 - Measures blood flow
 - Radioactive Sugar
 - Measures metabolism

Positron-Emission Tomography (PET)

- Subject injected with radioactive substance into blood-stream.
- Radioactive substance flows to brain regions that are more active.
- Several substances can have radioactive labels (e.g. sugars, neurotransmitters).
- Doughnut-shaped camera that records radiation and reconstructs 3D model of radioactive source.
- PET images blood flow, not neural activity directly.
- Radioactive labels have short half-life and are rather safe.



One more time...

- Neurons & Neurotransmitters
- Single Neuron recordings
- EEG/MEG/MRI/PET
- MRI vs fMRI
- TMS and related techniques