

Lecture 2: Research Methods

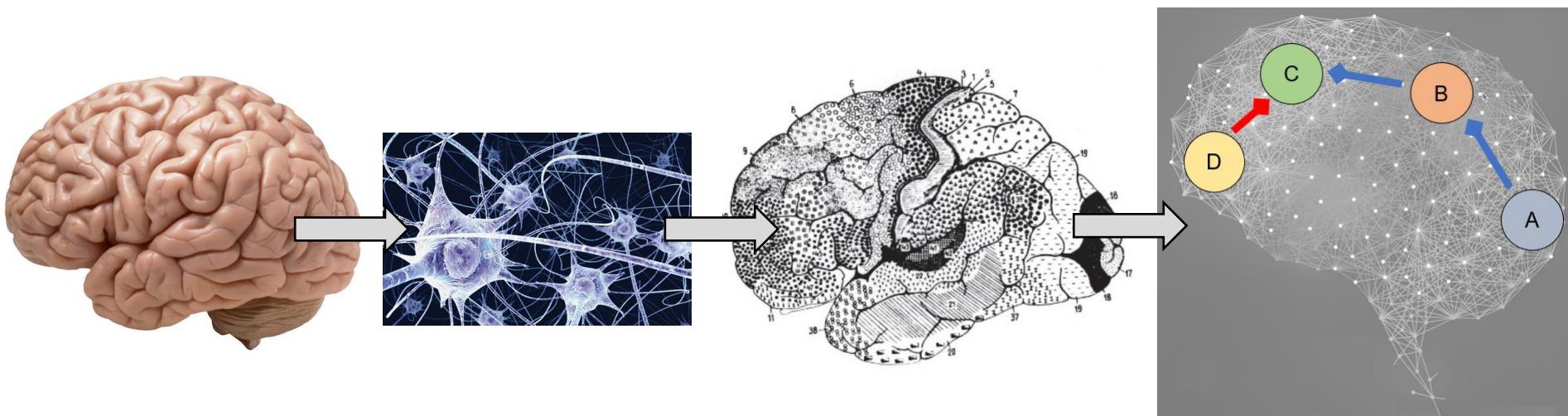
Cognitive Neuroscience (PSY493)
Paul Whissell, Ph.D.

Overview

- Part 1: Encoding information
- Part 2: Mental representations
- Part 3: Measuring brain structure and activity
- Part 4: Manipulating brain activity

Review

- Brain has ~90 billion cells, including **neurons**
- Neurons differ in structure/organization by area
- Distinct brain areas may exist and may form **networks**



Our perspective is that different cognitive processes are mediated by different networks.

Consider two experiences...

Falling in love

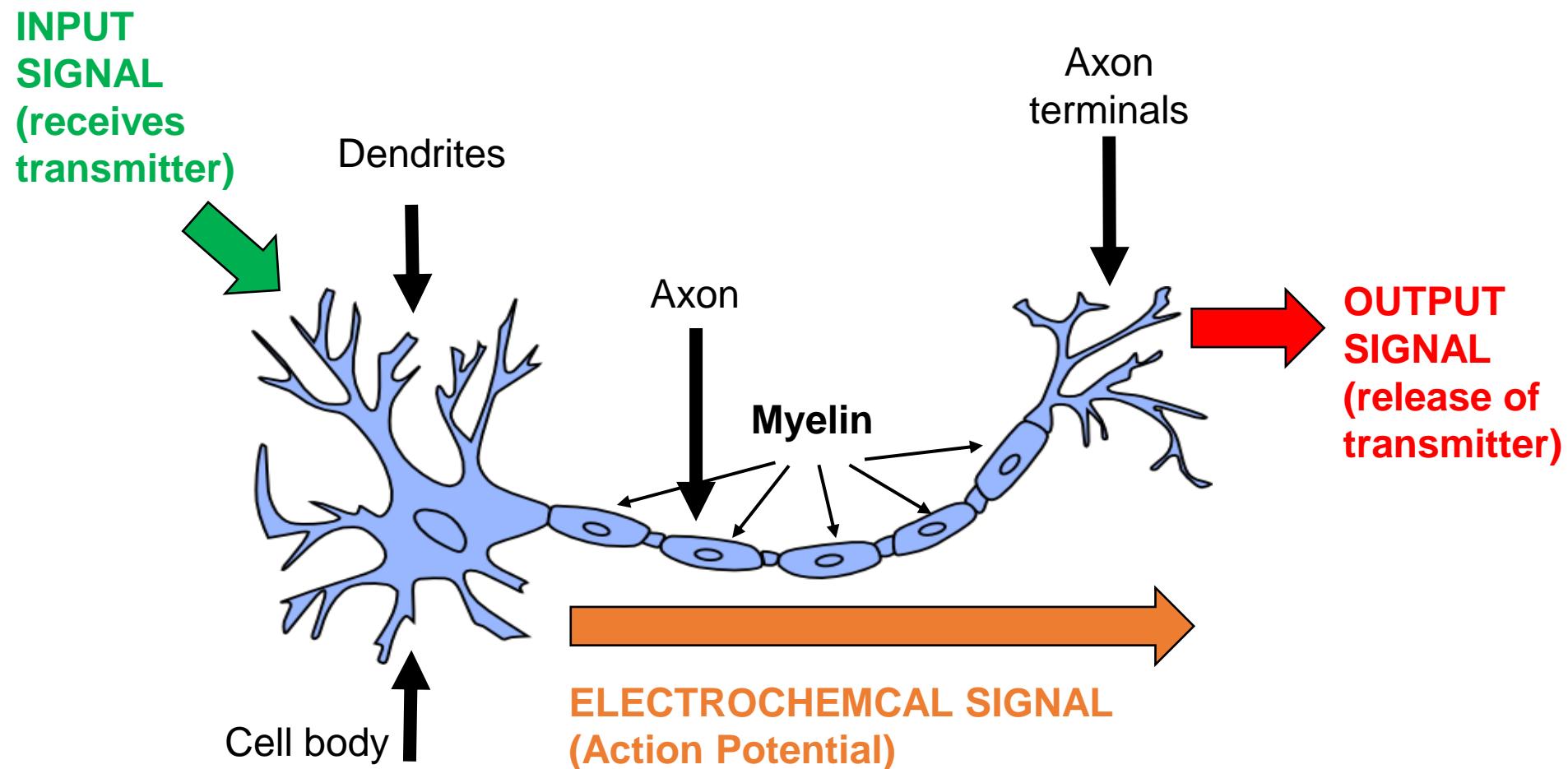


Presentation anxiety



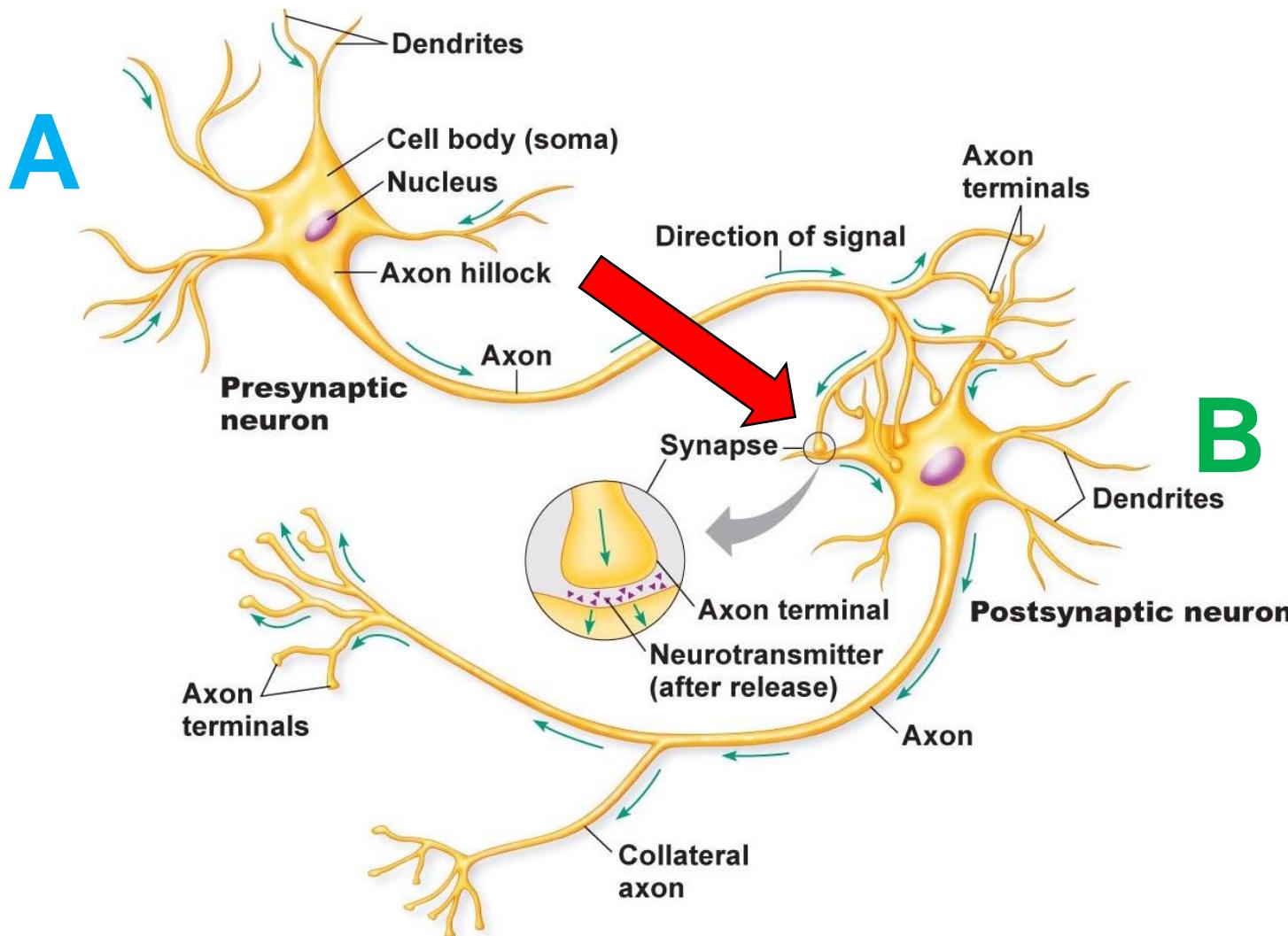
- Associated w/different thoughts, physiological reactions and effects on decision-making
- *How does the same brain (i.e. group of neurons) generate two radically different experiences?*

Neurons encode information



Excitable cells that generate and conduct electrochemical signals, provided they receive the necessary excitation.*

Neurons *intercommunicate*



Transmitter released by Neuron A travels across the synapse to affect Neuron B.

What *specific differences*
in action potentials are
meaningful for encoding?

Two main possibilities –

1. Different neurons are firing action potentials during different experiences (**population encoding**)
 - Is it *which neurons are firing* that matters?
2. The same neurons are firing action potentials during different experiences, but they do so at different rates (**rate encoding**)
 - Is it *how fast neurons are firing* that matters?

Let's investigate each of these possibilities!

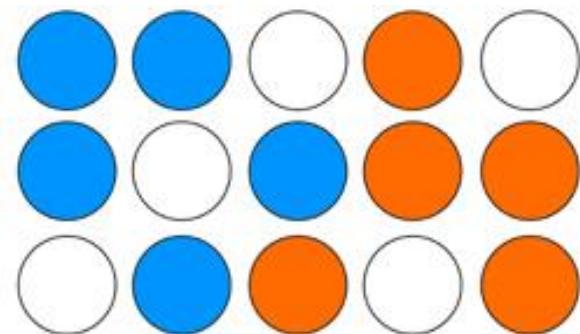
1) Population encoding

- Consider two different memories
- Each memory is associated with the activity of **different, non-overlapping populations of neurons**
- Theoretically, this **orthogonalization** could help us differentiate experiences

Memory 1



Memory 2

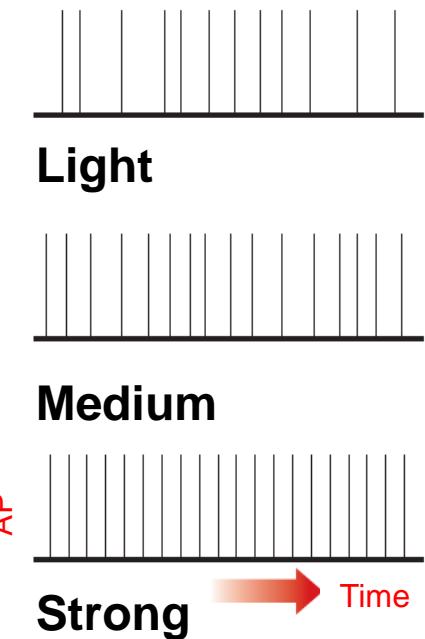
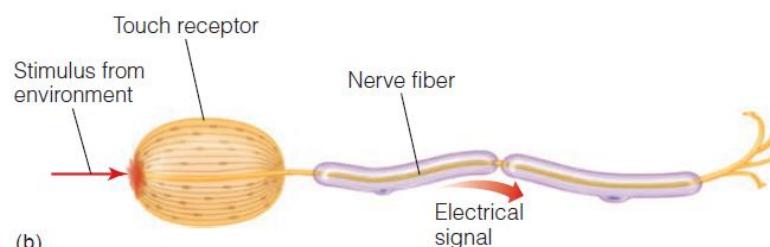
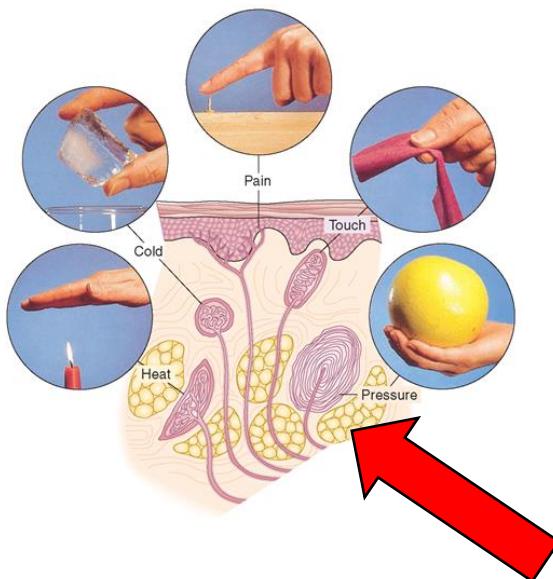


On population encoding...

- Consistent with the **localization of function perspective** mentioned earlier (L01)
 - Could explain why specific brain lesions impair specific cognitive processes
- **However, it is extremely unlikely** that all information is stored strictly through population encoding because:
 - Many neurons show spontaneous activity (fire without a particular stimulus being present)
 - Many neurons respond to more than one stimulus

2) Rate encoding

- The same neurons will fire in response to different stimuli, but at different rates
- Here, different levels of skin pressure elicit different firing rates in the same neuron



On rate encoding....

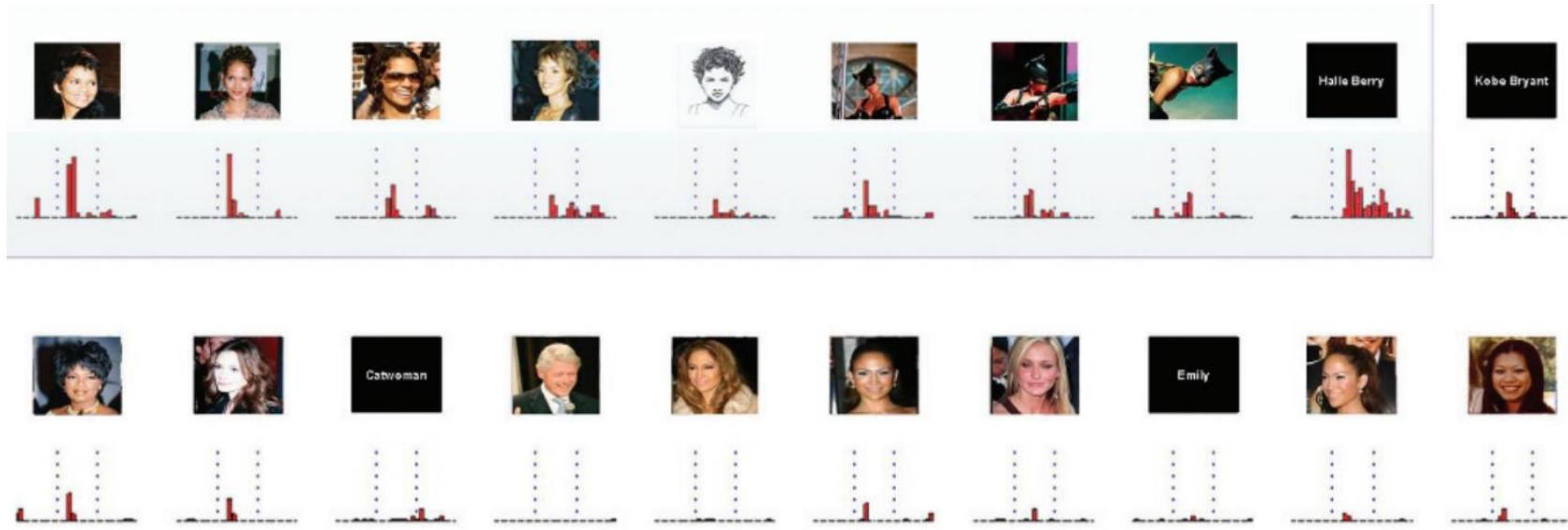
- **Huge advantage: economy of space and energy**
 - If each neuron is involved in many cognitive processes, you can handle many cognitive processes w/few neurons
- However, **it is also unlikely all processing is through rate encoding**, because:
 - Not every neuron fires constantly
 - Certain brain regions definitely appear to be more active during certain tasks and vital for certain tasks
- So, ***where do we go from here?***

An integrated solution

- The brain processes information using **both population + rate encoding**
- This reality has important implications for cognitive neuroscientists
- To understand a cognitive process, we must know **which neurons are active and how the activity of these neurons is changing**
- We will soon cover multiple techniques that allow us to measure brain structure and function (Part 3)

Example: The ‘Halle Berry’ Neurons

- Neurons that respond *most strongly* to pictures of Halle Berry (even when in costume) + the name ‘Halle Berry’

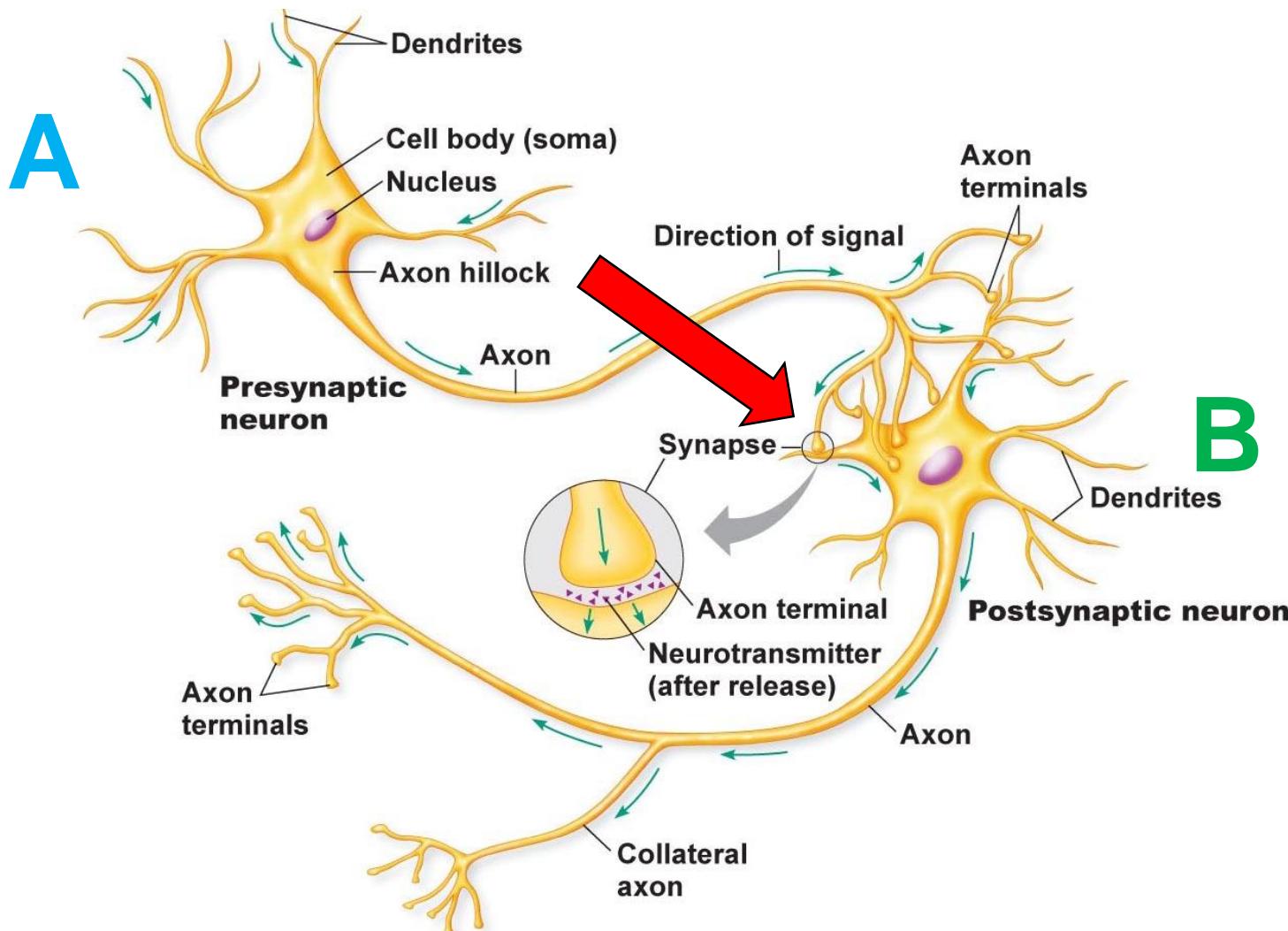


- These neurons are likely part of a larger population of cells that collectively ‘represent the concept of Halle Berry’ in your brain

There is also a ‘Jennifer Anniston neuron’ study.

If differences in firing rate
are meaningful, how are
they achieved?

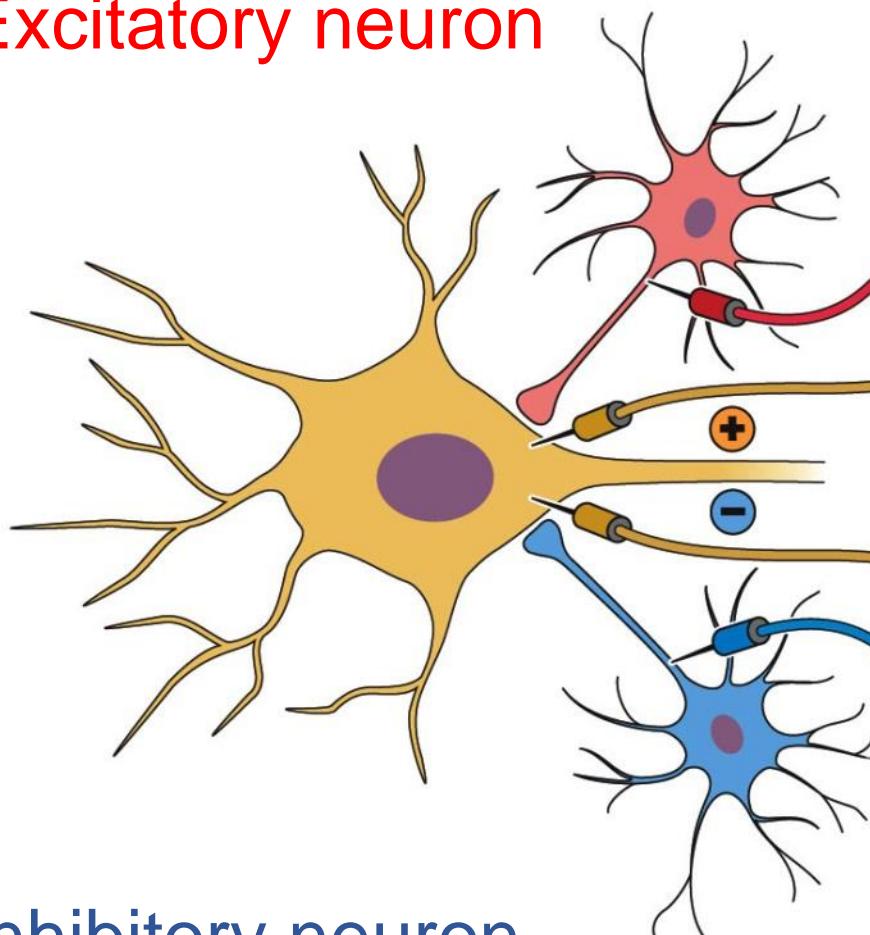
Modifying firing rate



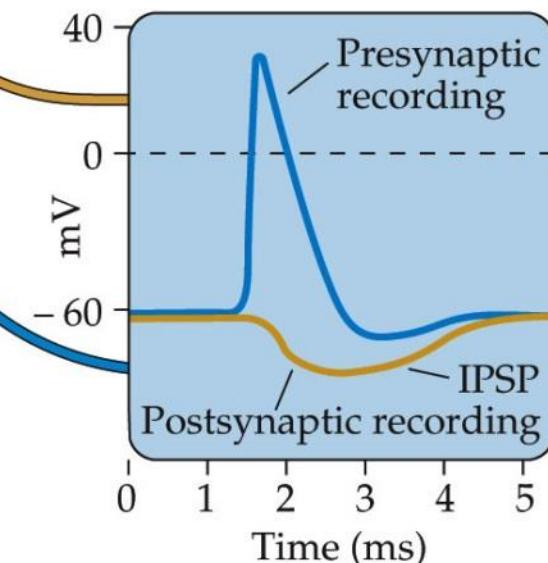
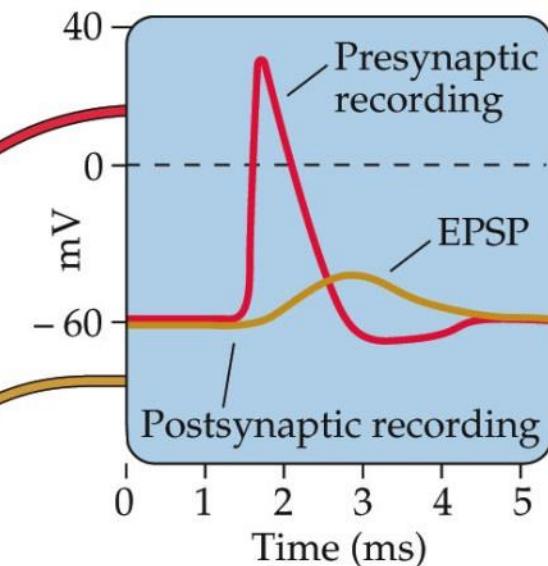
Neuron A can stimulate neuron B (**excitation**, increase firing) or inhibit it (**inhibition**, decrease firing)

Excitatory and inhibitory signals

Excitatory neuron



Inhibitory neuron



Different signals



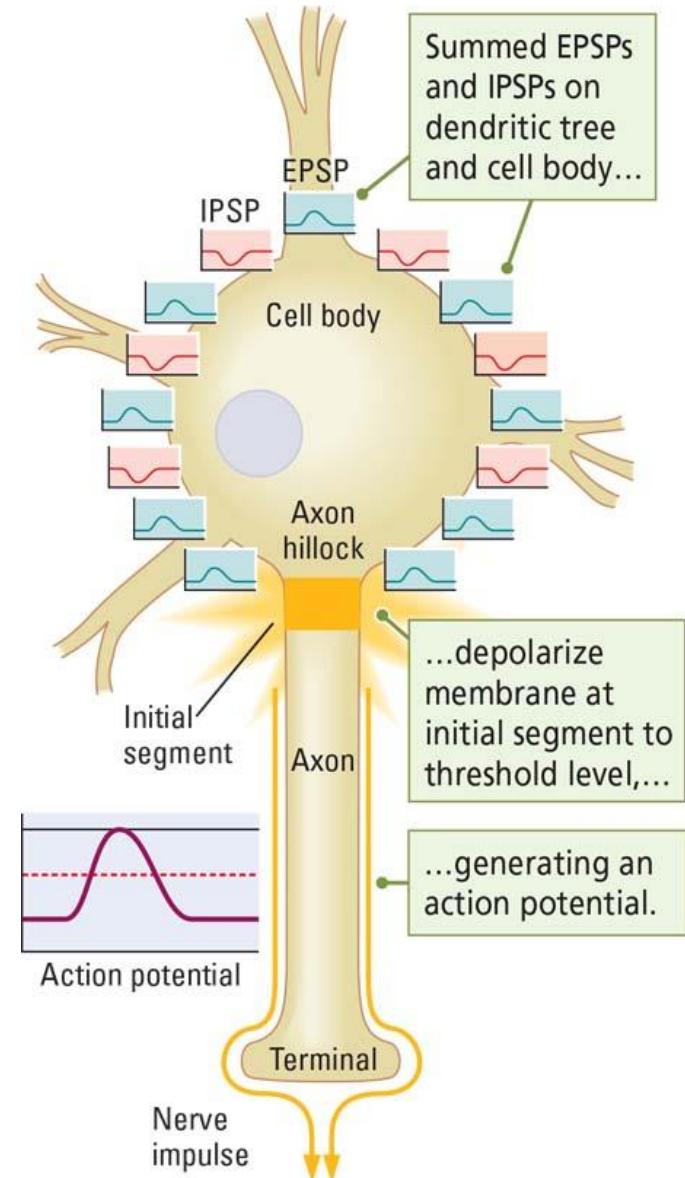
Glutamate = Neuron ON
(excitatory)

GABA* = Neuron OFF
(inhibitory)



Summation of signals

- Any one neuron receives many signals w/contrasting effects (**inhibitory** or **excitatory**)
- All signals are summed
- If the sum total exceeds a given threshold (excitatory >>> inhibitory), the neuron will fire
- Analogy: When a candidate gets just enough votes to win



Examples of transforming input

Distinguishing experiences

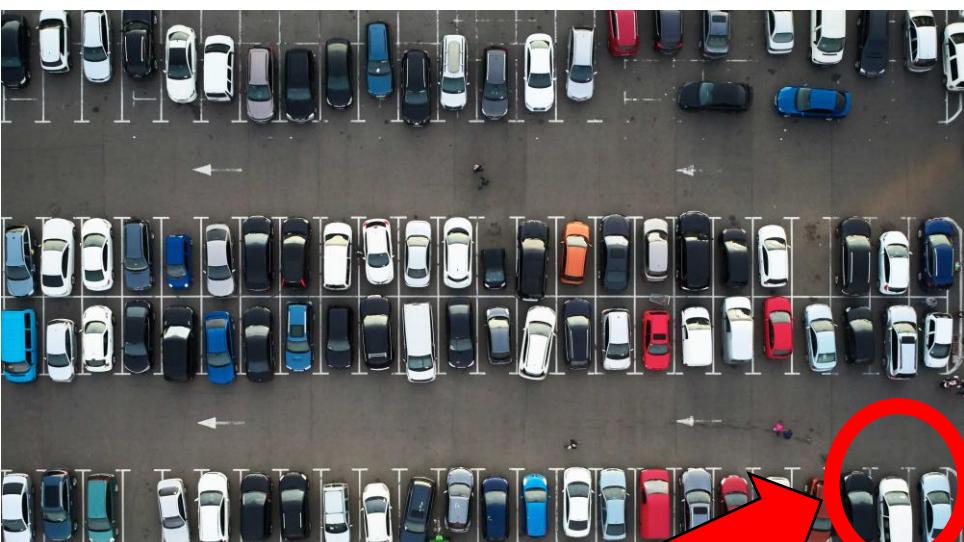
Two different parking spots in your memory.

Which did you use today?

Day 1
(X)



Day 2
(X')

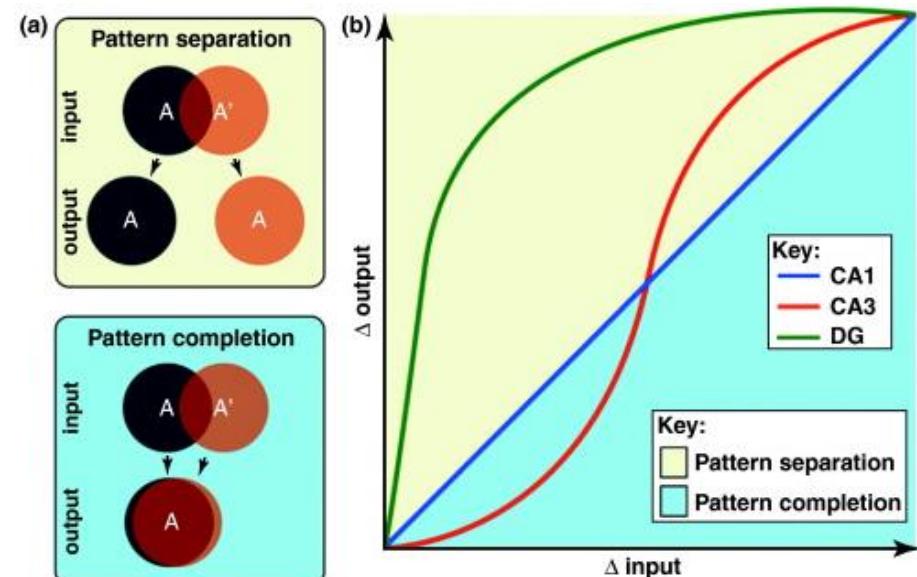
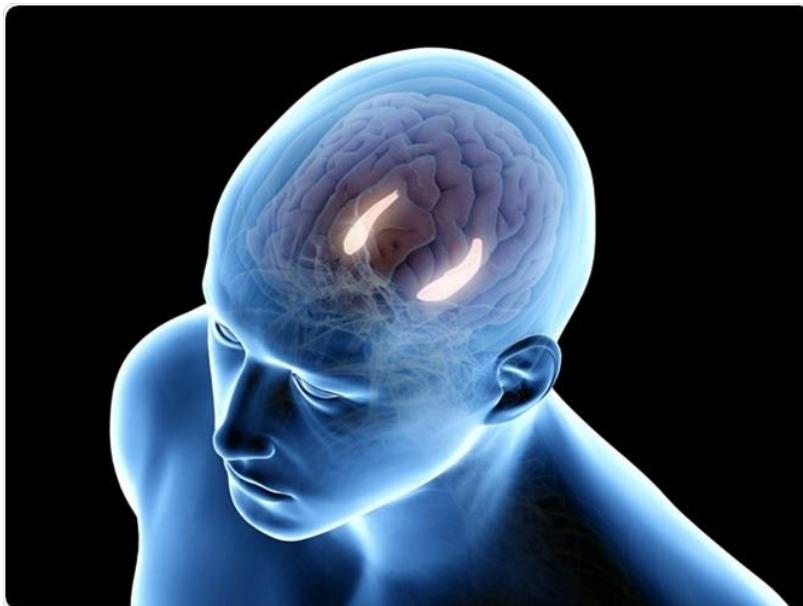


Distinguishing experiences

- *Theory: We can distinguish similar stimuli if each stimulus elicits a different neuronal activity*
- How can we ensure that different groups of neurons are active in each case?
- It has been proposed that your brain can transform similar inputs (e.g. X and X') into different outputs (X and Y), maximizing our ability to make distinctions
- This ability is termed **pattern separation**, and has been suggested to occur in the **hippocampus**

Pattern separation in the HPC

- According to this theory, the networks of the **hippocampus** transform inputs so that our ability to discriminate stimuli is improved

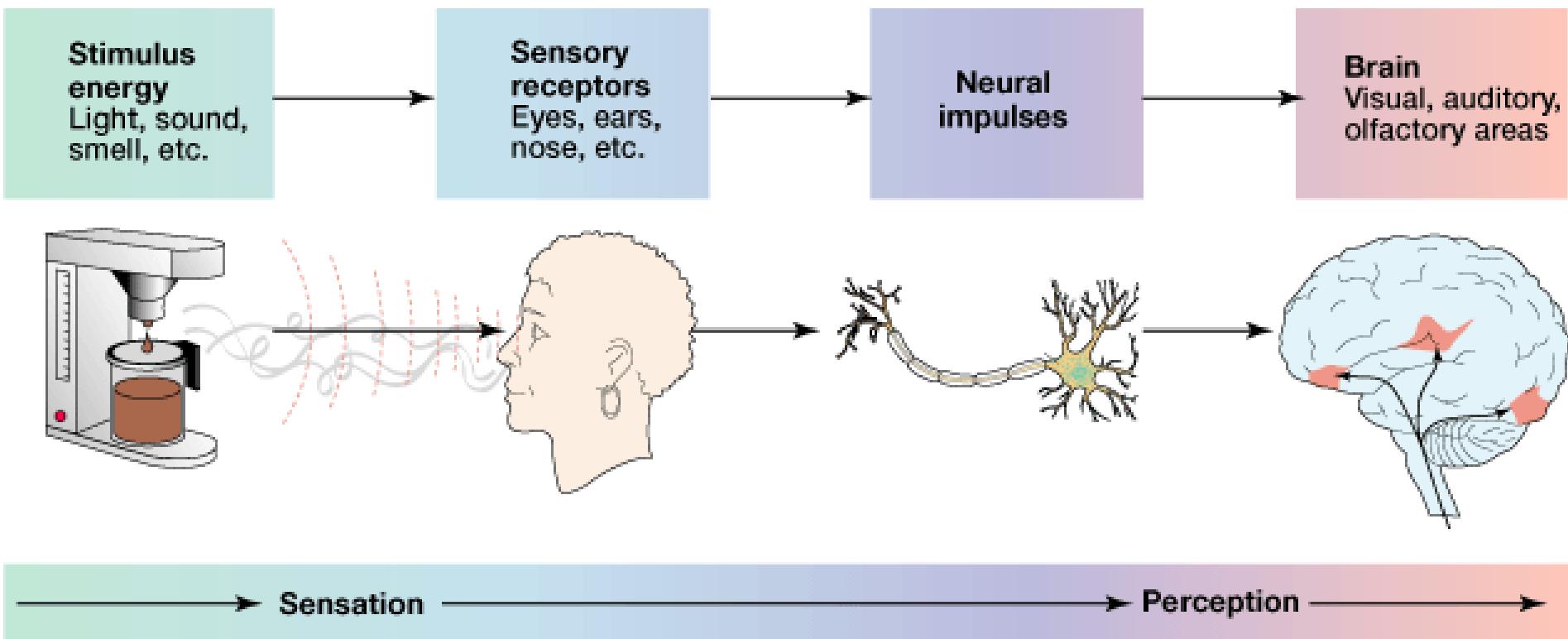


Summary

- Neurons encode information through action potentials
- The population of neurons firing, and the rate at which those neurons fire, matters
- A neuron's firing rate is modified by the inputs that it receives (inhibitory and excitatory)
- Similar inputs may be transformed by the brain so that differences are exaggerated and distinctions are easier (as in the theory of pattern separation)

Part 2: Mental Representations

Mental representations



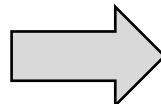
Mental representations

- Though we live in the real world, we are responding to a **constructed world** that exists in our head
- We are exposed to many different stimuli (lights, sounds and more)
- We create an **internal, mental representation** of each stimulus to which we can react
- Our mental representations of stimuli are complex, and do not always align with what is in the real world

Representing Stimuli

What you see

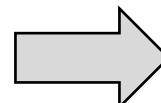
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Representation

According to a researcher...

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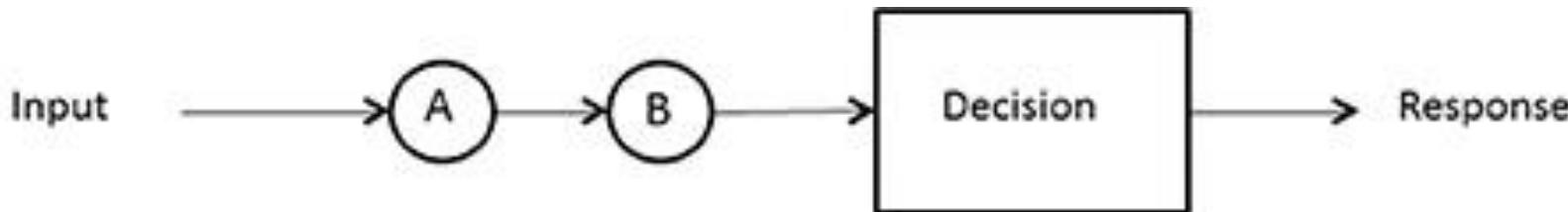
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The arrangement of letters in a word is very important for activating the mental representation of that word.

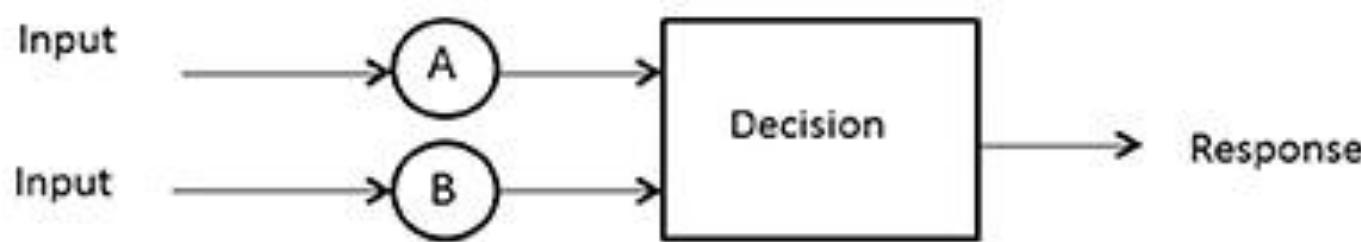
How can we still recognize a word when so many letters are wrong?

Processing letters in word

- **Serial:** Single letters in sequence (A then B....)



- **Parallel:** Multiple letters *at once* (A + B ...)

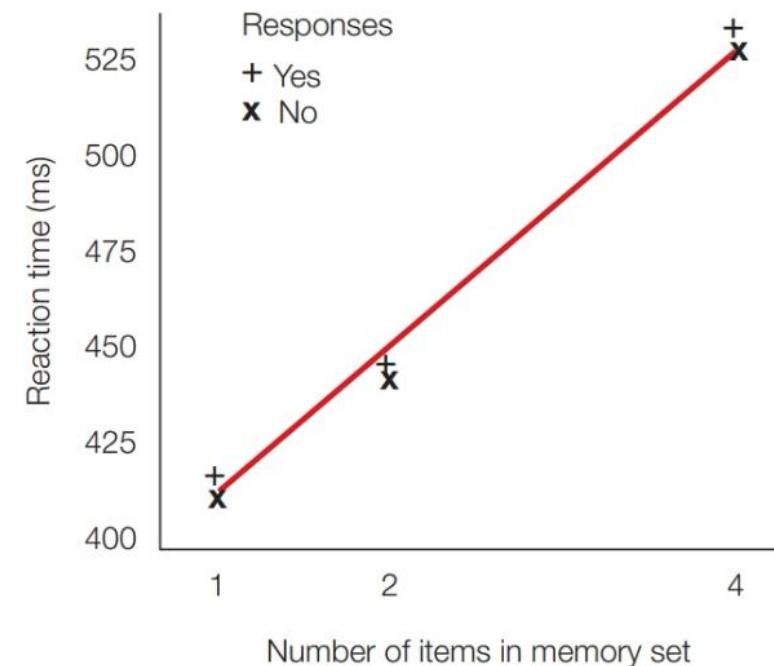
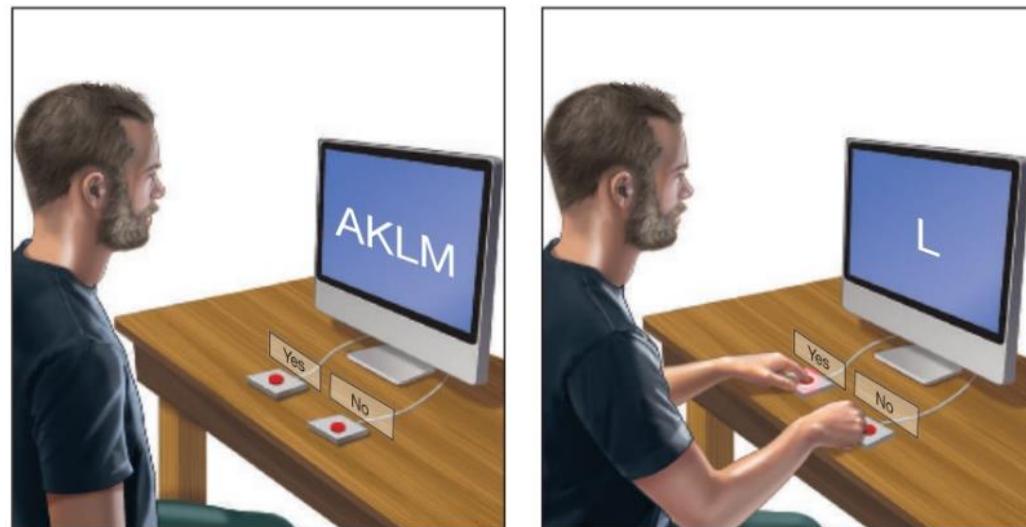


- Word recognition likely involves parallel processing,
with a particular focus on the first + last letters

Do we always process symbols (in this case, letters) in parallel?

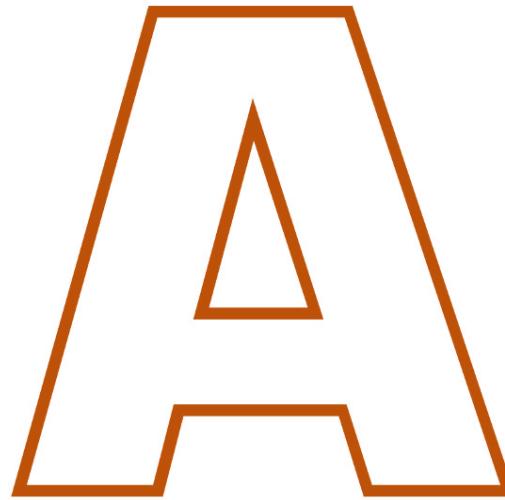
It depends upon the task

- When the goal is scanning for a letter, rather than reading a word, our cognitive processing is different



Does a particular stimulus
have only one
representation?

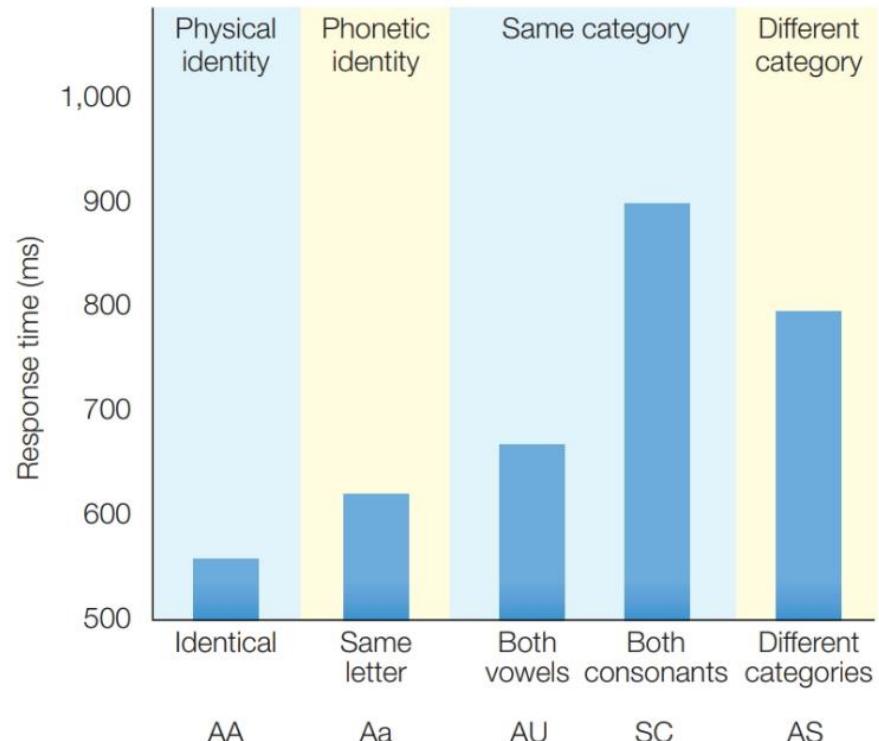
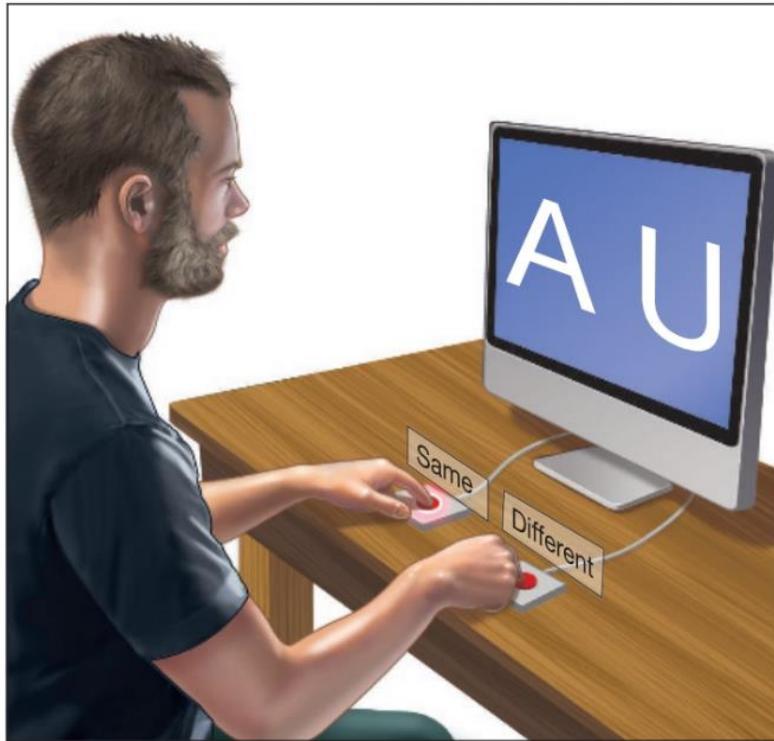
Multiplicity of representations



- This letter has **multiple properties** (capital/upper case, vowel, orange color...) and thus may have a 'multiplicity of mental representations'
- *Is there a way we could examine this possibility?*

Multiple representations

- *Differences in decision-making time* suggest that the letter A is represented in different ways (physically, phonetically and categorically)



Multiple representations

Does the stimulus contain an A or an E?

Condition	Stimulus	Accuracy
Word	RACK	90%
Nonsense string	KARC	80%
Xs	XAXX	80%

FIGURE 3.3 Word superiority effect.

Participants are more accurate in identifying the target vowel when it is embedded in a word. This result suggests that letter and word levels of representation are activated in parallel.

Competitive representations

- **RED**
 - Activates two representations: 1) the meaning of the word red + 2) the color red (**matched**)
- **RED**
 - Activates two representations: 1) the meaning of the word red + 2) *the color blue* (**mismatched**)
- *If we asked someone to read the words **RED** and **RED** aloud, what would we find?*

The Stroop Test

Color matches word	Color without word	Color doesn't match word
RED	XXXXX	GREEN
GREEN	XXXXX	BLUE
RED	XXXXX	RED
BLUE	XXXXX	BLUE
BLUE	XXXXX	GREEN
GREEN	XXXXX	RED
BLUE	XXXXX	GREEN
RED	XXXXX	BLUE

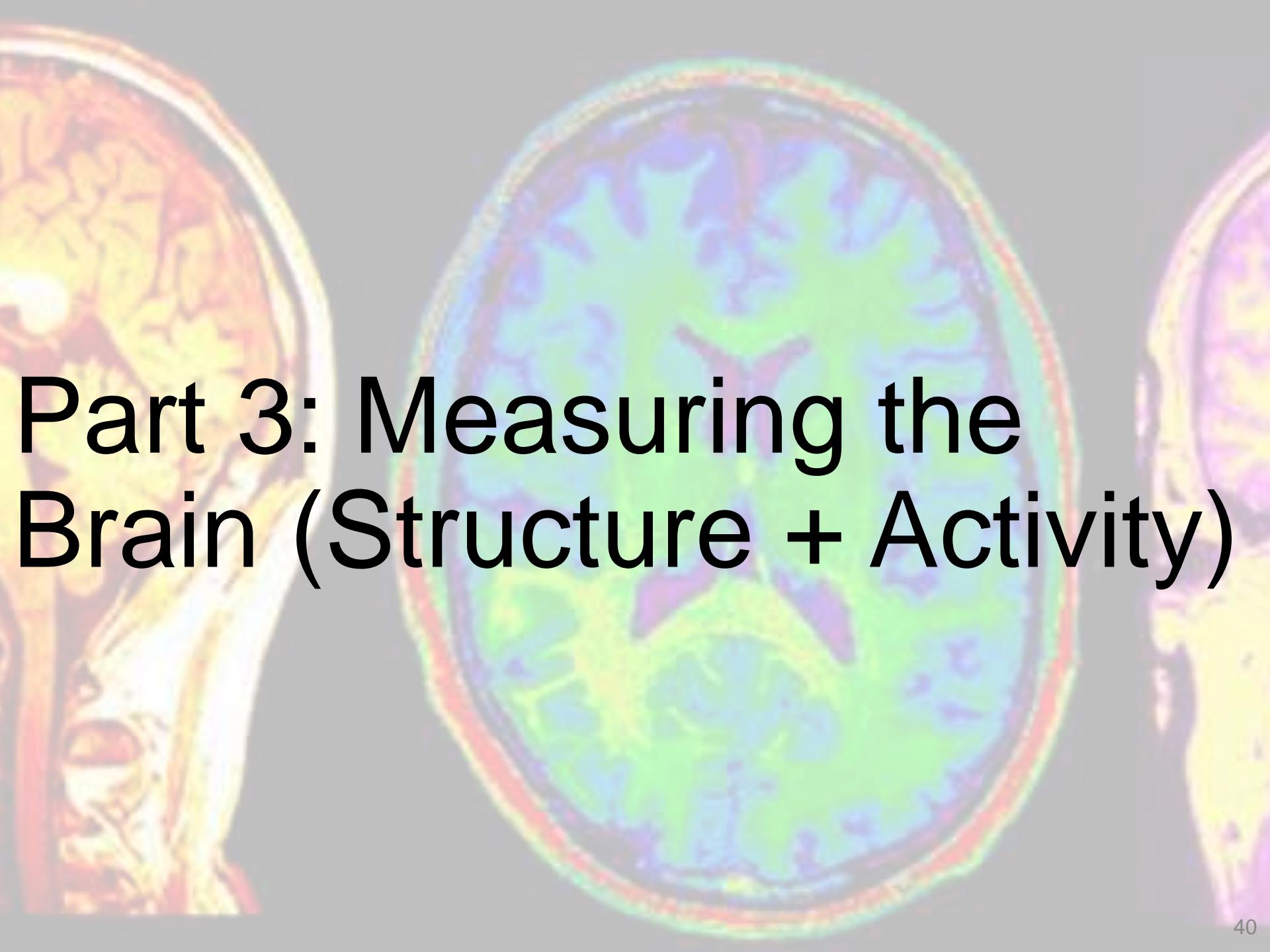
In cases of a mismatch, **response time** is higher + accuracy is lower (decision-making is tougher)

Summary

- We generate mental representations of stimuli
- One stimuli may have multiple representations, and these representations might sometimes be in conflict
- Processing of representations may be in series or in parallel, depending upon the task (e.g. reading versus scanning)
- Looking at decision-making time allows us to make inferences about representations

Interlude -

- Our central goal is to understand the neural mechanisms of cognition
- In other words, we want to know which brain areas are active in different cognitive tasks
- *How do we determine which brain areas are important for a given behavior?*
- Approaches fall into two general categories: measuring the brain (Part 3) + manipulating the brain (Part 4)



Part 3: Measuring the Brain (Structure + Activity)

Our reasoning

- If a cognitive process is impaired by damage to specific brain region, that region may be vital to that process
 - If injuries to the frontal lobe impair impulse control, we would argue that the frontal lobe is involved in this process
 - This is the logic of **lesion studies**
- If a cognitive process is associated with the activation of specific brain regions, those regions may be vital to that process
 - If listening to music strongly increases temporal lobe activity, the temporal lobe may be involved in this process
 - Logic behind all other studies we will cover

Techniques

- 1) Lesion studies (more correctly, an approach)
- 2) EEG/ERP
- 3) PET
- 4) MRI, DTI + fMRI
- 5) Single cell recording

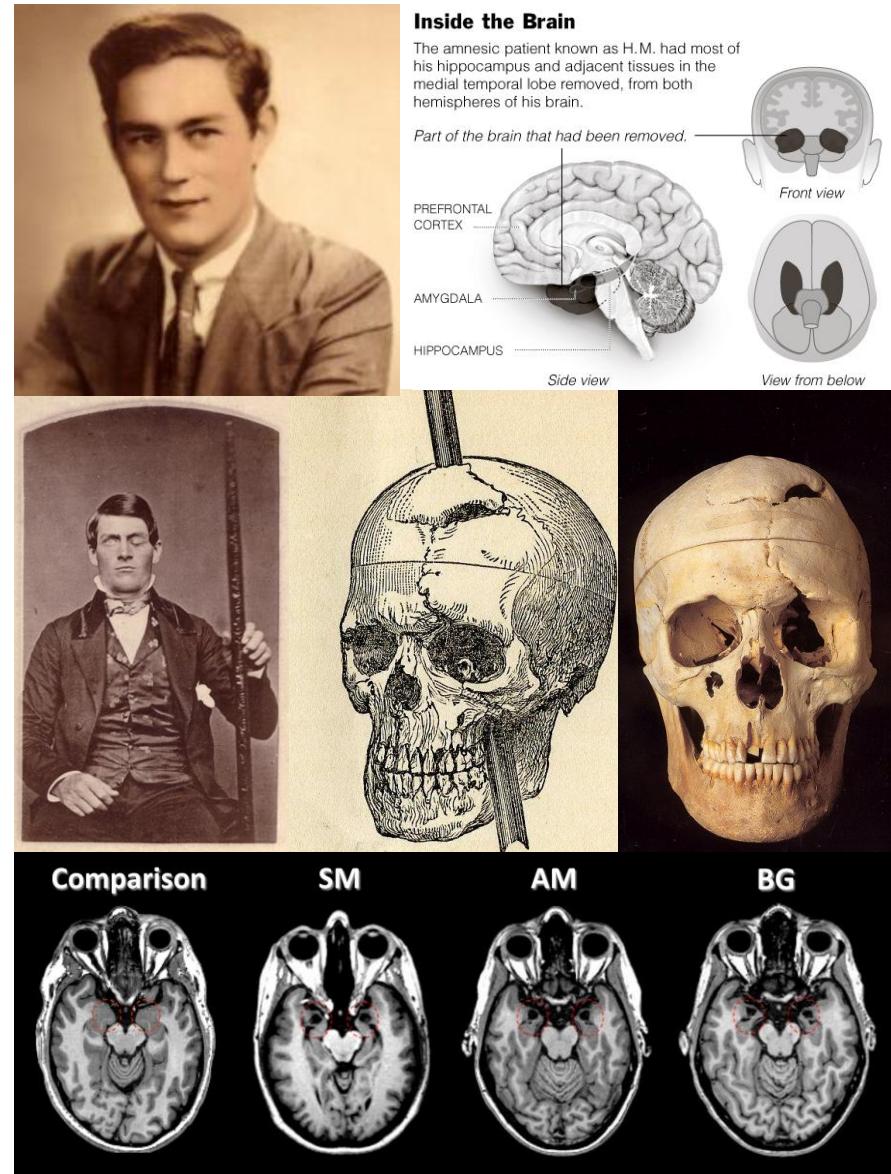
These techniques provide insight into brain structure and/or function.

1) Lesion Studies

- While brain damage is an unfortunate tragedy, important insights can be gained from its study
- Some lesions are associated with striking behavioral deficits
- *If damage to a specific brain region impairs a particular behavior, it is plausible that the brain region damaged controls the behavior impaired*
- Lesions studies are a major part of the history of psychology and cognitive neuroscience

Influential Lesion Studies

Patient HM – Removal of Hippocampus and adjoining areas; Impaired memory

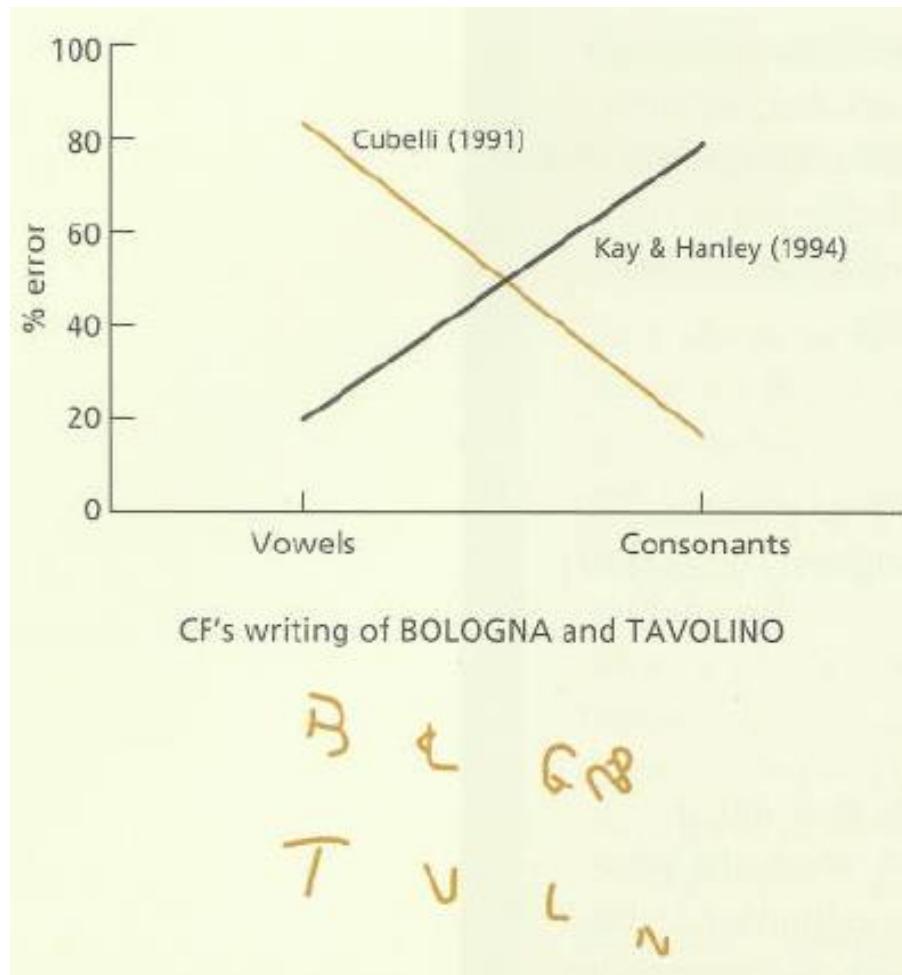


Phineas Gage – Lesion of Frontal Lobe; Impulsivity + Impaired Social Behavior

Patient SM – Lesion of Amygdala; Reduced fear

Dissociation in Lesion Studies

- Individuals w/different lesions show different impairments
- One person has more trouble vowel-writing, the other person has more trouble consonant-writing
- Vowel-writing and consonant-writing may be **dissociated functions (different areas involved)**



Single vs. Double Dissociation

Single dissociation

	Long-term memory	Short-term memory
Brian	Yes	No

- Function A is intact but Function B is not.
- A + B have different mechanisms and *may* be independent.

Double dissociation

	Can name Object	Can reach for Object
Alex	Yes	No
Ramon	No	Yes

- Requires two people with opposite impairments.
- **A + B have different mechanisms + are likely independent.**

On lesion studies...

- Lesions rarely specific; many areas are involved
 - Unwise to explain all behavioral deficits by changes in just one of these brain regions
 - Extent of lesions can only be verified post-mortem
- Damaged brain region may govern many other behaviors that we failed to measure
- Cases are very rare (often, $n = 1$); tough to build a conclusive argument based on them
 - Is the effect of the lesion likely to occur in many people? Or was it chance, and unique to one person?

Lesions studies involve measuring the brain after injury. While useful, they have limitations.

We should also look at the live brain in healthy individuals.

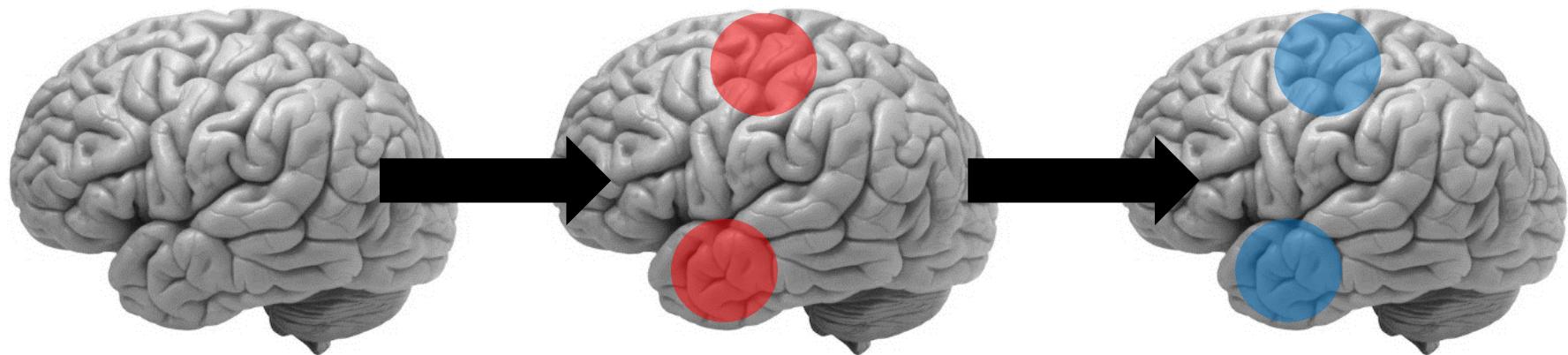
Measuring the Live Brain

- If we measure the structure/function of the brain in association with a cognitive process, we can get an idea of the brain regions involved in that process

Baseline (When a Person is Doing Nothing Special)

During Behavior
(Brain Areas Temporarily Active)

With Continued Behavior
(Long-term Structure + Activity Changes)



For each technique, consider...

- **Spatial resolution**
 - Ability to resolve details in brain structure (i.e. recognize different brain areas)
- **Temporal resolution**
 - Ability to resolve brain activity over time (or *correlates* of brain activity)
- Cost, expertise required and logistic factors (e.g. applying an fMRI when meditating is difficult, but applying an EEG is simple)

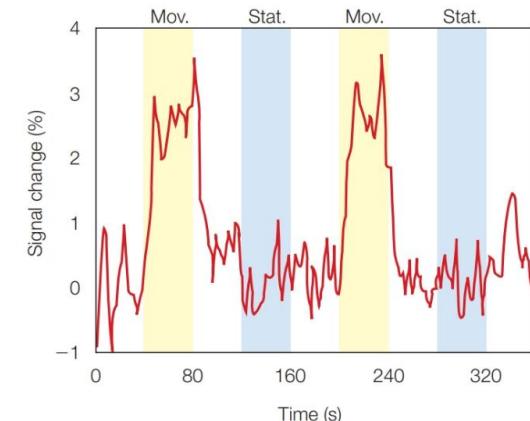
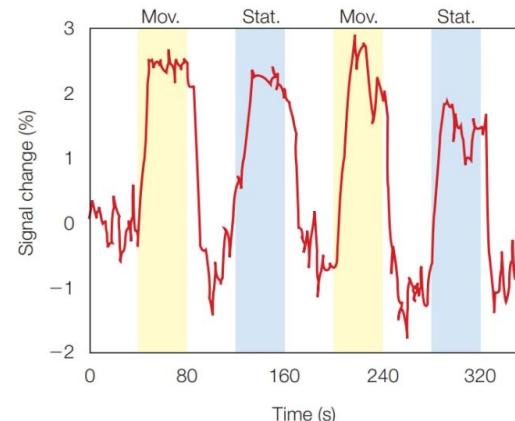
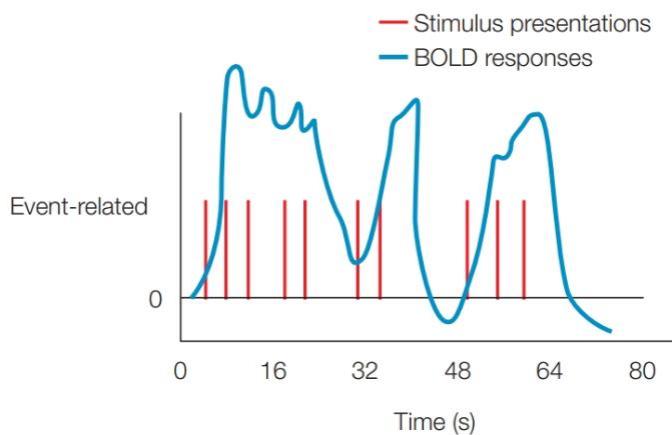
There are no perfect techniques. Most advantages are situational.

Managing temporal resolution

- Temporal resolution is a major concern
- The brain has incredible processing speed
- Many of your decisions are made quickly and unconsciously (in a matter of milliseconds)
- Capturing the time course of certain forms of cognitive processing is very challenging
- *How do we get around this issue?*

Managing temporal resolution

- In **event-related designs**, we measure signals during brief cognitive processes (i.e. the event)
 - This approach requires good temporal resolution
- To get around issues with temporal resolution, we may use a **block design** wherein people engage in cognitive tasks for an extended time (~40 seconds)



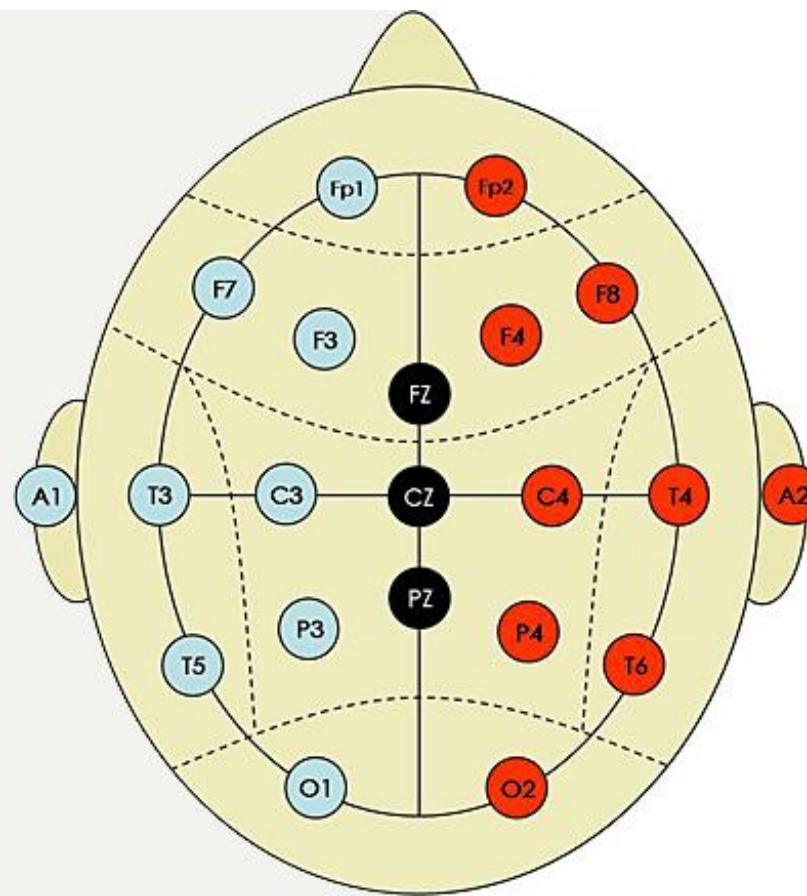
2) Electroencephalography

Measures *electrical activity in specific brain regions.*
Useful in studies of arousal, consciousness + epilepsy.

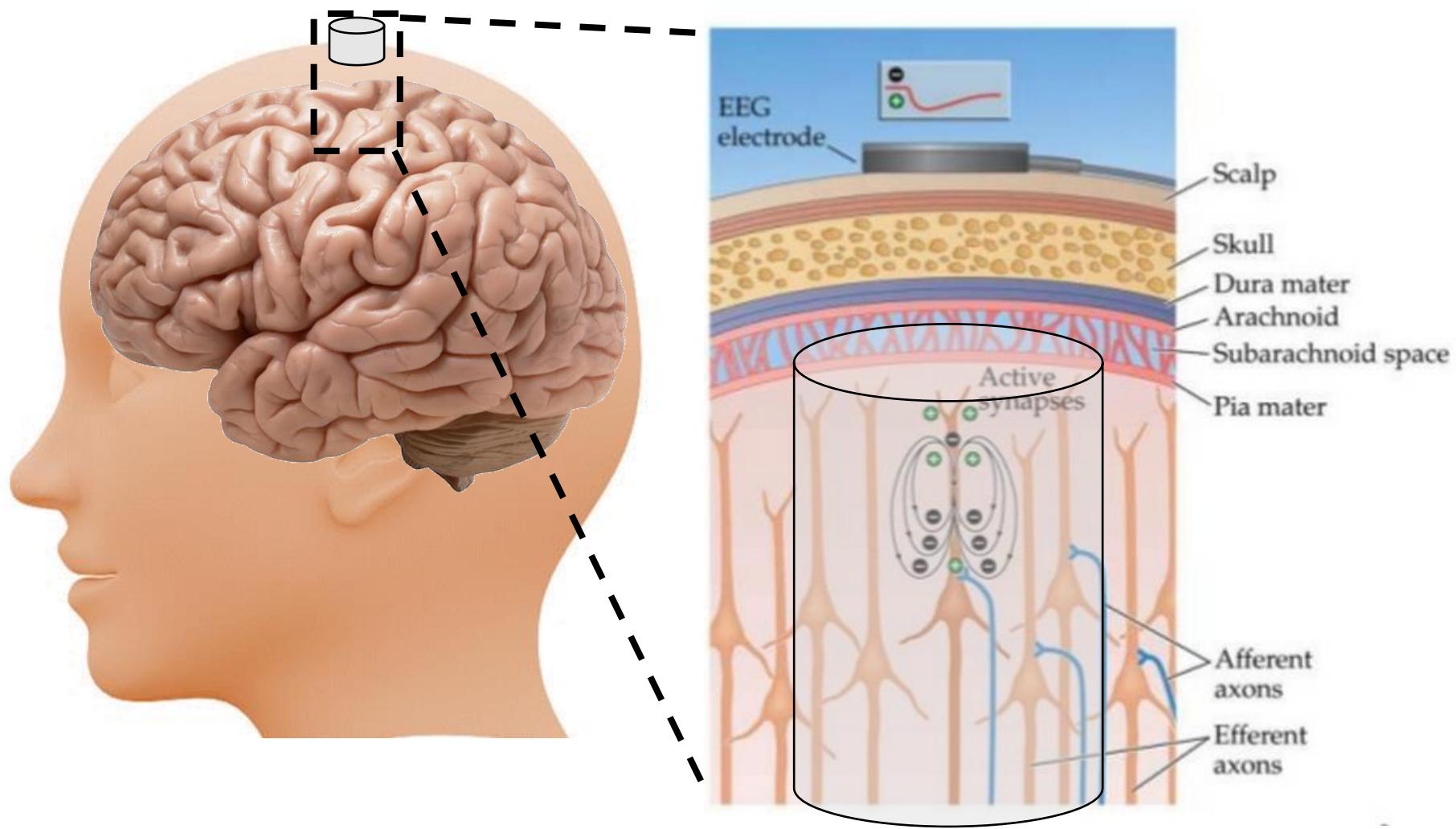
KEY:

- RIGHT Hemisphere
- LEFT Hemisphere
- Mid Line

F : Frontal Lobe
T : Temporal Lobe
C : Central Lobe
P : Parietal Lobe
O : Occipital Lobe
Z : Mid Line



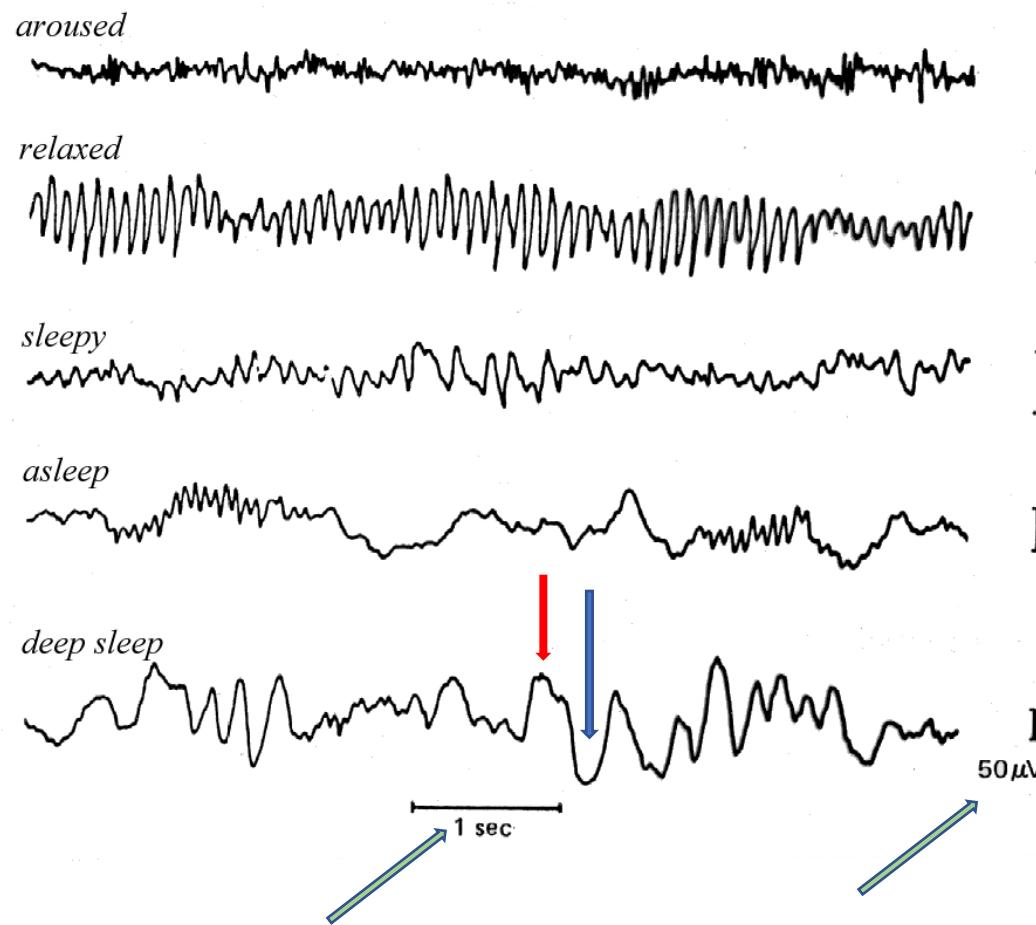
What is an EEG measuring?



Electrodes are placed above a small amount of neurons.

The EEG signal

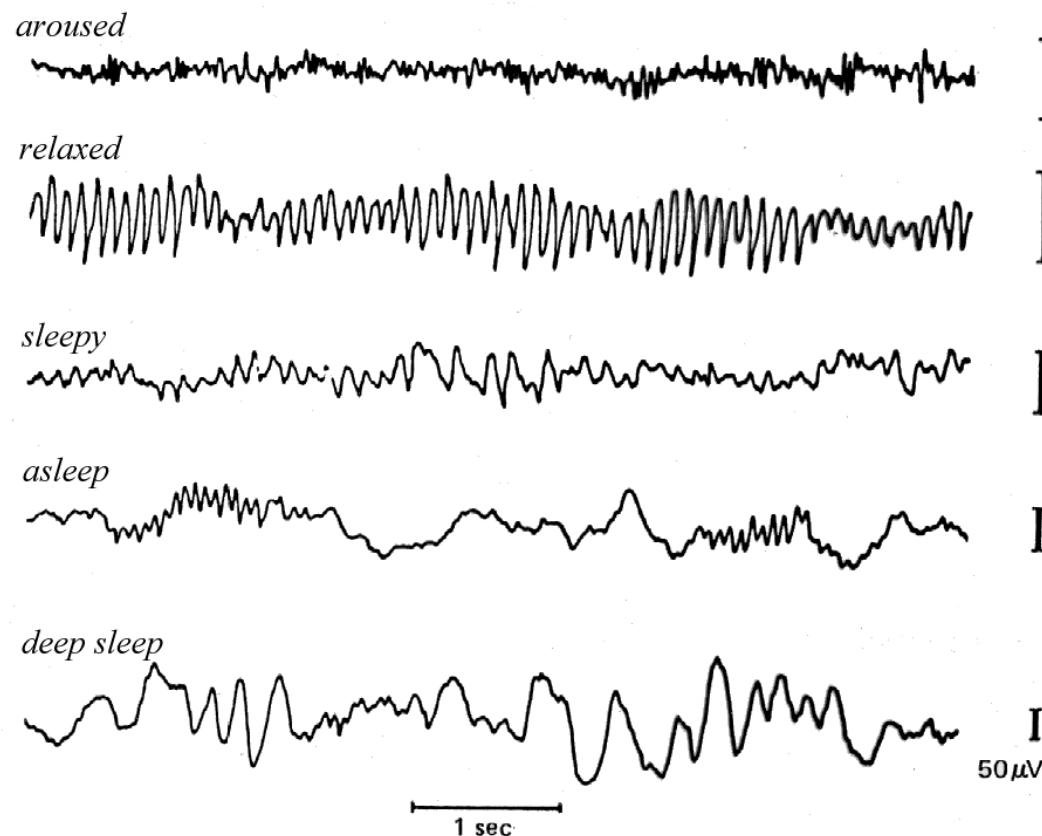
- *Potential difference (volts or V, y axis) over time (seconds or sec, x axis)*



- I • Notice how the voltage varies in a 'wave-like' manner over time, with **peaks** and **valleys**
- I
- I
- I
- I • The variation in voltage over time gives us **frequency**

The EEG signal

- *Potential difference (volts or V, y axis) over time (seconds or sec, x axis)*



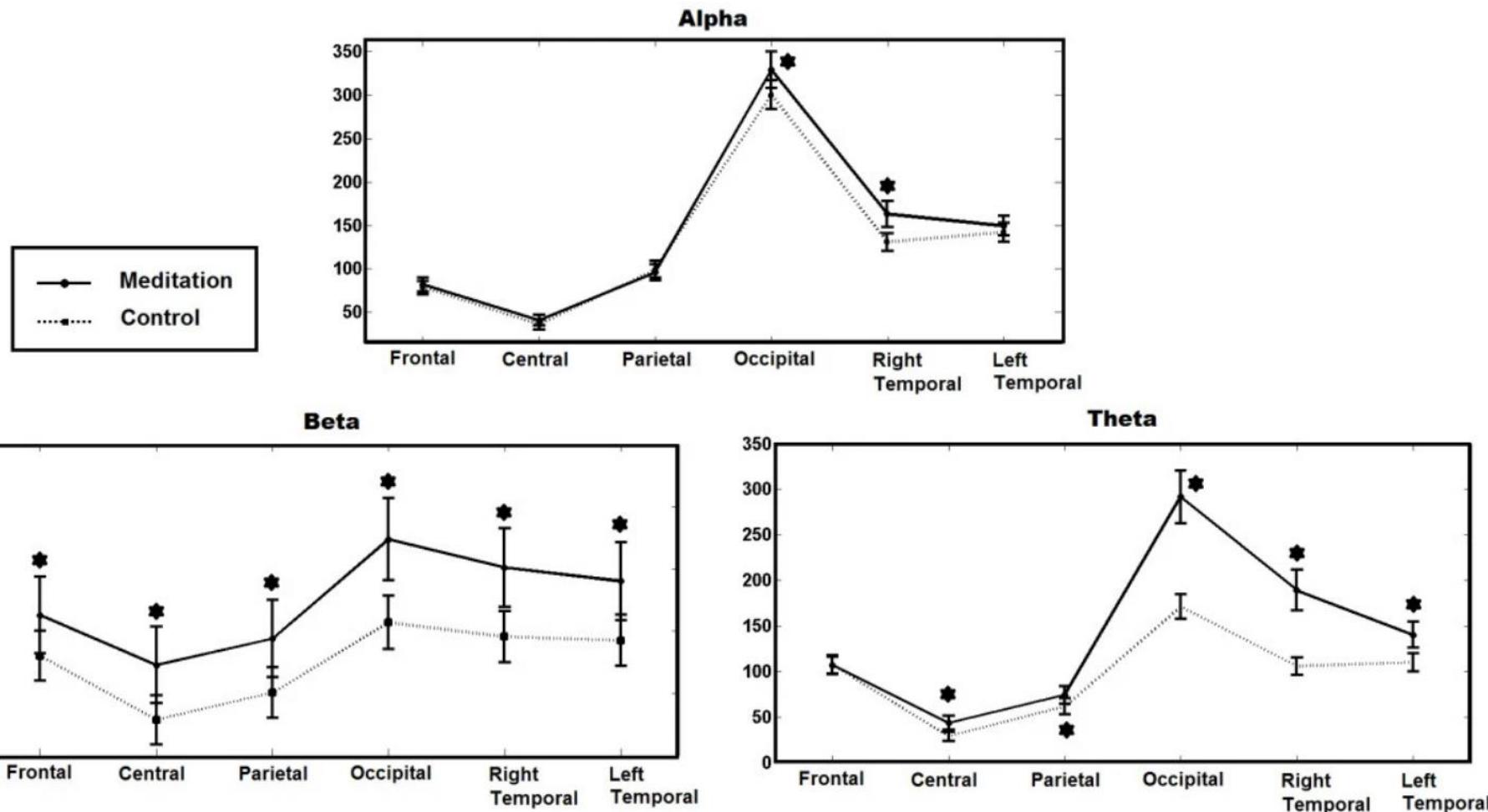
Frequency Ranges:

- | Beta = 13 - 30 Hz
- | Alpha = 7 – 13 Hz
- | Theta = 4 – 7 Hz
- | Delta = 1 – 4 Hz

What happens to activity as you 'fall asleep'?

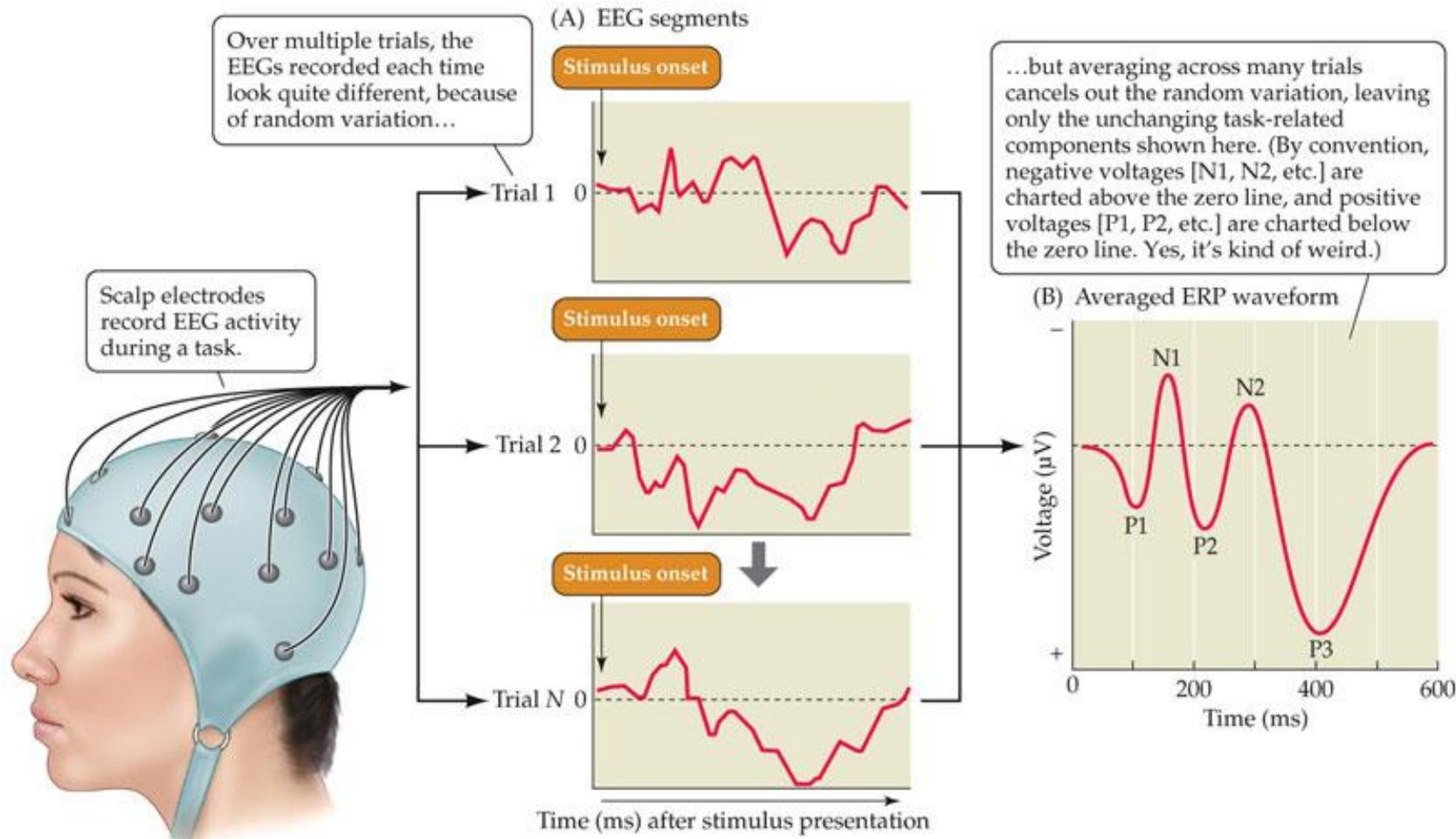
Studying Consciousness w/EEG

- In meditation, more beta and theta frequencies*



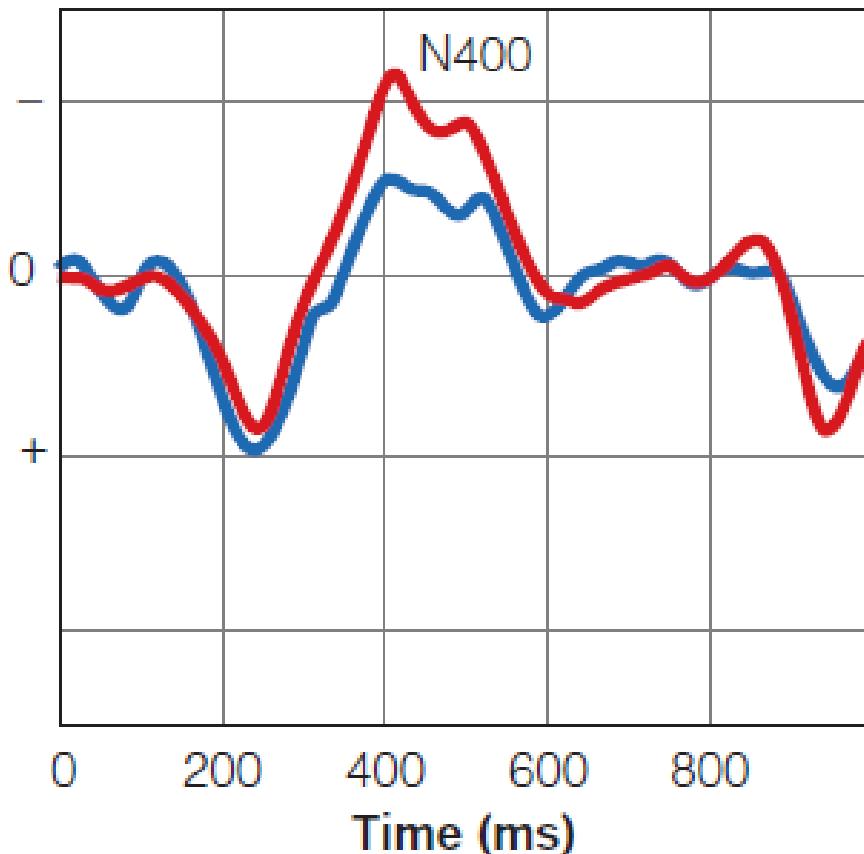
The Event-Related Potential (ERP)

- Neural activity related to a brief mental process
- ERP is measured using EEG equipment



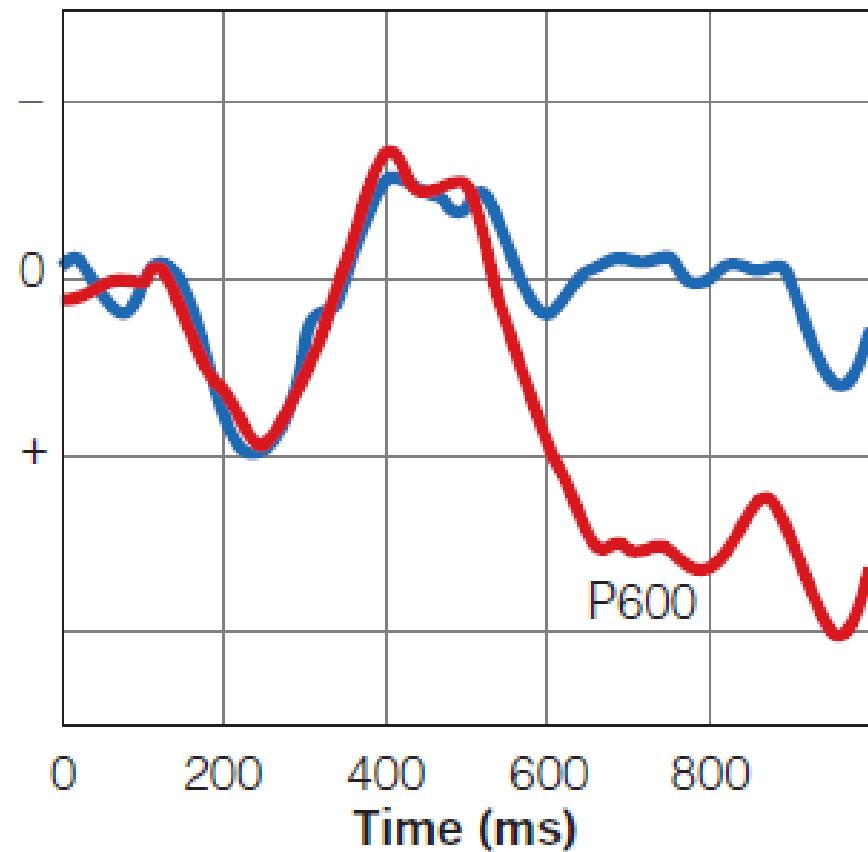
ERP w/Language Processing

— The cats won't EAT ...
— The cats won't BAKE ...



(a) How semantics affects N400

— The cats won't EAT ...
— The cats won't EATING ...



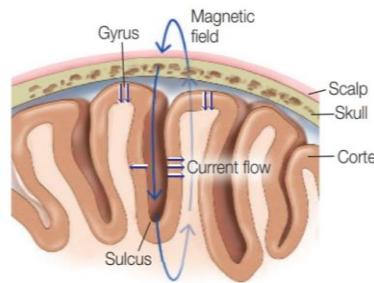
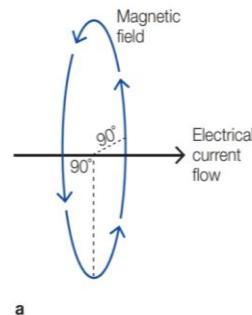
(b) How syntax affects P600

EEG + ERP – Summary

- **Great temporal resolution** (biggest advantage)
 - Millisecond scale
 - Great for measuring rapid changes in arousal/consciousness (regular EEG) and rapid cognitive processes (ERP)
- **Poor spatial resolution** (biggest disadvantage)
 - Difficult to determine which specific areas are active
 - Deeper brain areas cannot be measured

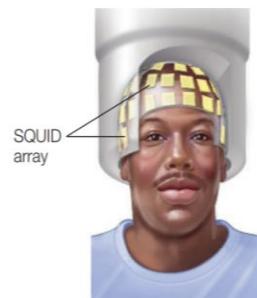
3) Magnetoencephalography

- Electrical currents accompanying brain activity generate magnetic fields in a perpendicular direction
- If we measure these fields during a task, we can approximate neural activity in that task

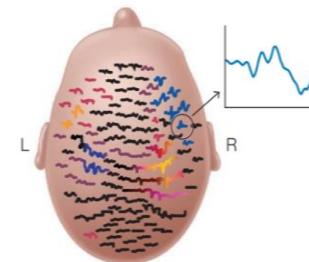


a

b



c Subject undergoing MEG procedure

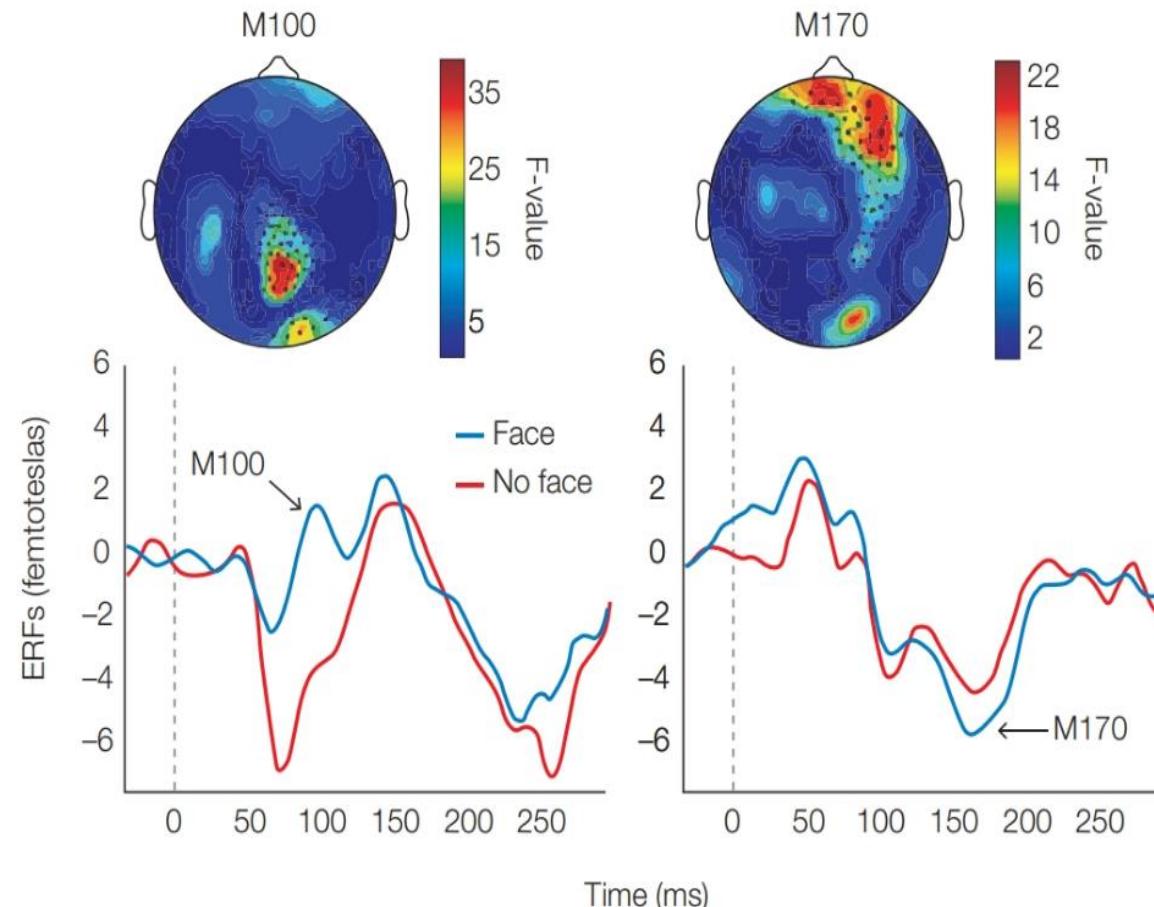


d MEG analysis of a response to a tone



MEG for specific events

- This study shows field strength (in microT, Y axis) over time (ms, X axis) during processing of a face

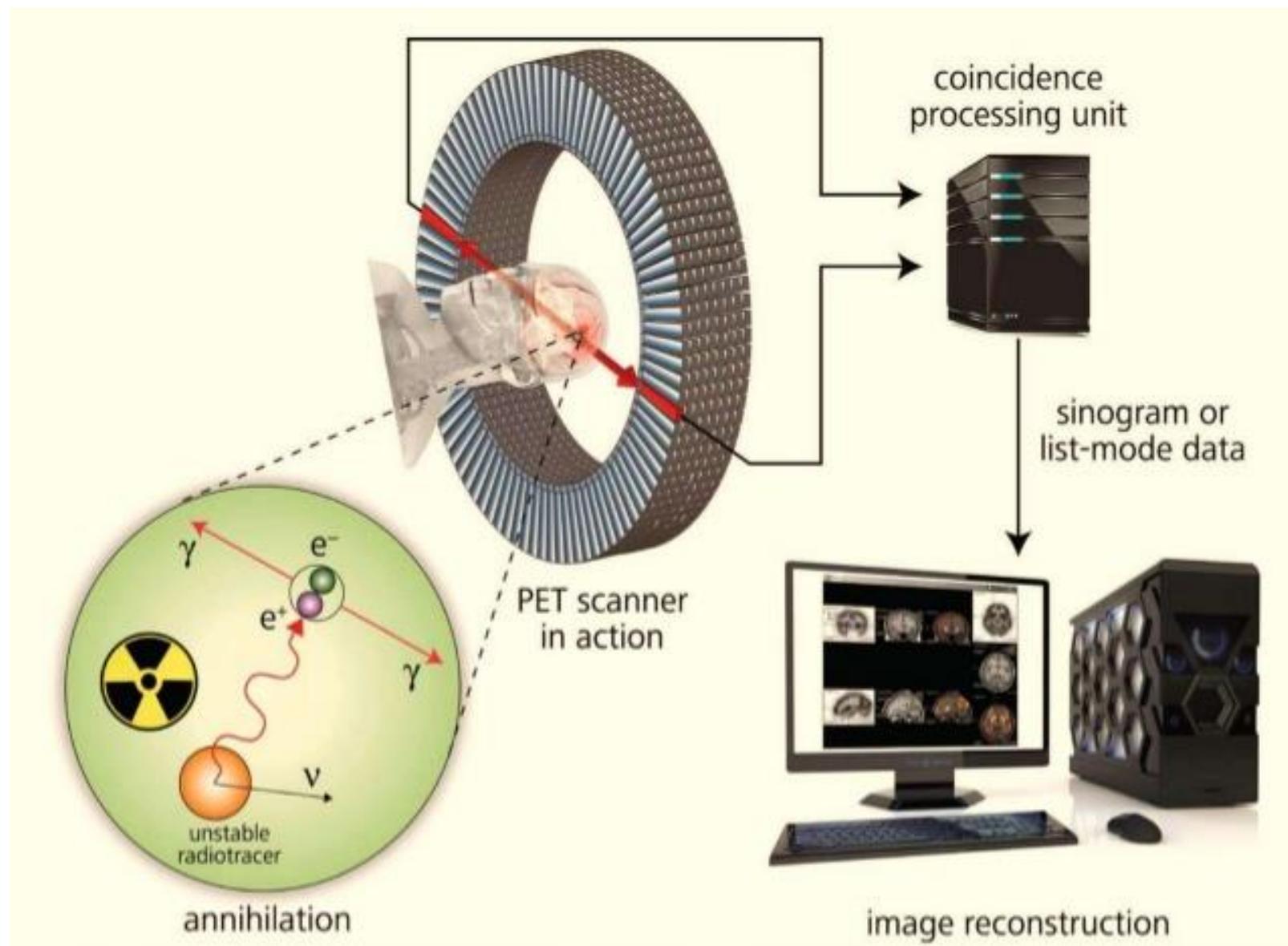


Is this an event-related design or a block design?

MEG - Summary

- **Great temporal resolution** (comparable to EEG)
- **Improved spatial resolution** (better than EEG)
 - Magnetic signals attenuate less with distance than do electrical signals
 - Overcomes one of the main problems w/the EEG
- Main disadvantage is the high expense and inconvenience
- Overall, MEG studies are relatively rare in the field

4) Positron Emission Tomography

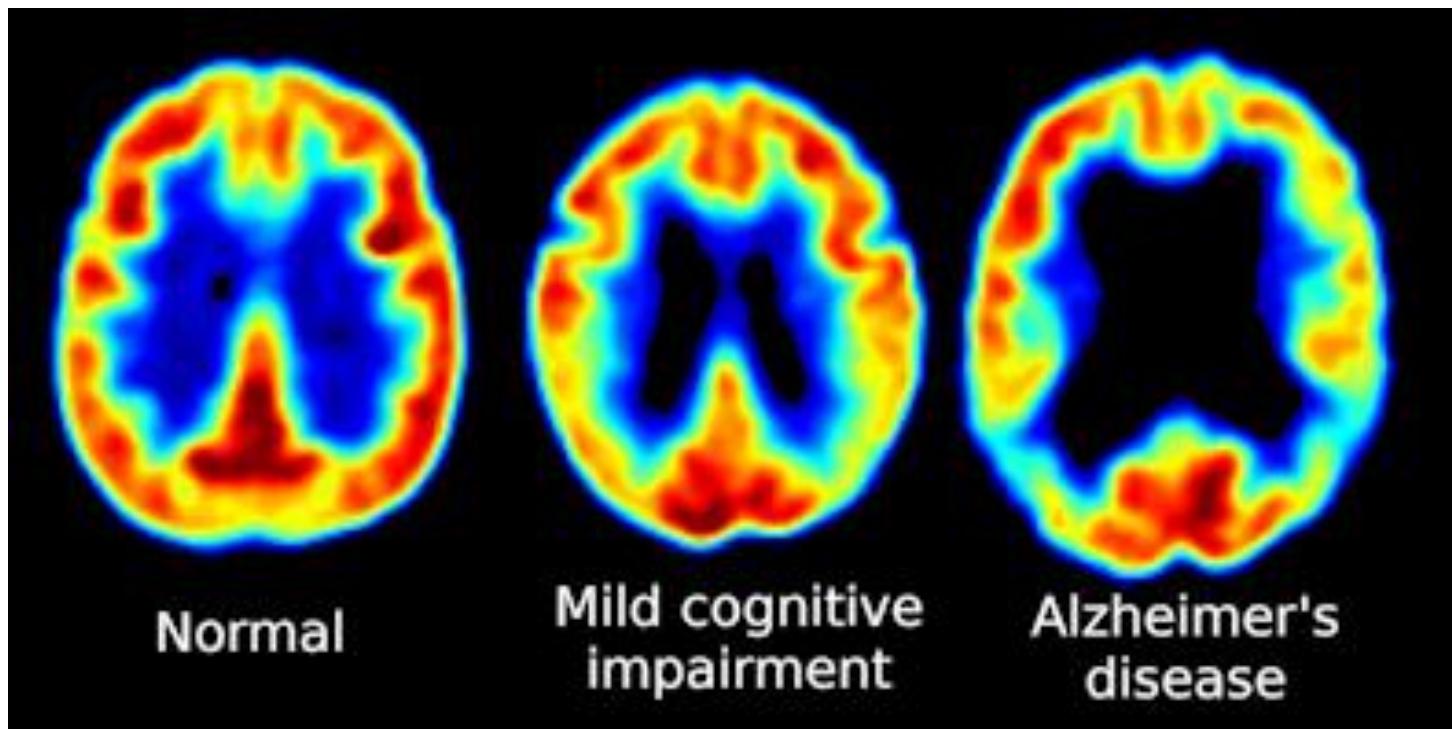


PET

- A **synthetic radiotracer** is injected into the subject
- This radiotracer reacts with tissue in the brain; this reaction produces a signal that can be measured with specialized equipment
- *Wherever the radiotracer goes in the brain, there will be a signal generated*
- Many radiotracers available for different purposes

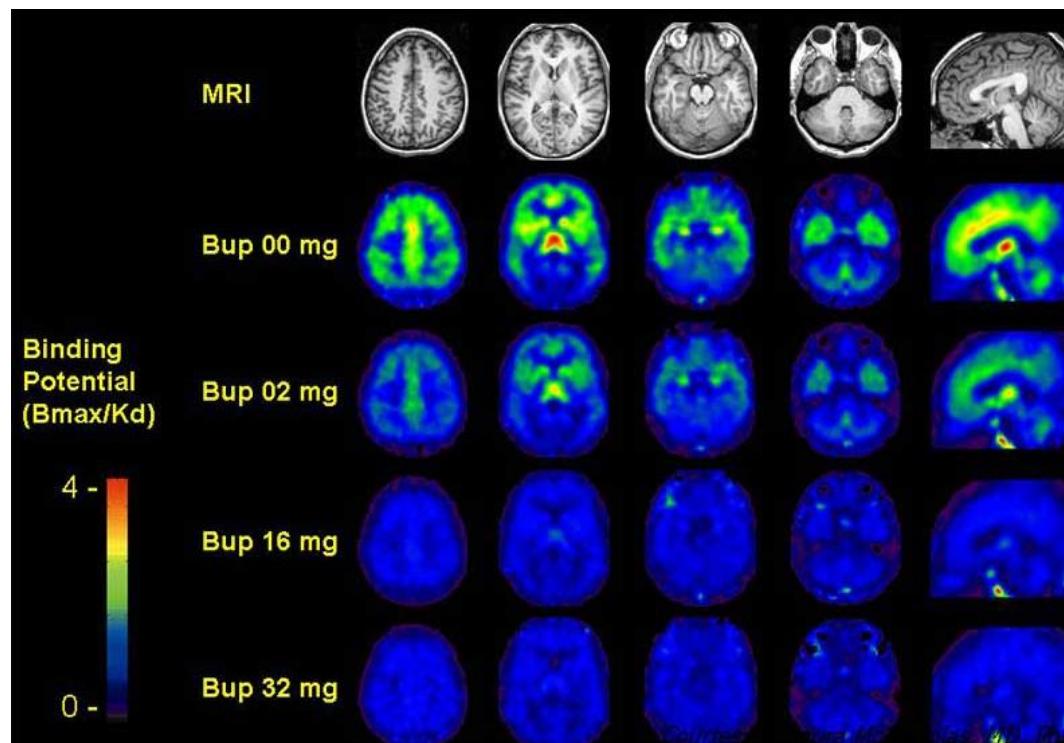
Measuring activity w/PET

- If we use a radiotracer similar to glucose (such as **Fluorodeoxyglucose (^{18}F)**, that tracer will ‘go where glucose goes’ (i.e. to active neurons)
- Signal differences between brain regions reflect differences in glucose demands (+ neuronal activity)



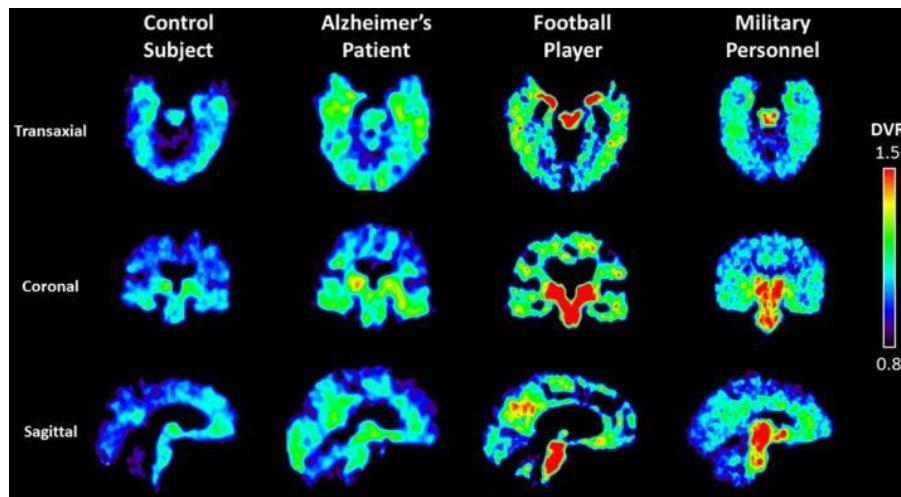
Measuring substances w/PET

- If we use a radiotracer similar to opiate transmitters, that tracer will go where opiate transmitters go (it will bind to opiate receptors)
- Signal differences between brain regions reflect differences in opiate receptor occupancy



Diagnosing disorders w/PET?

- Certain proteins are upregulated in pathology (e.g. B-amyloid in Alzheimer's Disease)

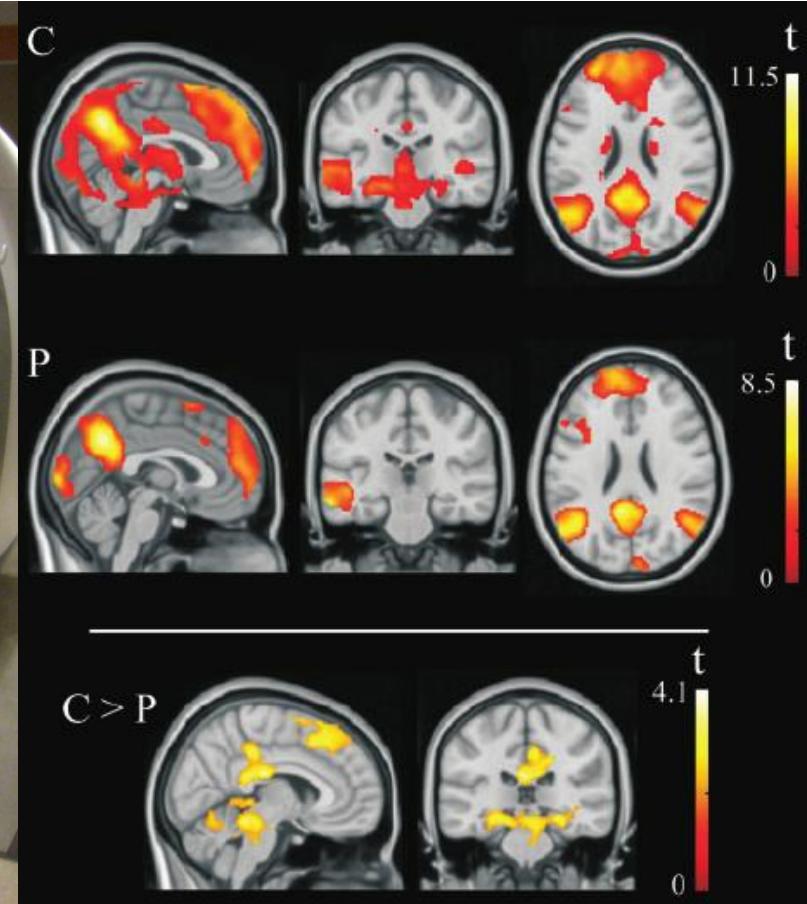


- If we can develop a radiotracer which interacts with these proteins, we can track them in the living brain
- While intriguing, these techniques are not reliable enough to be used in formal diagnosis

PET – Summary

- **Decent spatial resolution**
 - Better than EEG but worse than MRI
- **Poor temporal resolution**
 - Difficult to resolve rapid changes in neural activity
- Due to its resolution issues, PET is *no longer preferred* as a structural/functional measure
- Main current use is in characterizing substances (e.g. receptors, proteins)

5) MRI + related methods



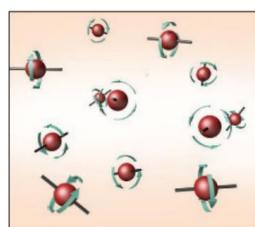
MRI = Magnetic Resonance Imaging

MRI + related methods

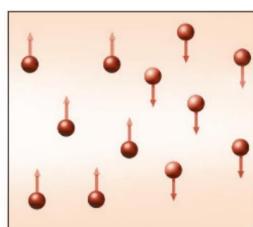
- MRI (structural - for grey matter/cell bodies)
- DTI (structural - for white matter/axons)
- fMRI (activity)
- rs-fMRI (activity, specifically connectivity patterns)

MRI method in brief

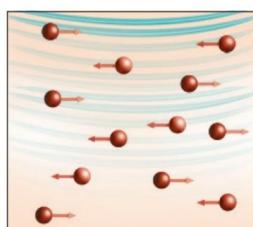
- Brain tissues are first magnetized in a strong magnetic field; strength of the field matters
- When hit with a radiofrequency pulse, the magnetized tissues emit a signal *which depends upon their structure*
- If we capture these signals, we can use them to artificially reconstruct the tissues of the brain



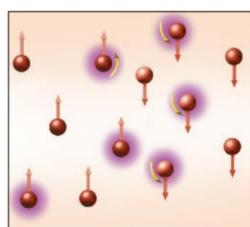
In normal state, the orientation of spinning protons is randomly distributed.



Exposure to the magnetic field of the MRI scanner aligns the orientation of the protons.

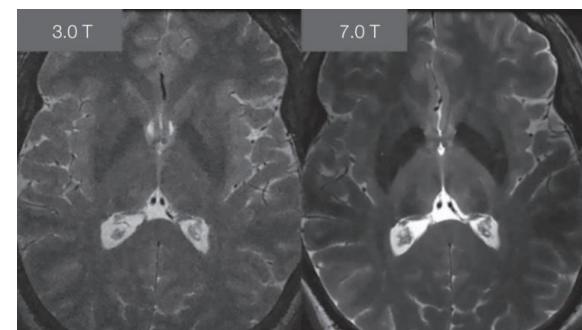


When a radio frequency pulse is applied, the axes of the protons are shifted in a predictable manner and put the protons in an elevated energy state.



When the pulse is turned off, the protons release their energy as they spin back to the orientation of the magnetic field.

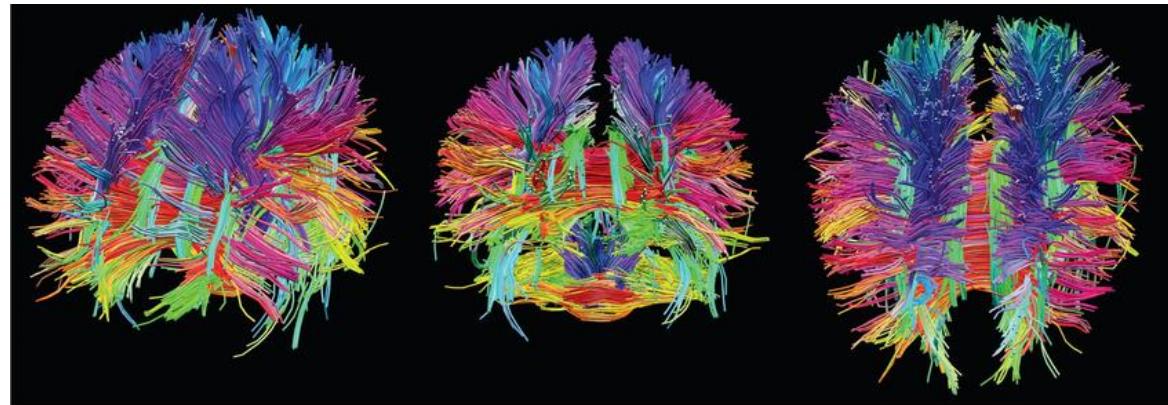
a



Traditional MRI....

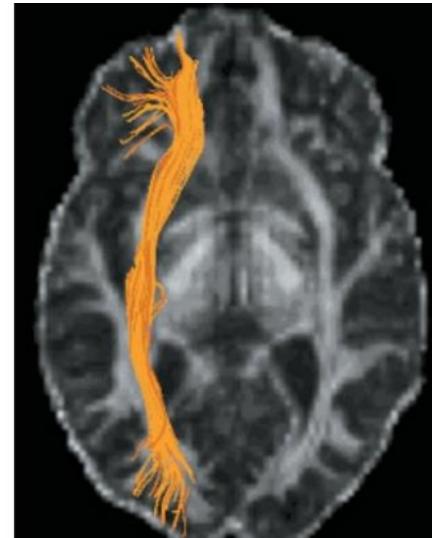
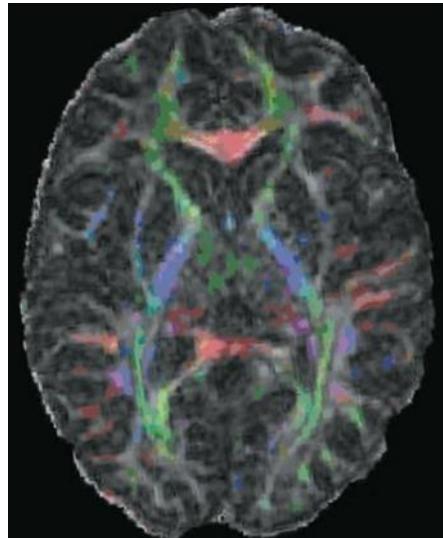
...is great for imaging grey matter (cell bodies)

- What about white matter (axons)?
- An adapted form of MRI, **diffusion tensor imaging (DTI)**, is often used for studying white matter



How DTI works

- Water flows through most tissues, but not all tissues
- Myelinated axons are fatty, water flows parallel to them
- When you measure water, you are measuring boundaries corresponding to myelinated axons



DTI and white matter pathology

- Cannabis use during adolescence is associated with reduced growth of tracts + poorer verbal performance

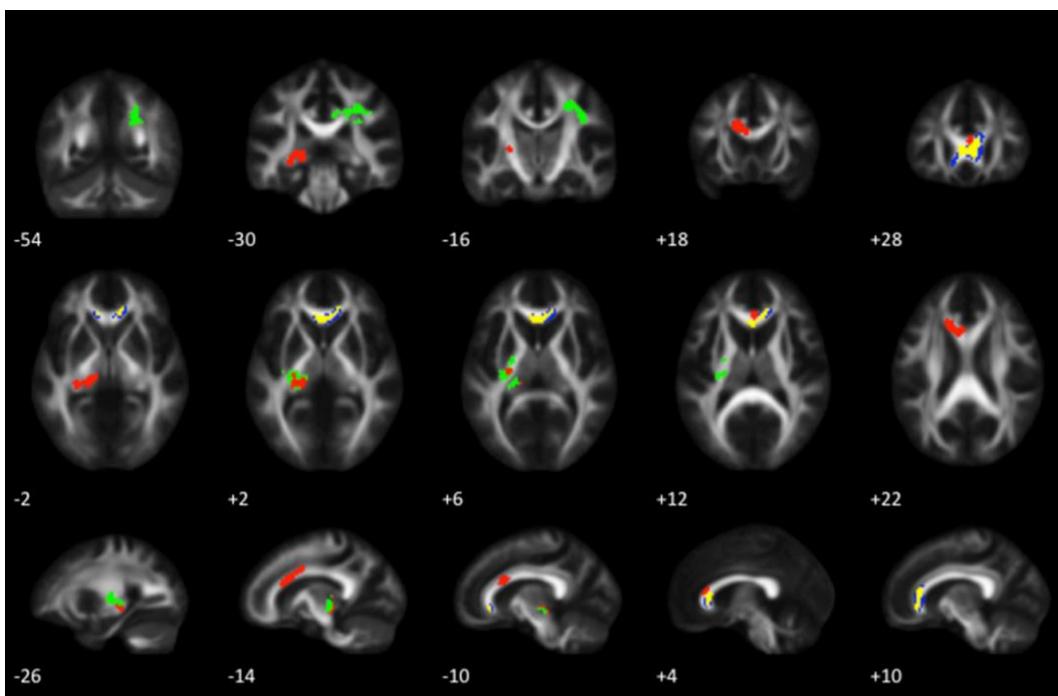


Table 5

Partial correlations of cluster mean fractional anisotropy (FA) change values with RAVLT scores. Partial correlations between cluster mean values and total scores on the Rey Auditory Verbal Learning Test (RAVLT), controlling for sex, age at baseline, time interval between baseline and follow-up assessments, average 12-month alcohol use, and IQ. Abbreviations: ATR = anterior thalamic radiation; CC = corpus callosum; CST = corticospinal tract; FOF = fronto-occipital fasciculus; SFG = superior frontal gyrus; SLF = superior longitudinal fasciculus; CU = cannabis user; L = left hemisphere; R = right hemisphere.

FA cluster	RAVLT: Baseline	RAVLT: Follow-up
<i>CU > Controls</i>		
L anterior CC (-14,16,26)	-0.226	-0.504**
L thalamic white matter (-10,-24,-6)	-0.407**	-0.342*
<i>Controls > CU</i>		
R SLF/CST (32,-32,40)	0.350*	0.364*
L CST (-16,-28,50)	0.360*	0.334*
R ATR (26,16,12)	0.288	0.210
L SLF/CC forceps major (-38,-44,24)	0.319*	0.317*
L SFG white matter (-18,16,42)	0.315*	0.357*

* $p \leq 0.05$.

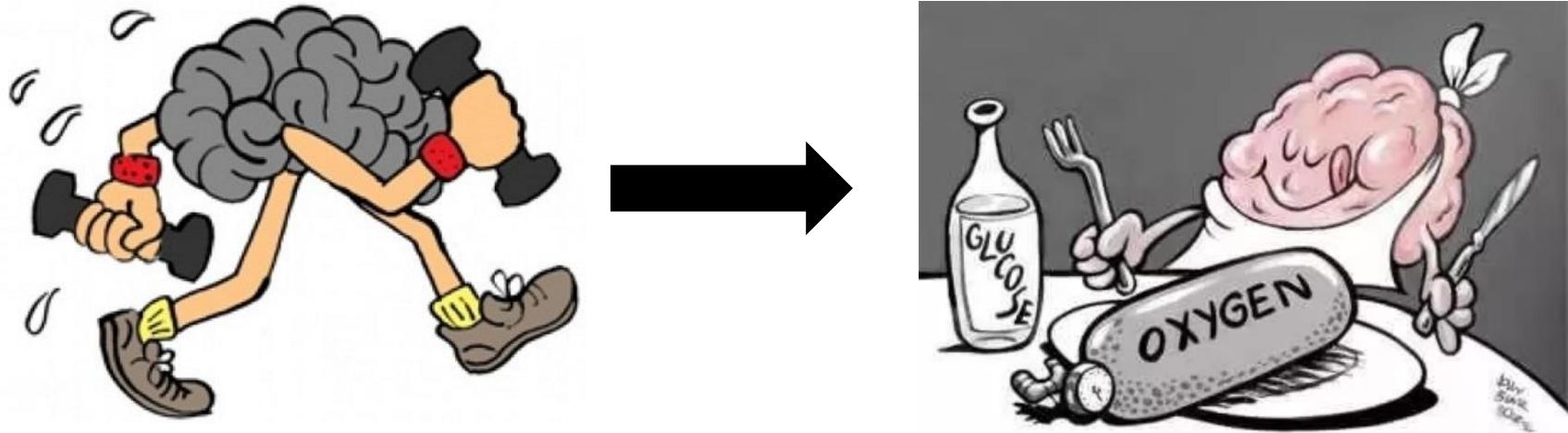
** $p \leq 0.01$.

The MRI and DTI are used to assess brain **structure** (grey and white matter, respectively).

An adapted version of MRI, fMRI, is used to assess **function**.

Basis of the fMRI signal

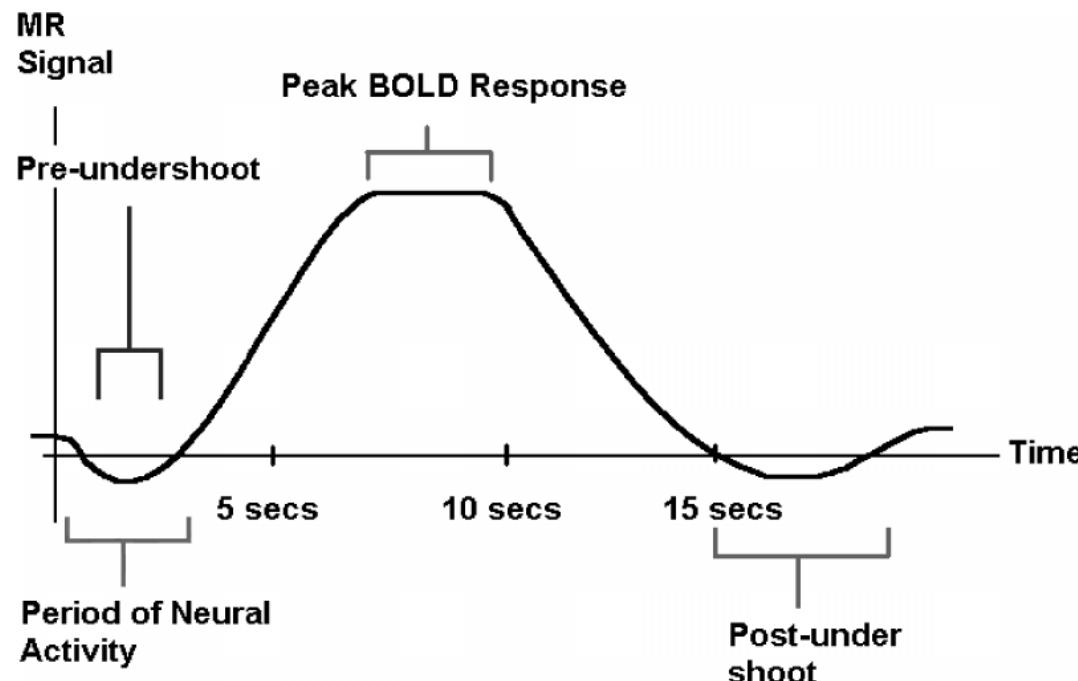
- Active neurons use glucose + oxygen



- After blood delivers oxygen, it becomes *deoxygenated*
- *If you knew the regions changing in blood oxygenation, you would know the regions changing in activity*

Basis of the fMRI signal

- Oxygenated and deoxygenated blood have different magnetic properties which can be measured
- If you measure blood oxy/deoxy ratio in a given area, you'll have a correlate of neuronal activity in that area



fMRI outputs

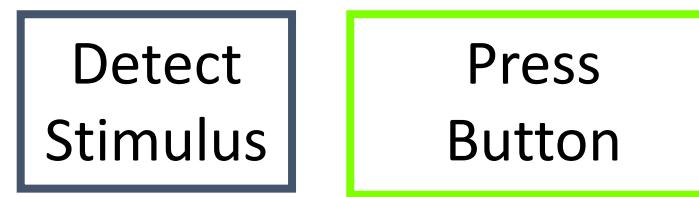
- An fMRI reveals that large portions of your brain are active at any given time
- Again, remember that any one neuron does many things (see earlier section on encoding)
- To interpret ‘noisy’ fMRI outputs, we must first process them carefully
- When processing fMRI outputs, we use **subtraction logic**

Subtraction Logic

Task 2



Task 1

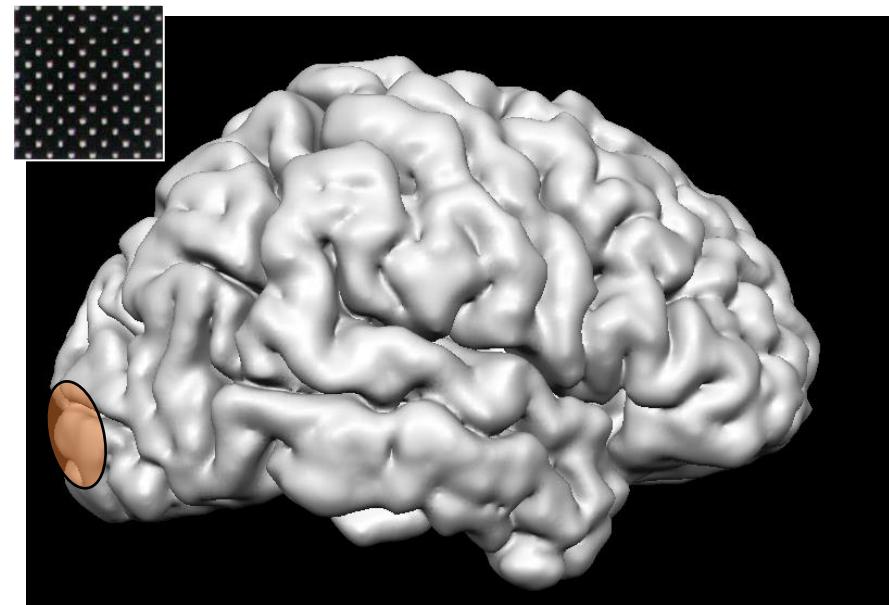
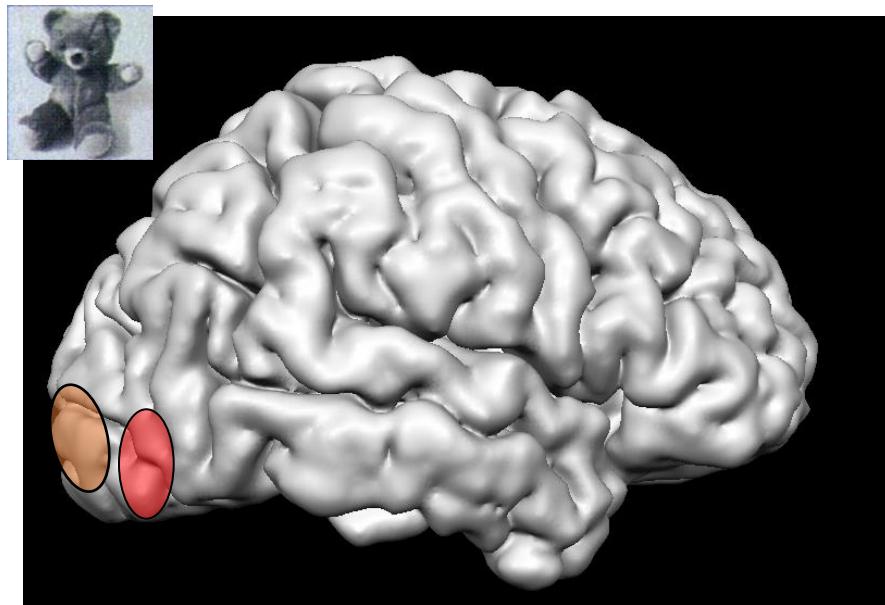


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Discriminate
Color

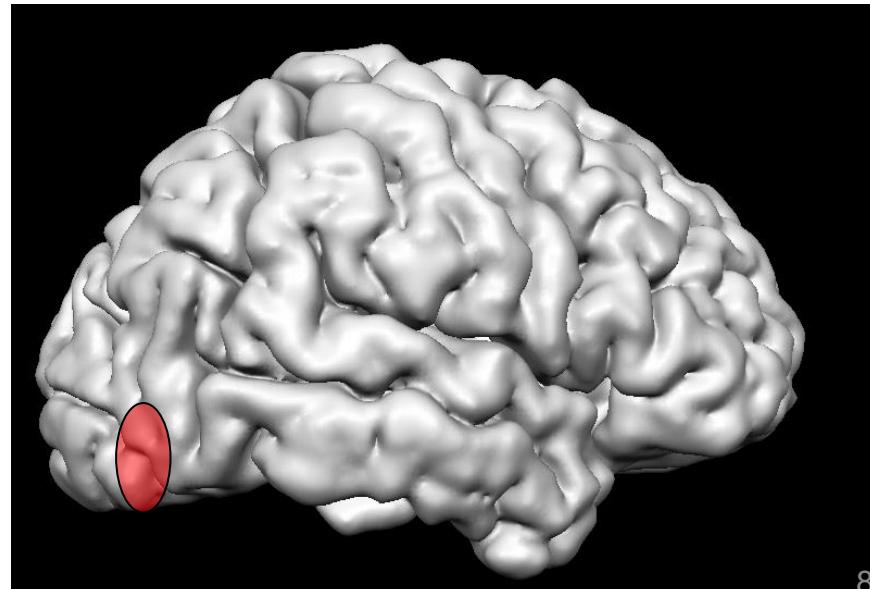
fMRI Subtraction



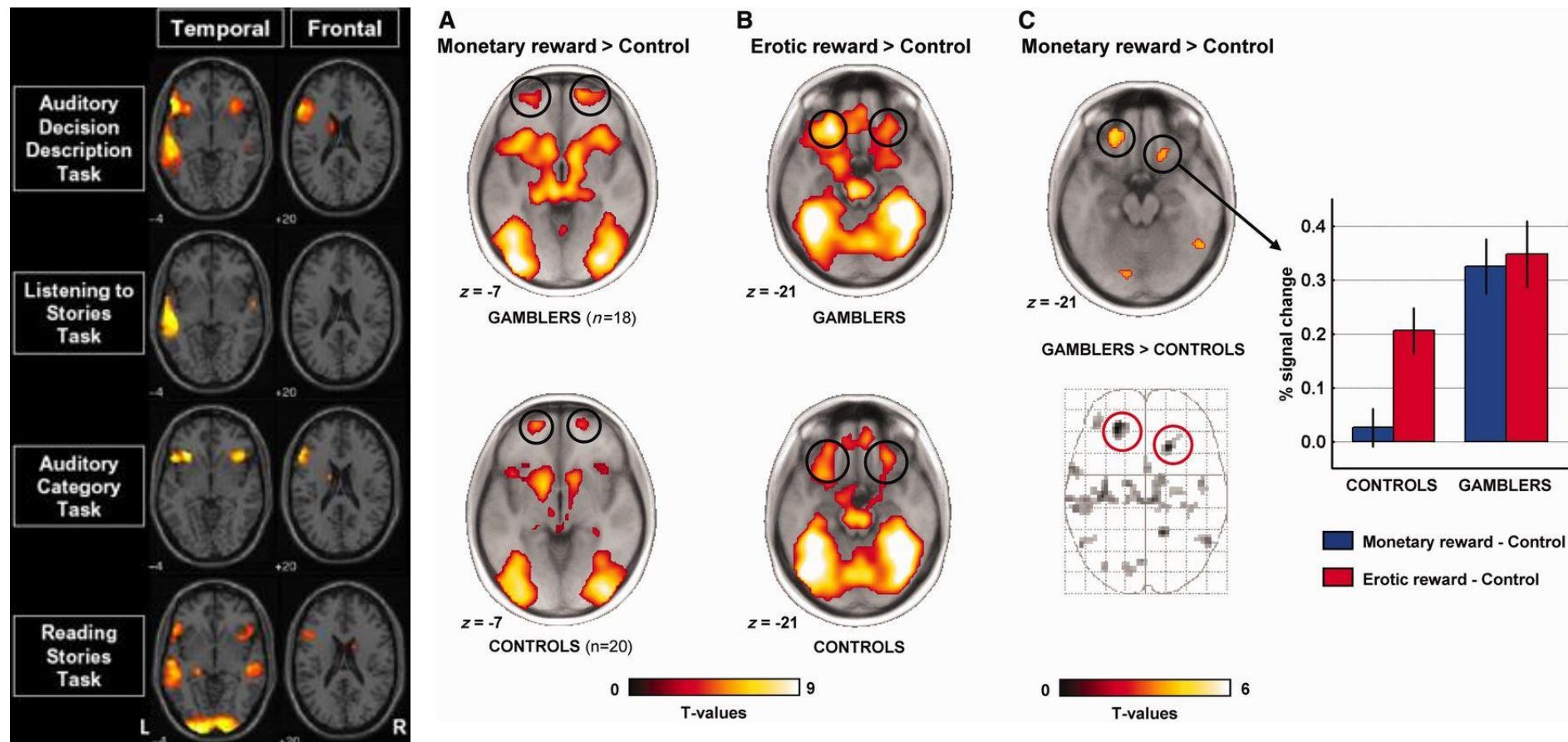
Teddy Bear stimulus = activates yellow + orange neurons

Control stimulus = yellow neurons

Via subtraction, we infer that the red neurons are specific to the teddy bear



fMRI for Behavior + Disorders



Brain activity differs in different tasks.

Brain activity may differ with personality characteristics and mental health disorders (such as addiction).

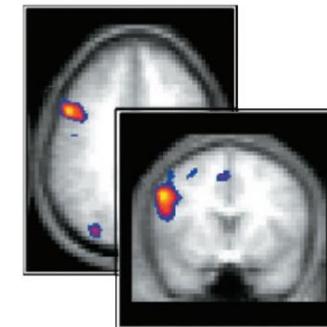
fMRI example: Studying memory

- If given a list of words and asked to recall them later, we'll always forget a few
- One explanation is that we have an encoding failure during our initial exposure to the words
- To test for this possibility, we can measure brain activity during the encoding phase

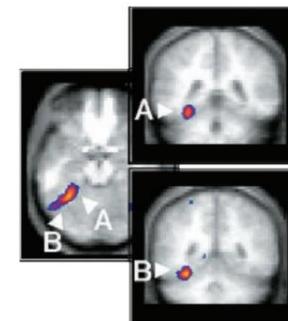
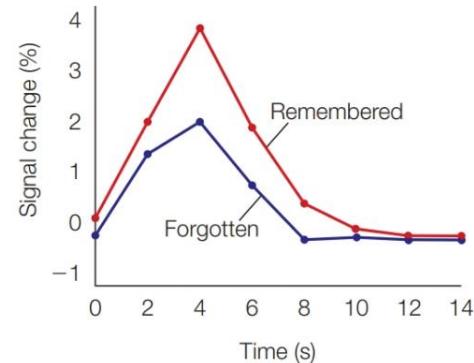


fMRI in memory mechanisms

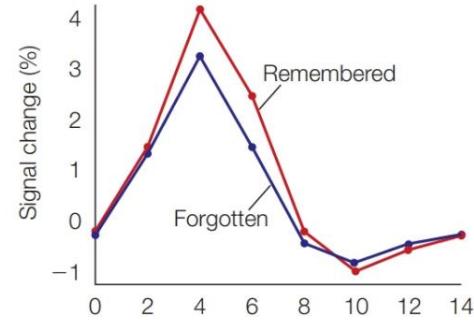
- Activity during the encoding is correlated w/successful recall
- In other words: If I study your brain while you're learning (i.e. encoding phase), I can predict what you'll retain later
- Suggests some memory failures are encoding failures



a Posterior LIFG



b Parahippocampal/fusiform gyri



This data is all
CORRELATIONAL, not
experimental.

*We are observing, not
manipulating anything.*

Why is this a problem?

The Problem of ‘Reverse Inference’

Psychological
Function X

Forward inference

Brain activity
in Region Y

“Manipulating X leads to changes in Region Y, so Y must be involved in X”

Problematic! Why???

Reverse inference

“Psychological function X must be engaged because Region Y is active”

Because Region Y can do many, many, many, many other things!

Credit Dr. Spaniol.

Do you love your iPhone?



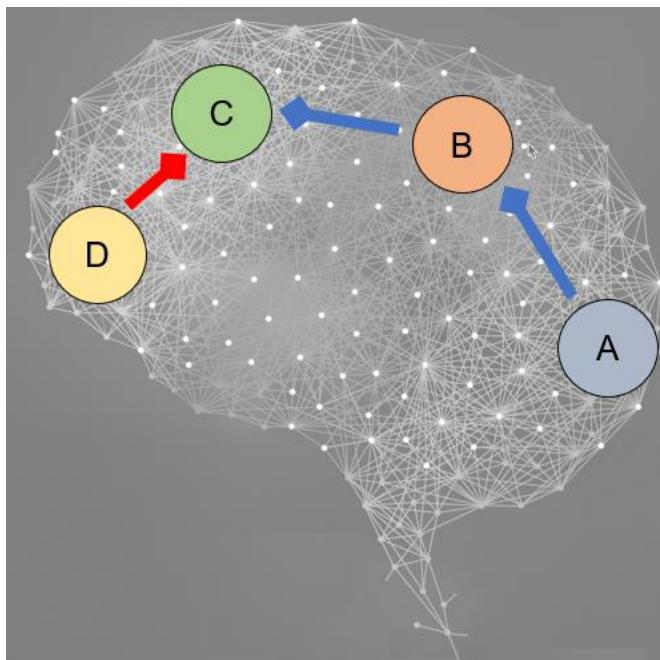
<https://www.youtube.com/watch?v=b64qvG2Jgro>; 5 – 7 minutes

fMRI - Summary

- **Great spatial resolution** (great for studying brain structure)
 - Best out of techniques we have covered today
 - Can be ‘paired’ w/other techniques (e.g. PET)
- **Decent temporal resolution**
 - Better than PET (arguably), not as good as EEG
 - Lag of several seconds between neuronal activity and signal
- Probably the most popular technique for **cognitive neuroscience**, but should be interpreted with care

fMRI to measure connectivity

- Recall that we are interested in neural networks (i.e. groups of inter-connected brain structures, A-B-C...)
- How might we identify neural networks in the brain?

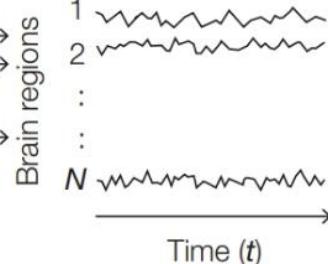
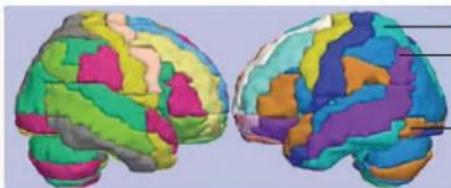


Logic:

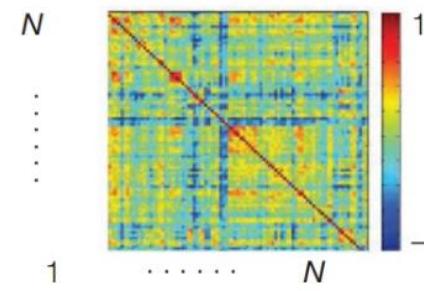
If A + B are interconnected in a network, you would expect that the activity of A + B is correlated

MRI to measure connectivity

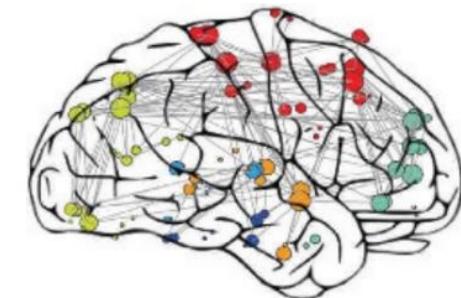
- Look at activity in different brain areas (A, B, C...)
- See what areas show highly correlated activity
- These areas may be interconnected
- Look at all linked areas to build a **connectivity map**



① Anatomical nodes



③ Association matrix



④ Connectivity map

rs-fMRI

- We can measure the connectivity of the brain **at rest** (i.e. while not doing a specific task) (**resting state fMRI or rs-fMRI**)
- Brain connectivity at rest may be related to your cognitive abilities (e.g. intelligence), mood + more
- Connectivity is plastic and modifiable with experience
- In a controlled study, we can observe how the strength of connectivity at rest changes after experience (e.g. before learning vs. after learning)

Measuring changes in connectivity

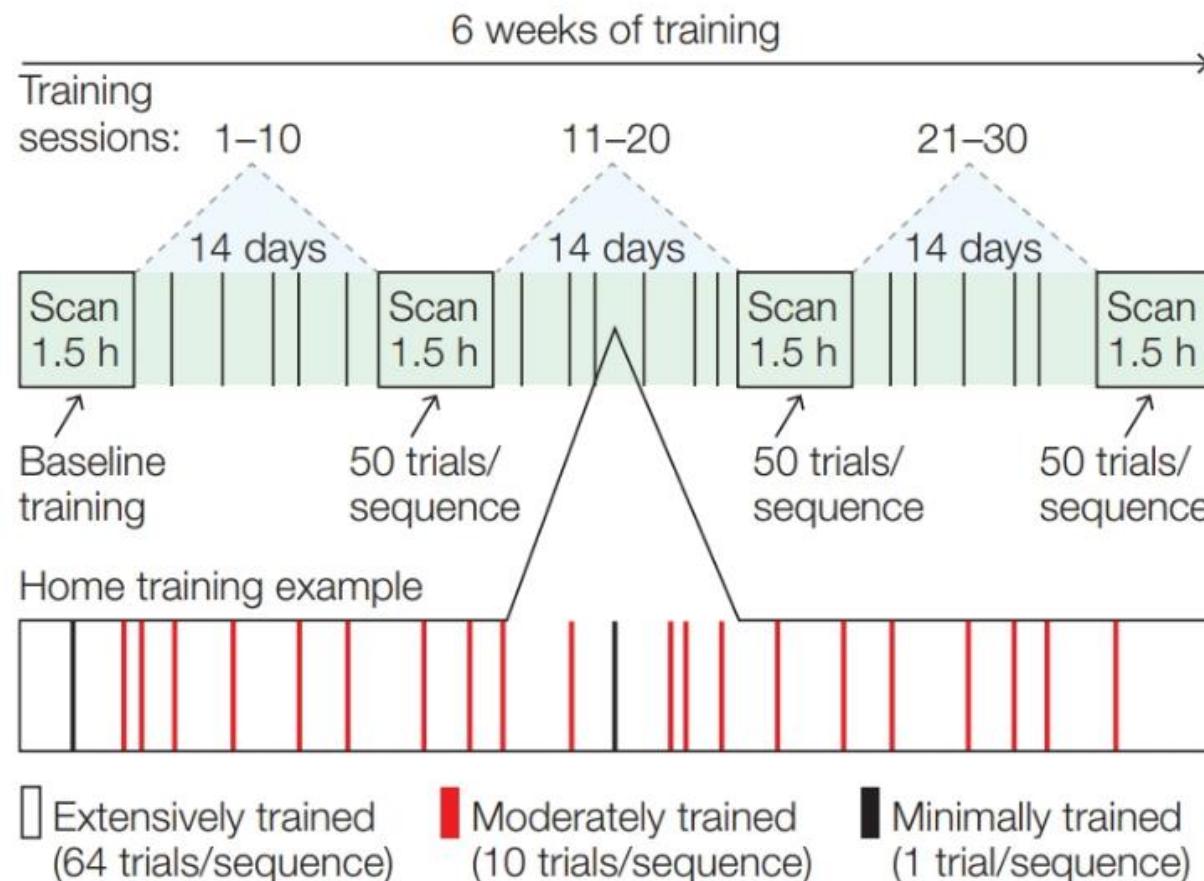
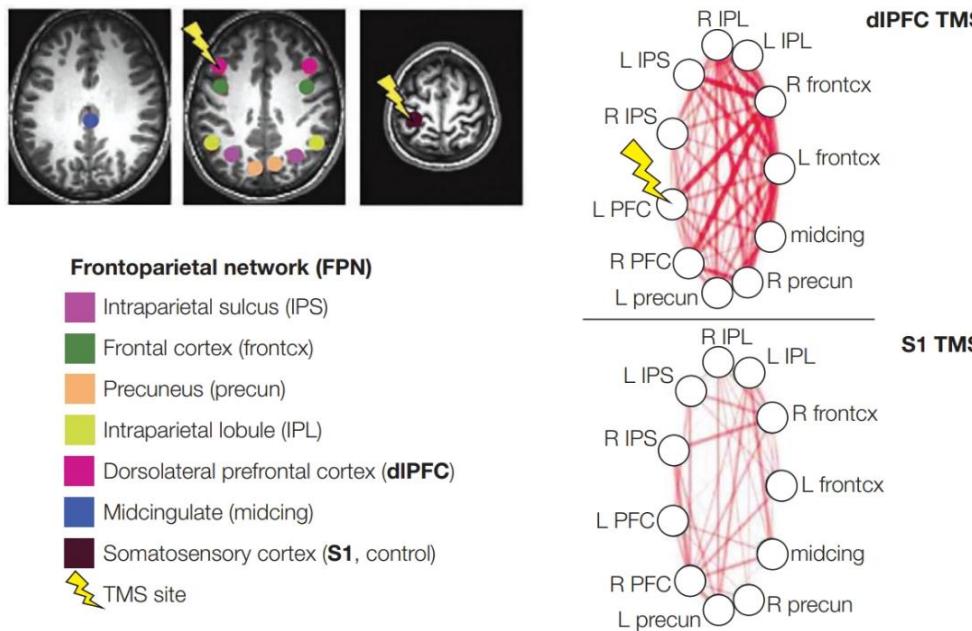


FIGURE 3.38 Training schedule for measuring learning.
Participants underwent a resting-state scan and an active-state scan before training, and then again every 2 weeks for the following 6 weeks.

Changes in connectivity

- In this study, stimulation of the brain area influenced the connectivity pattern of multiple brain regions
- Connections that increased in strength are shown in thick red lines



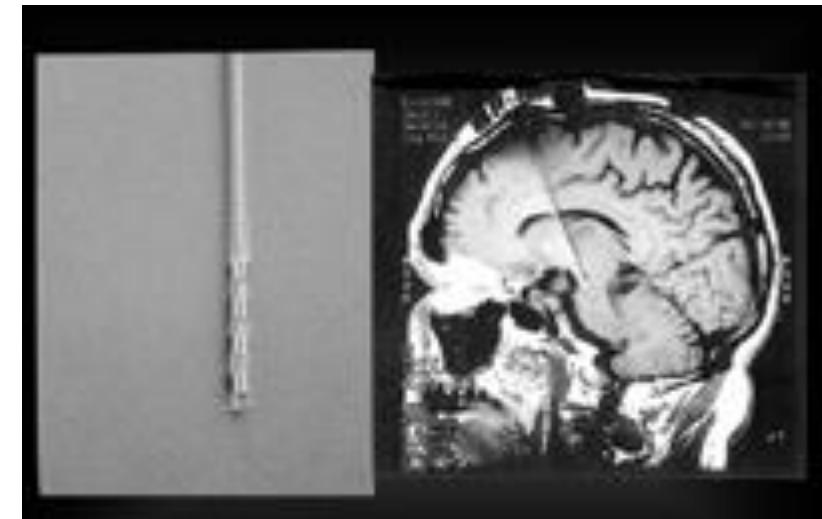
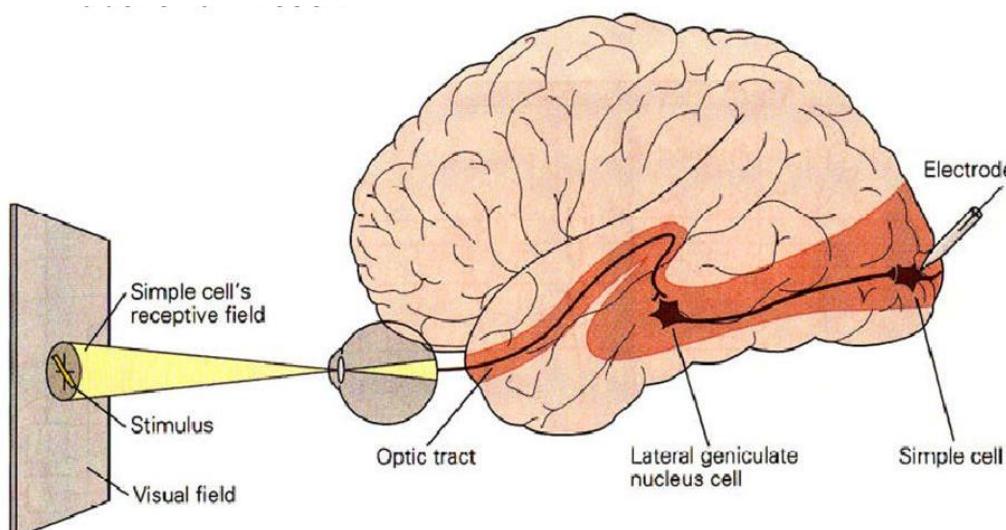
All these methods have focused on overall, large scale brain structure + function.

Can we get more specific?

Can we get down to the level of the cell?

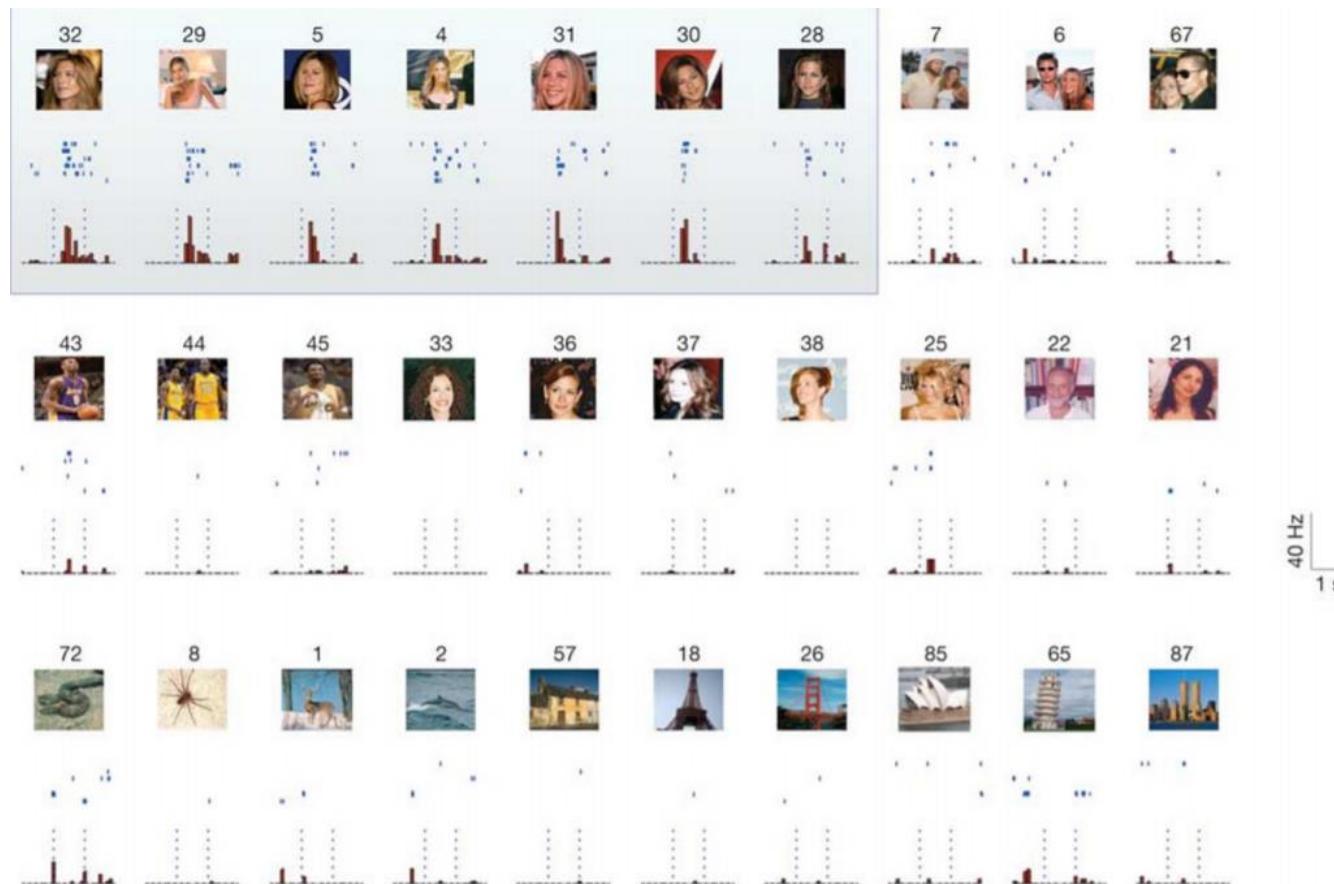
Single-cell Recording

- Recording activity of individual neurons during behavior
- **Highly invasive**; we rarely get the opportunity (unless we are already performing surgery on someone)

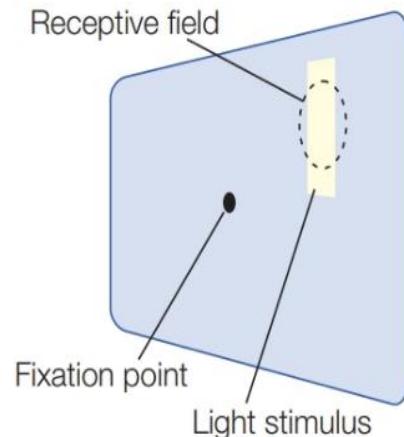


The ‘Jennifer Aniston’ Neurons

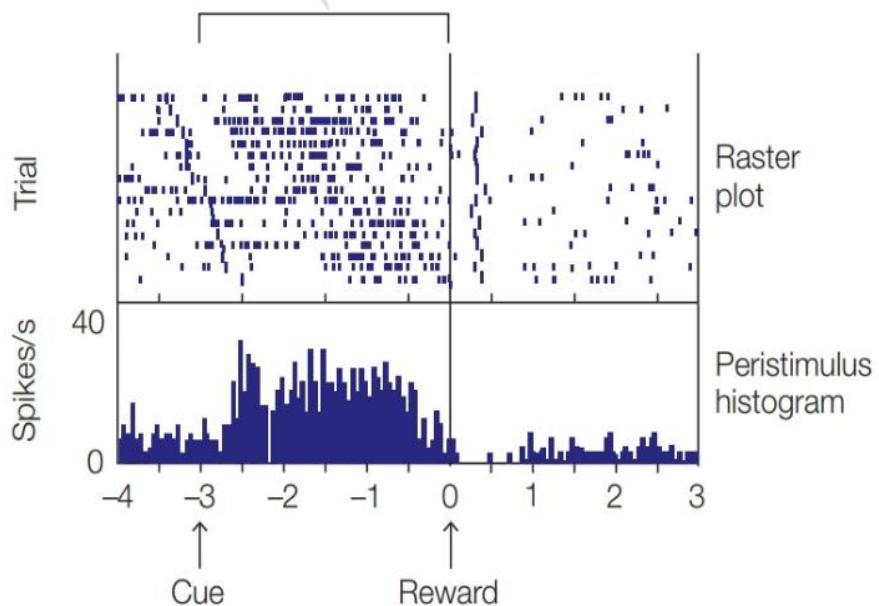
- In this experiment, they found neurons that fire specifically to different pictures of the same person



Cell recordings in animals

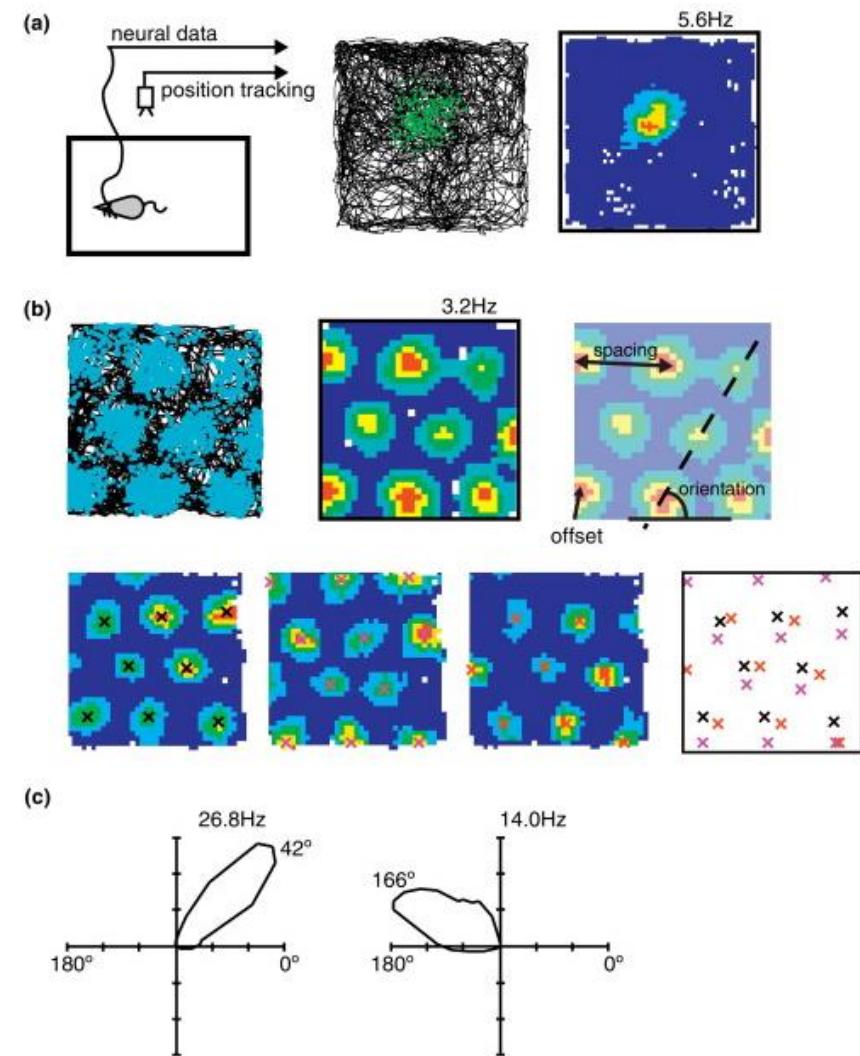


Cell is responsive when a stimulus is presented in its receptive field.

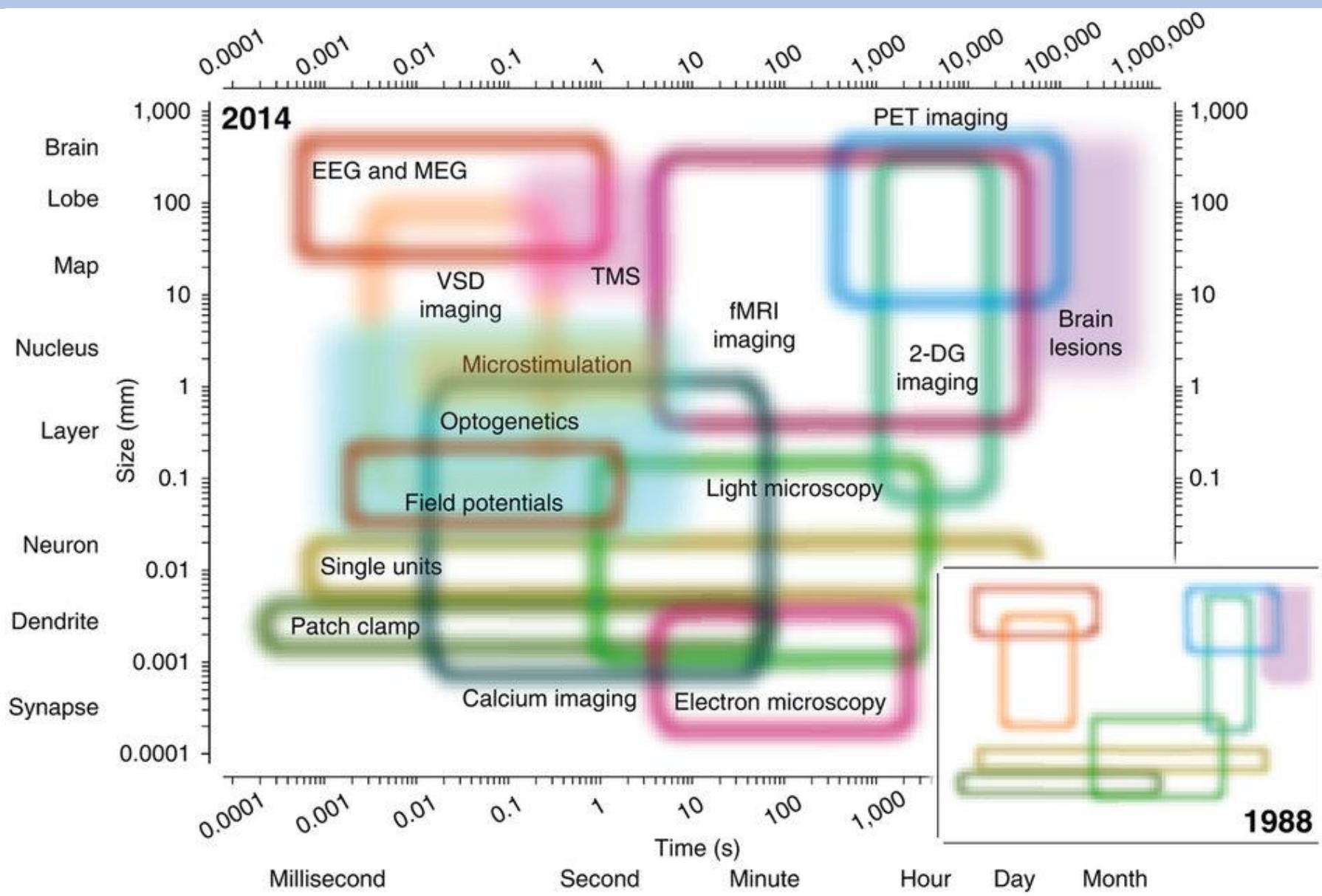


Cell recordings in animals

- Shown here are recordings from hippocampal cells while the mouse explores an area
- Cell activity depends upon mouse position
- Many cells in the hippocampus have this property (**place cells**)



Comparing Techniques



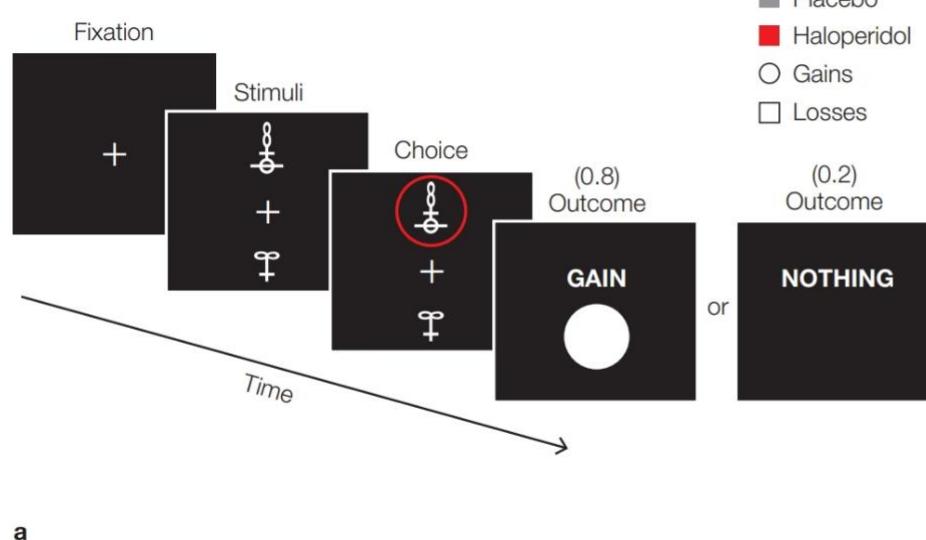
Part 4: Manipulating Brain Activity

Moving forward -

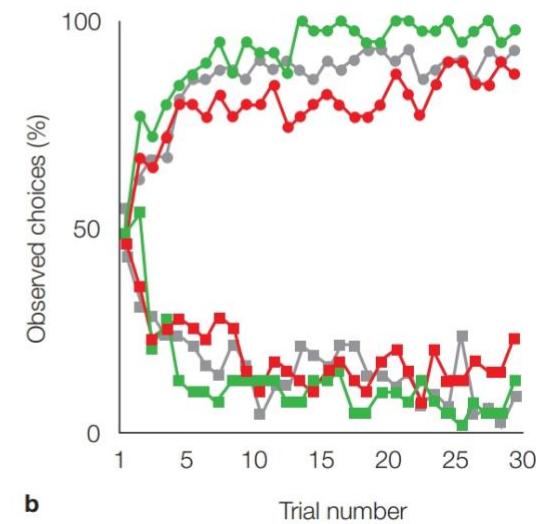
- So far, we've discussed techniques for observing brain structure and function (correlational data)
- None of these techniques give us compelling evidence of causal relationships between brain activity and mental processes
- *To identify causal relationships, we must manipulate brain activity in a controlled, experimental setting*
- Three main ways of doing this in humans: drugs, magnetic stimulation and electrical stimulation

1) Drugs

- Compare behavior under normal conditions to behavior while taking a drug (X, Y) or a placebo (Z)
- Example: In a reward-based task, **individuals learned faster w/L-DOPA** and **learned slower w/haloperidol**

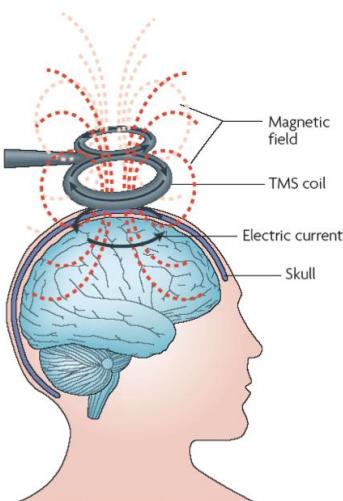


■ L-Dopa
■ Placebo
■ Haloperidol
○ Gains
□ Losses



2) Transcranial Magnetic Stim.

- Neuronal activity is manipulated by magnetic fields
- In a standard TMS study, we apply TMS to a particular brain area during a certain behavior
- If TMS changes that behavior, we can infer that the brain area targeted is involved in that behavior¹



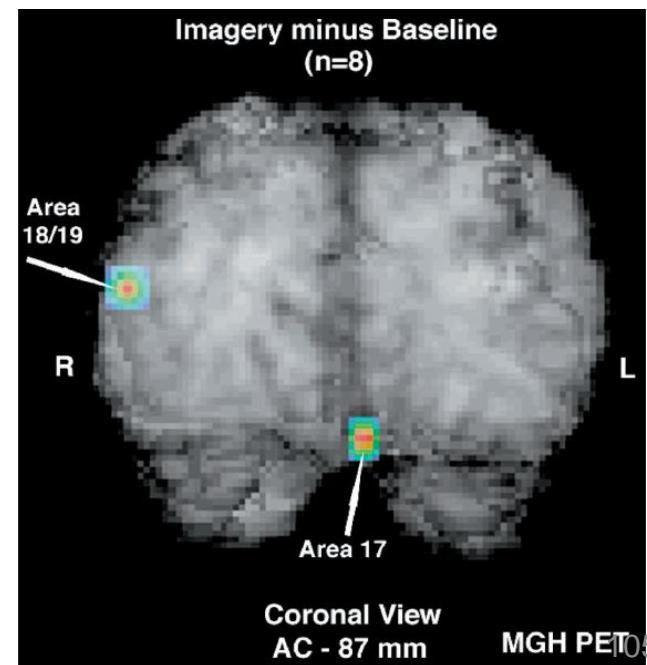
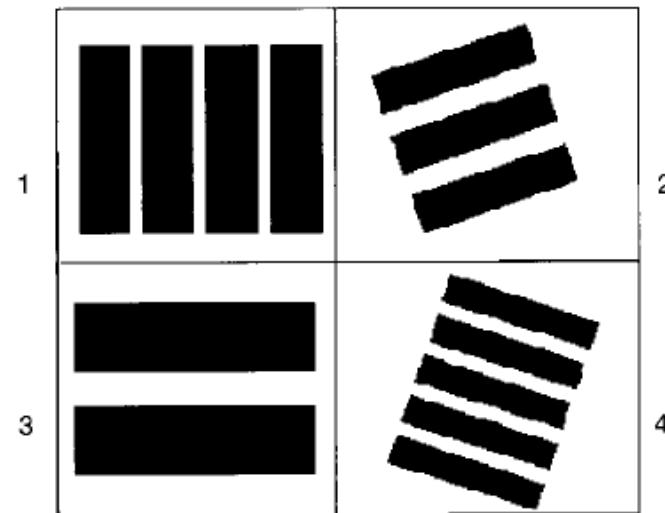
TMS also has therapeutic applications in treating depression (see Dr. Downar's amazing work)²

1. <https://www.youtube.com/watch?v=mD34o-sW22A>

2. <https://rtmslab.com/>

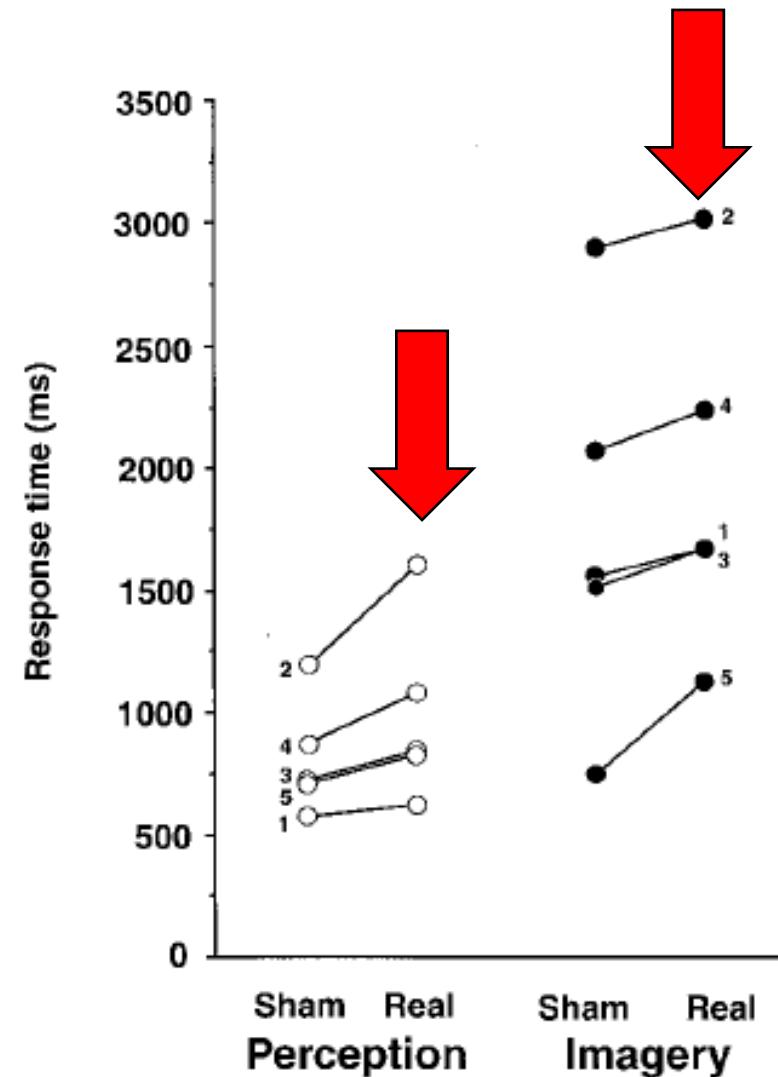
TMS + the neural basis of Imagery

- Subjects were asked to answer a question about a panel of objects
- Subjects did **perception trials** (w/objects) and **imagery trials** (objects absent + had to be visualized)
- While answering, TMS was applied to the primary visual cortex (*real treatment*) or a non-visual area (*sham/control*)



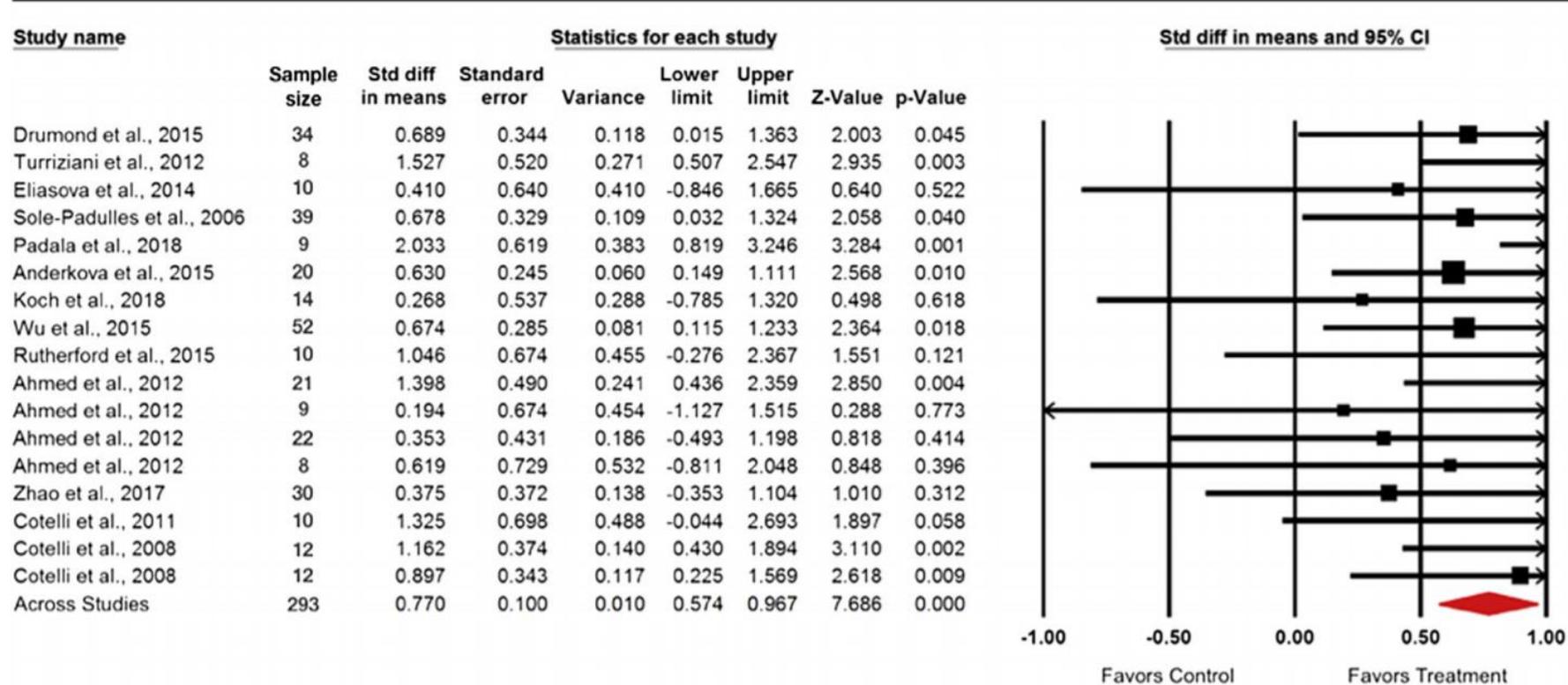
TMS + Imagery

- When TMS inactivated the visual cortex (**real**), judgments during perception and imagery trials took longer (increased RT)
- This suggests that the visual cortex activation is important for imagery + perception
- This TMS study allowed us to make causal inferences!



TMS – Therapeutic Applications

- New data suggests that TMS applied to the frontal lobe may rescue cognitive + memory in Alzheimer's Disease

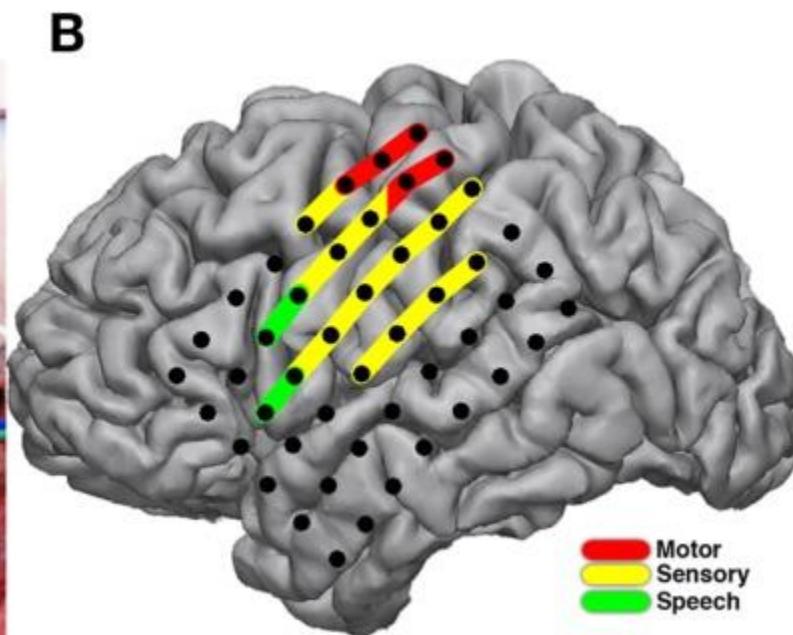
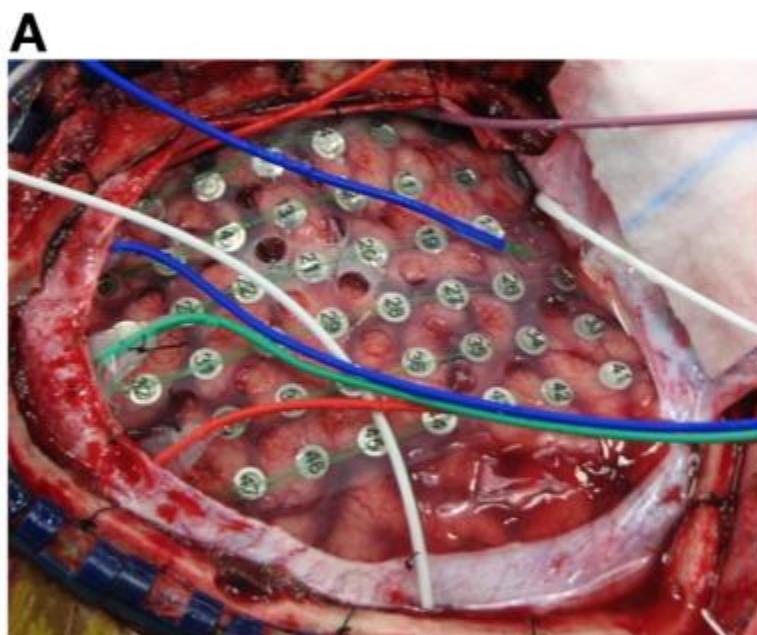


TMS – Summary

- Many great advantages
 - Non-invasive
 - Can be used multiple times in one subject
 - Relatively fast
- However, there are some notable disadvantages
 - Unclear what stimulation parameters to use
 - Difficulty precisely targeting certain deep brain areas
 - Relatively new; still underused

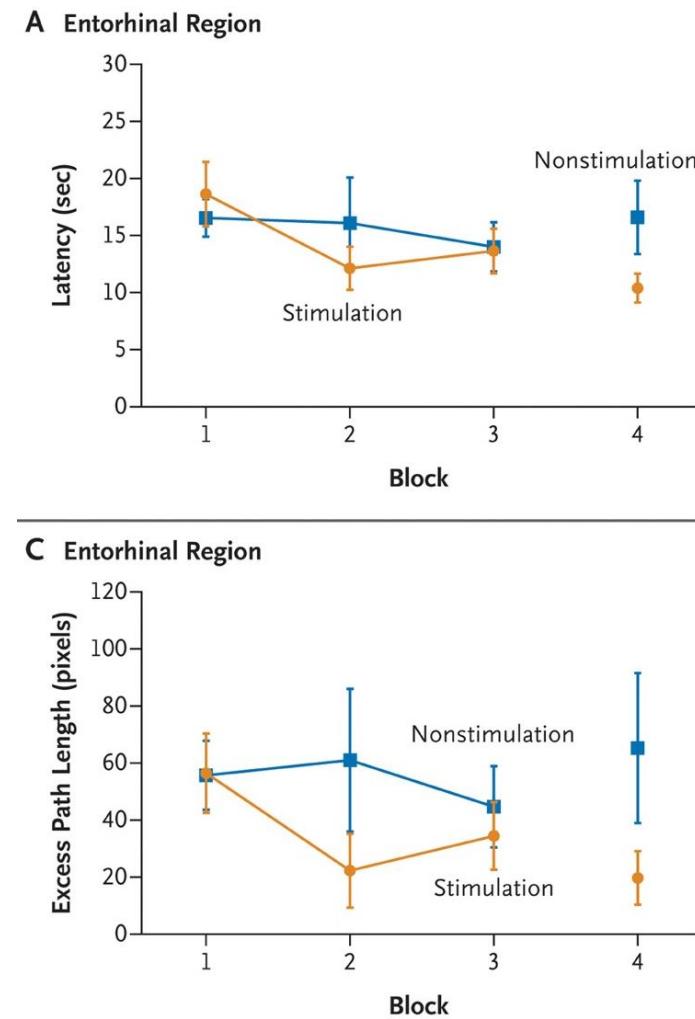
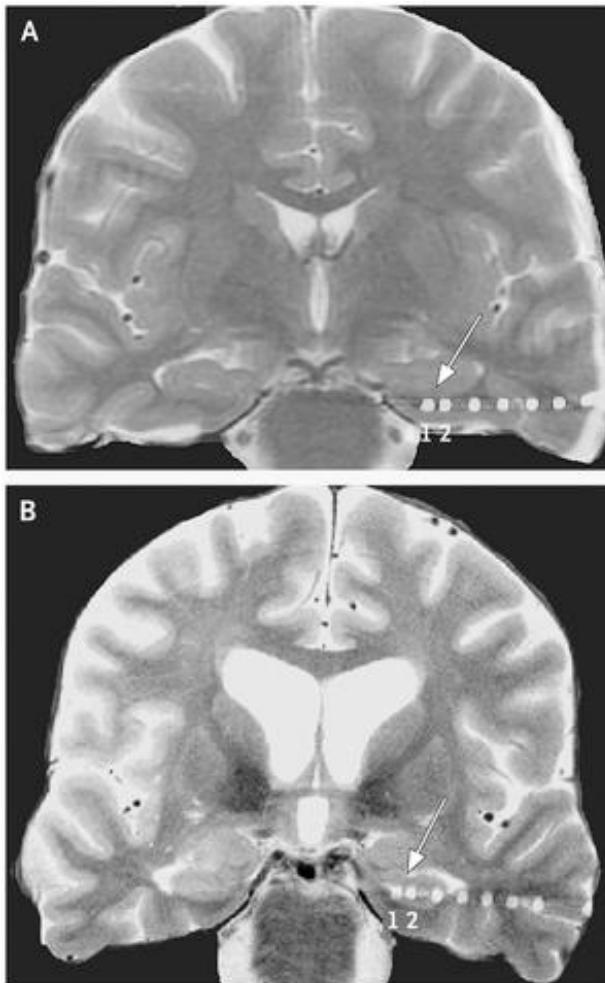
3) Electrical Brain Stimulation

- Pioneering work by Penfield with this technique lead to the development of influential cortical maps (i.e. sensory and motor homunculi)



- Also can be used to locate epileptic foci (source of seizures)

Stimulation to enhance memory?



Activation of certain brain areas (e.g. **entorhinal cortex**) using electrodes can facilitate spatial memory

EBS – Summary

- Informative of causal relationships, but comes with many drawbacks
- Highly invasive
- Only used when there is already another pathology present (eg. epilepsy) (potential confound)
- Few opportunities for use (small sample size)
- Concerns about generalization of findings