9.13 The Human Brain Class 6
Experimental Design

Outline:

I. Leftovers from Cog Neuro Face Methods
- TMS
- animal research

II. The Snake Region Assignment
- A few comments from me
- The you will work in groups to hash out details of design.
- Then we will discuss

III. Multifactor Experiments
- main effects and interactions

Review of Last Two Lectures: Face Recognition: What we want to know & Which Methods Can Answer Which Questions

Key Questions about Face Recognition:

1. What is the nature of the problem of face perception? (inputs, outputs, challenges)
   Marr computational theory level
2. What is the nature of the representations we humans extract form faces?
   Measure behavior!
3. Is face perception a distinct system from the rest of vision/cognition?
4. How *fast* are faces detected and recognized?
5. How is face recognition implement in individual neurons/circuits?
6. What is the causal role of each brain region in face recognition?

Methods Discussed Last Week:

Monday: Computational theory & Behavioral measurements

Wednesday: fMRI, ERP/MEG, intracranial recording, studying patients with brain damage, brain stimulation.

Wrapping this up Today: TMS and animal studies

Behavioral Methods: Advantages & Disadvantages

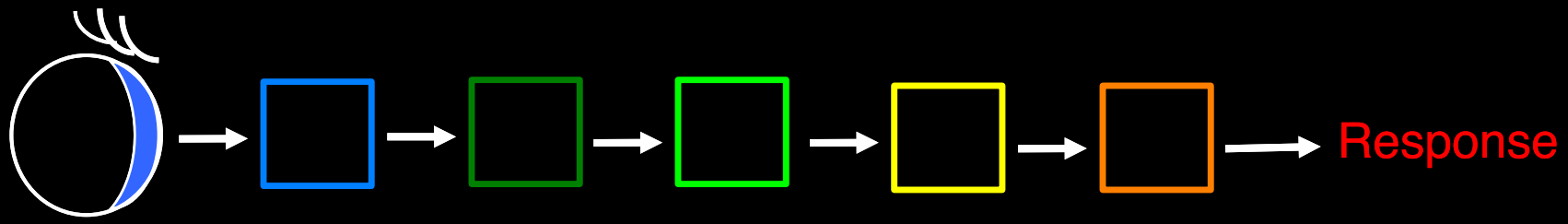
Advantages:

1. Good for characterizing internal representations.
   at least qualitatively
2. Good for dissociating distinct mental phenomena.
   e.g. face versus object processing
3. Cheap!

Disadvantages:

1. No relationship to the brain, at least not without further information

2. Data are sparse: all we have is the output of the final stage,
   but we would like to characterize each stage in the whole sequence of processing.



fMRI: Advantages & Disadvantages

Advantages:

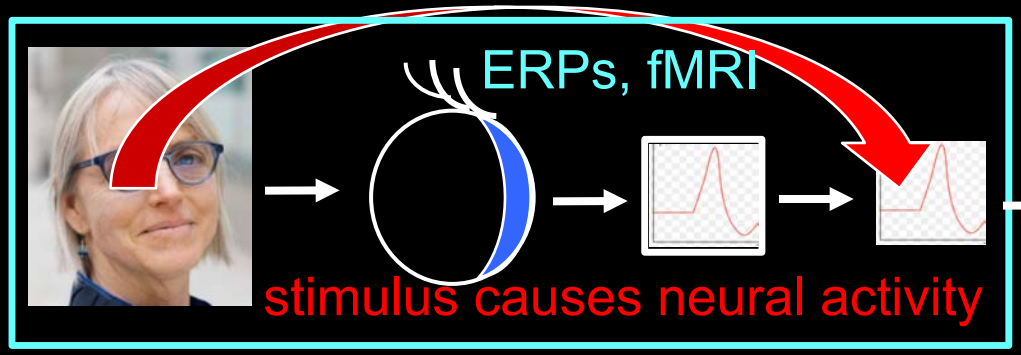
- The best spatial resolution available for studies on normal subjects.
- Noninvasive.

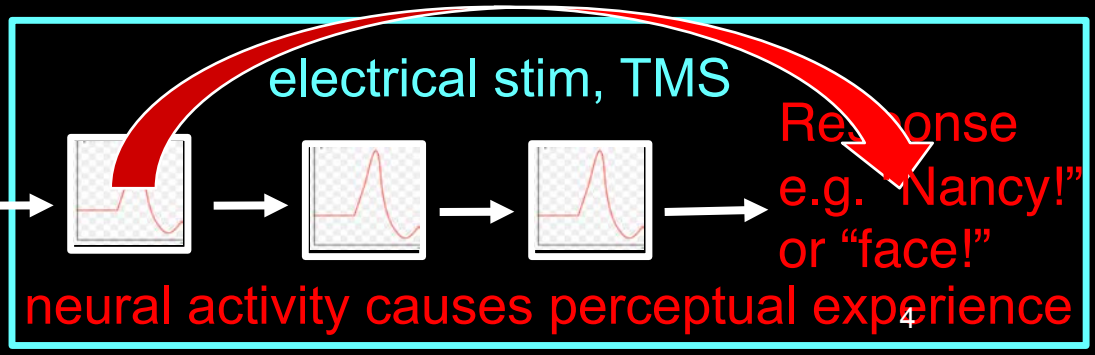
Disadvantages:

- Temporal resolution not on a par with visual information processing.
- Doesn't test causal role of neural activity in cognition/behavior.
- Can't tell if activity measured plays a causal role in cognition/behavior!
- The physiological basis of BOLD is unclear (synaptic activity vs spikes).
- Spatial resolution a ~1 mm at best (difficult to see cortical columns),
- Expensive (>$600/hour!).
- Loud banging noise.

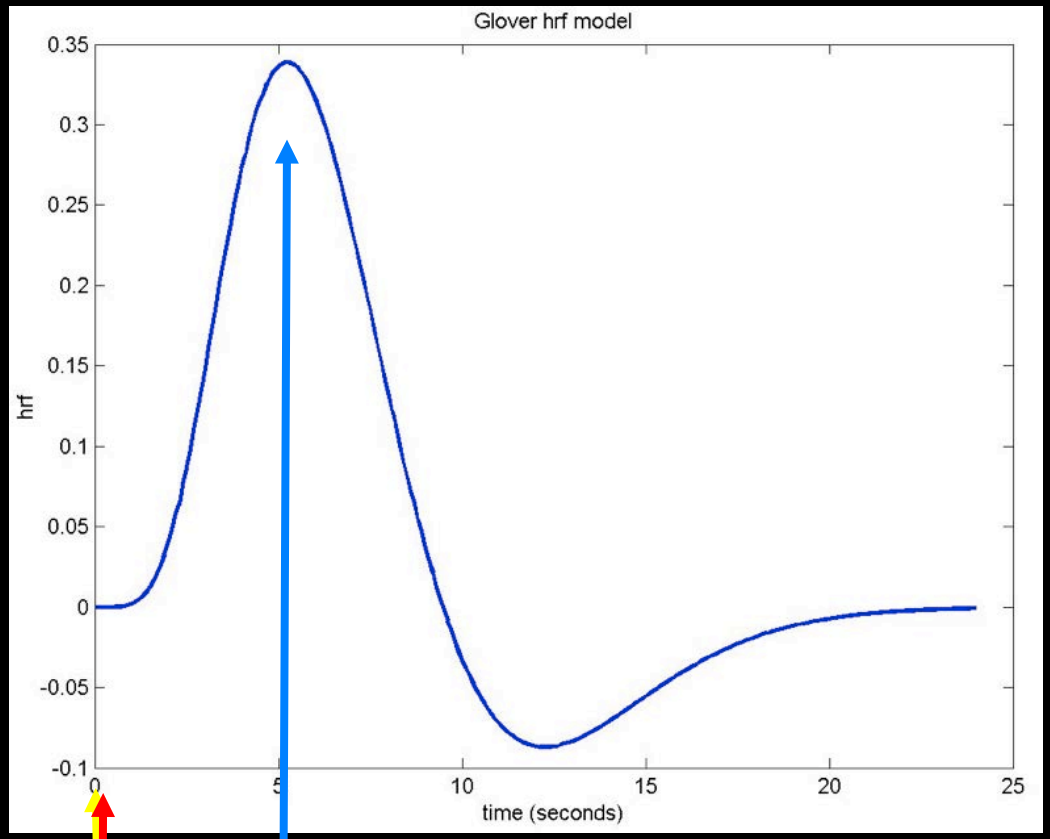
BTW *which* causal role are we talking about here?

Can only test causal role of X in producing Y if you manipulate X.





BOLD Response, or "hemodynamic response function (HRF)"



Visual stimulus on

Neurons fire

BOLD response

>>>> BOLD fMRI response peaks 5-6 seconds after neural activity.

So, it is hard to distinguish neural events that happened within a second.

EEG & MEG

Advantages:

- Excellent temporal resolution.

  [Why would we care about time?]

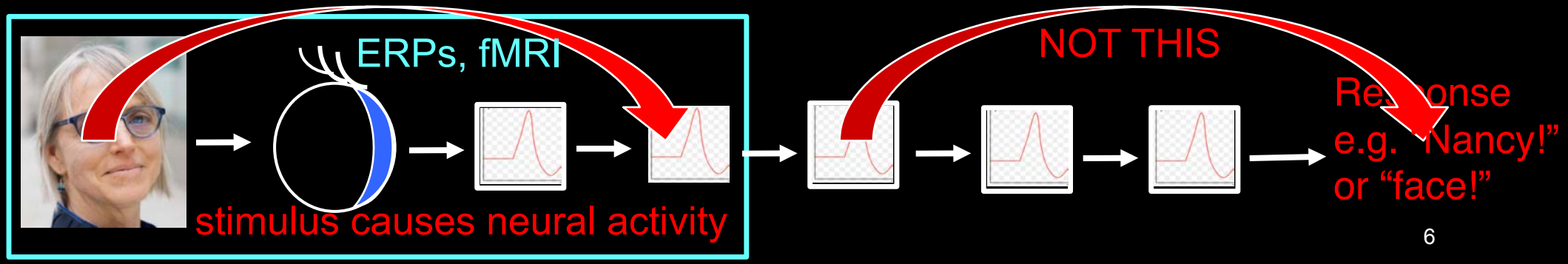
- Noninvasive
- The methods described so far rely on finding specific selective responses.

  But new ML methods can ~ "decode" from ERP and MEG responses what the person saw/thought.

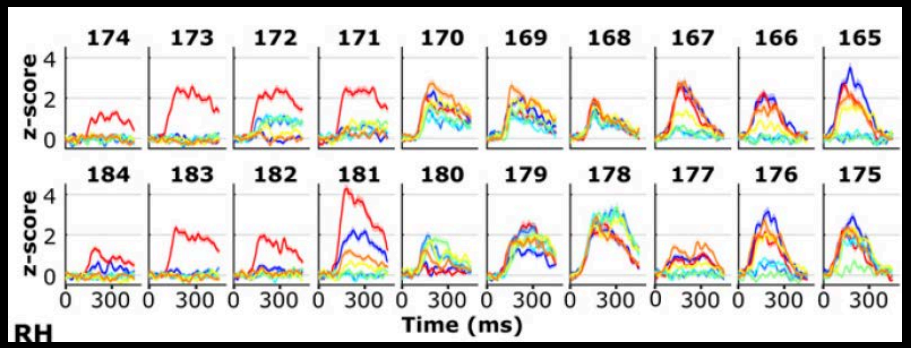
  More on that later.

Disadvantages:

- Lousy spatial resolution. (Ill-posed "inverse problem".)
- Doesn't test causal role of neural activity in cog/behavior.



Intracranial Recording



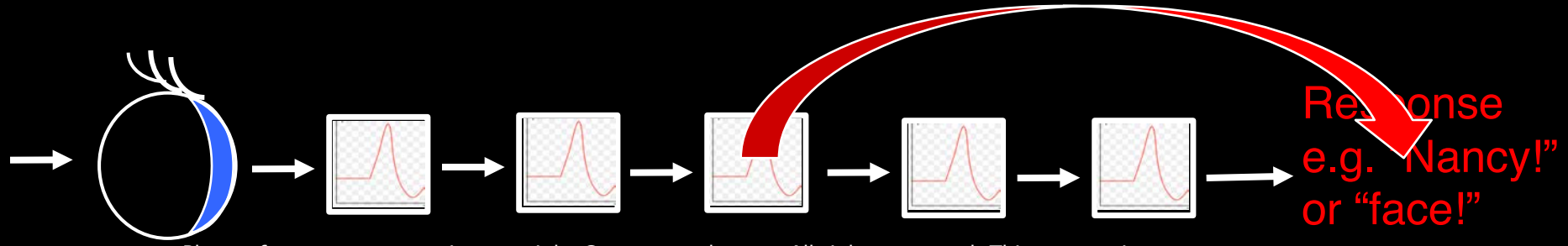
Advantages:

- The only method in humans w/ high spatial *and* temporal resolution

Disadvantages:

- Invasive; Only possible in patients with neurological problems.
- Data are rare and hard to control.

Question:
Does intracranial recording test causal role of neural activity in perception/behavior?



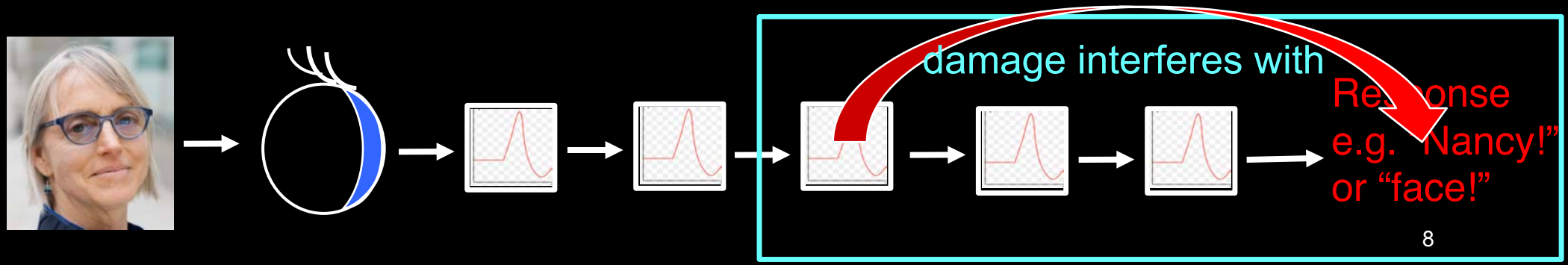
Studies of Patients with Focal Brain Damage

Advantages:

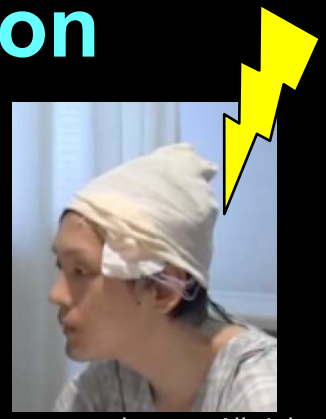
- Strong link between brain and behavior: evidence that the damaged region plays a necessary (causal) role in face perception.
- Two opposite patterns of deficits collectively represent a "double dissociation", suggesting independence of the two processes.

Disadvantages:

- Damage is usually large, covering multiple areas.
- In humans, only "natural experiments": cannot chose your site;
- Lack of disruption could be due to compensatory mechanisms.
- No before versus after.
- Ambiguity: damage to a processor vs a *connection* betwn processors.



Direct Intracranial Electrical Stimulation



In human neurosurgery the surface of the brain can be electrically stimulated. Can lead to disruption or sometimes positive percepts.

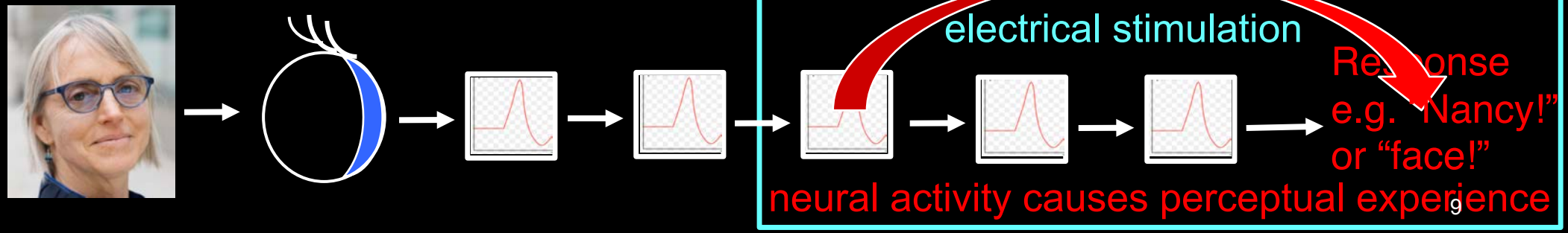
Example: Hallucinatory face percepts when FFA is stimulated.

Advantages:

- Stronger evidence (than observation studies) for a direct causal role
- Excellent temporal and spatial resolution.
- Reversible (a major advantage over lesion studies)

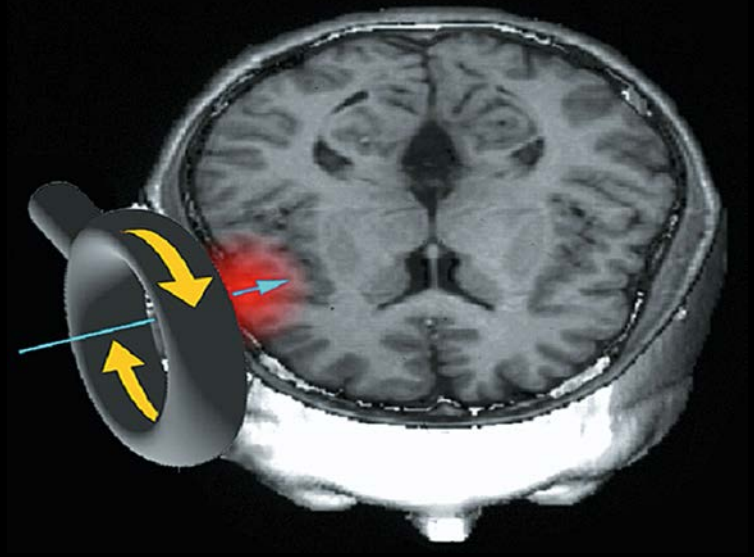
Disadvantages:

- Very Limited data: only a few trails & only subjs w/ abnormal brains.



Challenge: Can we test the causal role of a particular part of the brain *in a normal subject*?

The only method that can disrupt specific brain regions in normal brains:
transcranial magnetic stimulation (TMS)



TMS induces a brief, strong, transient magnetic field over scalp.
What should that do to underlying cortex?

watch me get zapped with TMS in video at nancysbraintalks

Transcranial Magnetic Stimulation

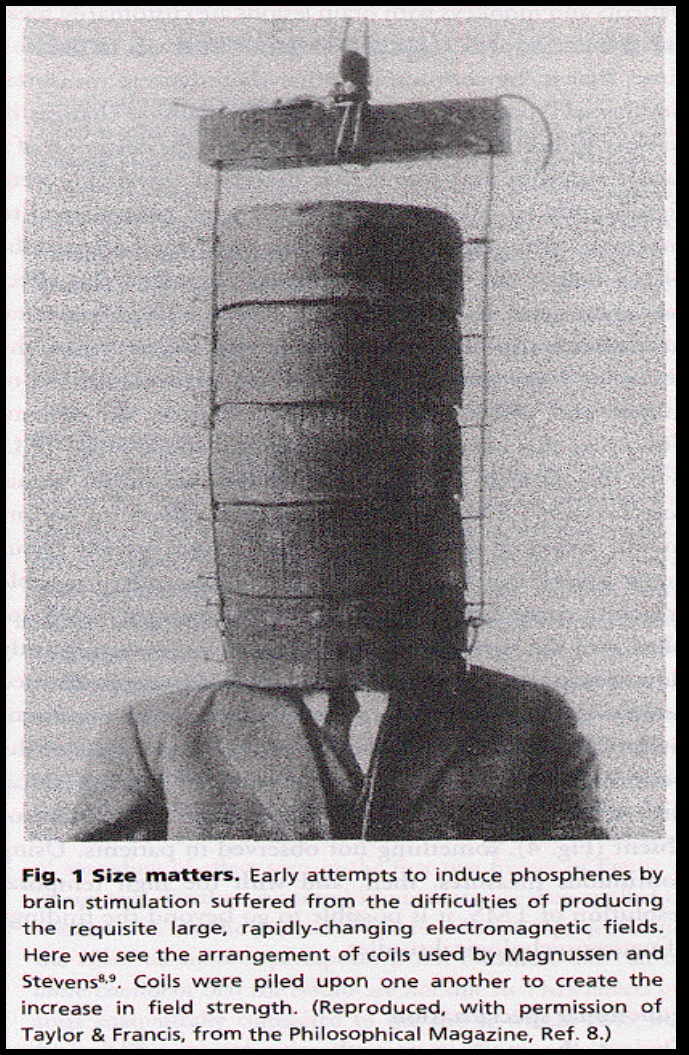


Fig. 1 Size matters. Early attempts to induce phosphenes by brain stimulation suffered from the difficulties of producing the requisite large, rapidly-changing electromagnetic fields. Here we see the arrangement of coils used by Magnussen and Stevens[8,9]. Coils were piled upon one another to create the increase in field strength. (Reproduced, with permission of Taylor & Francis, from the Philosophical Magazine, Ref. 8.)

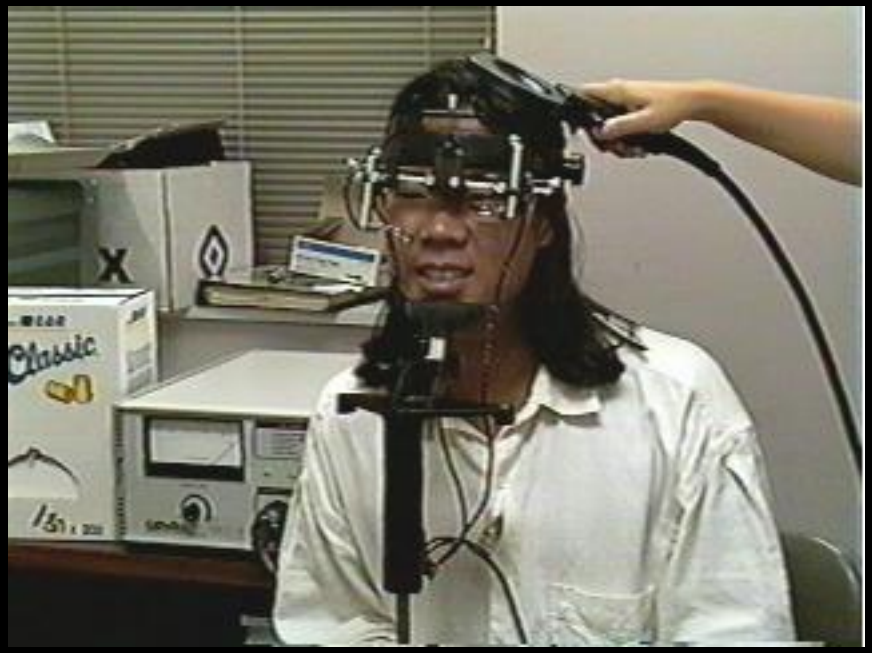
An early TMS device.

Transcranial Magnetic Stimulation
Can TMS tell us anything about Face Perception?

Can briefly and focally disrupt neural activity in surface regions of cortex.

Spatial resolution is low: ~ 1-2 cm.

Can guide placement of coil to specific locations mapped with fMRI in that individual.



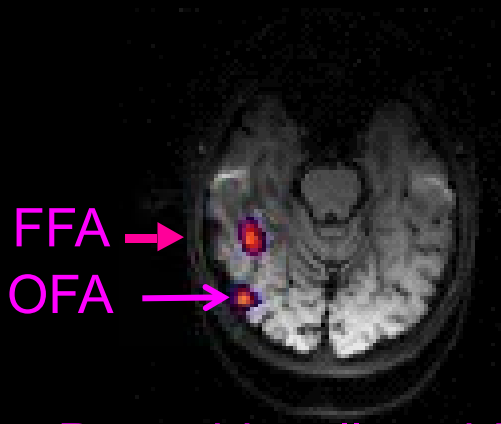
A more recent TMS device.

Transcranial Magnetic Stimulation
Can TMS tell us anything about Face Perception?

Problem: cannot reach the FFA.

David Pitcher's good idea:

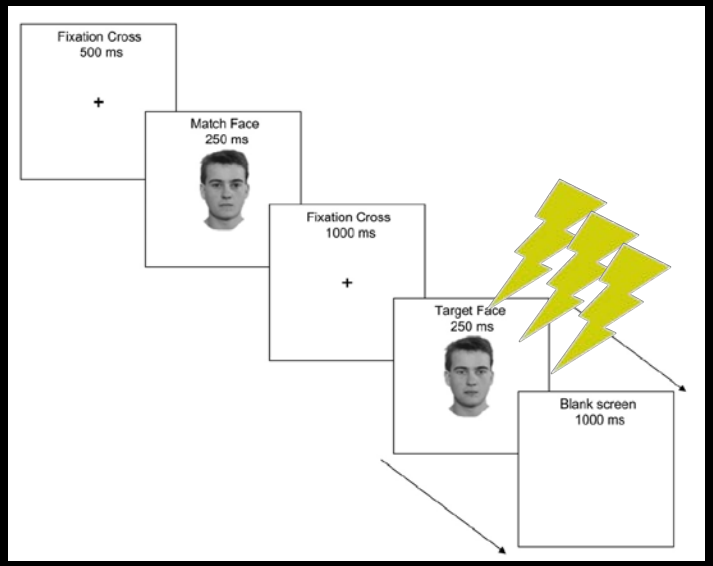
If you cannot zap the region you love, love the region you can.

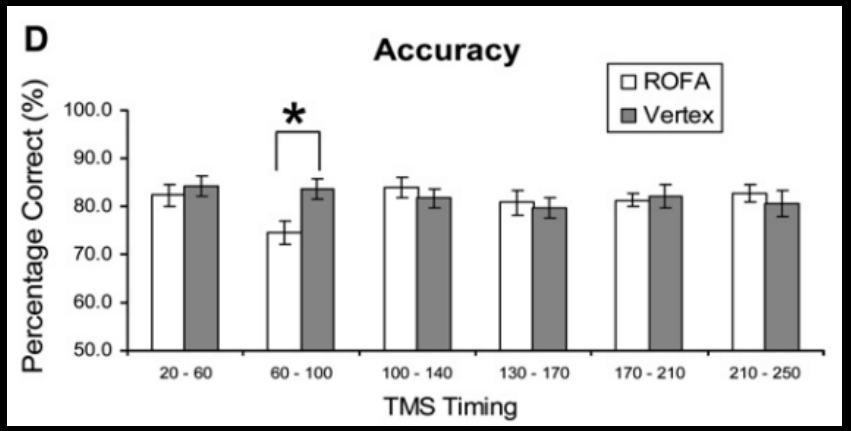


Does this tell us this region is specifically involved in face perception?

Same-different task.

Zap OFA @ diff times after presentation of face 2.





What does this tell us?
What else do you want to know?

Figures source: Pitcher, D., Walsh, V. & Duchaine, B. Exp Brain Res 209, 481 493 (2011). https://doi.org/10.1007/s00221-011-2579-1

Transcranial Magnetic Stimulation

Advantages:

- Strong evidence for a direct causal role of this part of the brain in perception.
- Good temporal information (unlike patients).
- The only disruption method that can be done on normal humans.
- Reorganization/adoption of new strategies unlikely.

Disadvantages:

- Spatial resolution not fantastic (~1-2 cm)
- Underlying basis not well understood.
- Does not reach far below scalp*

OK where have all these methods gotten us?

*Stay tuned,
Ed Boyden
is working on this

Face Recognition: What we want to know

Key Questions about Face Recognition:

1. What is the nature of the problem of face perception? (inputs, outputs, challenges)
   Marr computational theory level
   Major challenge: huge variation across images of a single face
2. What is the nature of the representations we humans extract form faces?
   Not image invariant for unfamiliar faces.
   Orientation specific
3. Is face perception a distinct system from the rest of vision/cognition?
   Looks like it, from both behavior and fMRI, but we have not yet nailed the case.
   Think about why.
4. How *fast* are faces detected and recognized?
   Face detection begins by 170 ms, maybe earlier.
   Face recognition we don't yet know. Stay tuned.
   Does this tell us what kinds of computations are involved? Not really yet but…
5. What is the causal role of each brain region in face recognition?
   FFA is causally involved in face perception, apparently not object perception.
   (So maybe we need different theories of how face vs obj recognition works.)
6. How is face recognition implement in individual neurons/circuits?

This is all great, but there are so many questions we have not yet answered….

Face Recognition: Questions we cannot answer well with methods in humans

1. What is actually represented in each region and how is it represented?
   i.e., what is the neural code for faces?
2. What is the actual series of computations that extract these representations, and how do those computations unfold over time?
3. Anatomical connections of each face region?
4. What is the causal role of each region in face perception?
5. How does this system get wired up over development?
   e.g. what is the role of experience?

The sad truth:
For the most part, we do not have good methods that enable us to answer these questions in humans.
Mostly these questions can only be answered with research in animals.

Ethical Issues in Animal Research

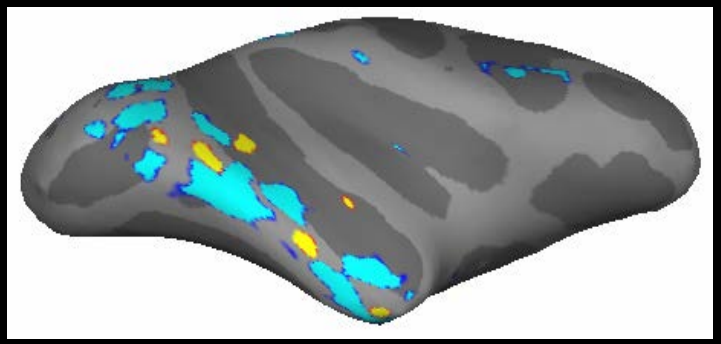
It is not unreasonable to have qualms.
Causing animals pointless suffering is unacceptable.
A difficult tradeoff between avoiding animal suffering and
research that has saved countless human lives
(including mine)
But a few things to inform your thoughts on this tradeoff:
1. In the US animal research is heavily regulated
animals receive excellent vet care
pain is minimized and infrequent
2. The bigger issue: what kind of life is this for lab animals?
increased housing in social groups
many monkeys play video games all day
perhaps they would be happier in nature
though nature can be pretty nasty
3. Benefits of research are forever,
vastly more justifiable in my view than
eating meat/buying leather

and methods available in animal research are vastly more powerful than methods available in humans. For example

What Invasive Studies in Monkeys have Taught us about Face Recognition

Doris Tsao &
Winrich Freiwald

Faces>objects in monkeys



1. What is actually represented in each region and how is it represented?
   what is the neural code for faces?
   record response of each of 100s of neurons to each of 100s of stimuli
2. What is the actual series of computations that extract these representations, and how do those computations unfold over time?
   watch representations change over time within and across face patches
3. Anatomical connections of each face region?
   tracers and other methods reveal precise anatomical connectivity
4. What is the causal role of each region in face perception?
   electrical stimulation targeted to specific regions
5. How does this system get wired up over development?
   raise monkeys without ever letting them see a face

9.13 The Human Brain Class 6
Experimental Design

Outline:

I. Leftovers from Cog Neuro Face Methods
- TMS
- animal research

II. The Snake Region Assignment
- A few comments from me
- The you will work in groups to hash out details of design.
- Then we will discuss

III. Analyses of fMRI Data
- standard group analyses versus fROIs

IV. Multifactor Experiments
- main effects and interactions

Basic Concepts & Terminology in Experimental Design

Independent variable: The factor the experimenter manipulates. (e.g. stimulus type)
usually this is varied across several conditions (e.g., faces, objects)
Dependent variable: The thing the experimenter measures
e.g., magnitude of fMRI (BOLD) response in a given voxel or region
Hypothesis: The key idea you are testing in the experiment.
Prediction: The precise finding in your data that should be found if the hypothesis is true.
Confound: A difference between your conditions other than the one you are trying to manipulate, that hence provides an alternative account of your data.
Contrast: an activation is generally based on a contrast of two conditions,
e.g. finding voxels that respond faces > objects.
The point of a contrast is to isolate a mental process…

How do we Decide What Contrast to Use?

Step 1. State the precise hypothesis you are testing. Often it will concern a specific mental function (e.g. face recognition).

Step 2. Recall that fMRI can only show differences in brain activity between conditions, not absolute amounts.

- So in any imaging experiment, you will need to compare two (or more) conditions.
- To isolate a particular mental function, you need to turn it on and off (or on more vs less strongly).
- Usually you cannot conduct a single mental function without also doing others.
- So, you design 2 tasks that differ in just one mental process, and you compare them.

F. C. Donders
Dutch physiologist
1818-1889

This idea is called "subtraction logic" and it comes from earlier work applying the same logic to behavioral studies on reaction time.

What you aspire toward with your contrast is...

Minimal Pairs

To isolate a single mental process (like snake perception) the two conditions you are comparing should differ only in that single mental process and not in anything else.

Such contrasting conditions are called "*minimal pairs*".

The single most important aspect of experimental design is the choice of these conditions.

The most common problem with imaging experiments is that the conditions compared differ in many respects, not just one.

That is, the two conditions are not "*minimal pairs*".

The other differences between conditions are *confounds* in the experiment.

[If an entire experiment is run on only male subjects, is that a confound?
If all snake pix have grassy backgrounds, and all nonsnake conditions do not?
A confound is not just any problem with an experiment.
Confounds create specific alternative accounts of your data.
e.g. this thing I thought was a snake-selective brain region is really just responding to grass]

Minimal Pairs:
Not usually *fully* realizable,
More of an ideal to aspire toward.

Decisions toward an Actual Experiment

1. What exact conditions will you run in each experiment?
2. What task will subject do in the scanner?
3. Will you have “baseline” conditions? Of what? Why?

Suppose you get to scan ten subjects for one hour each.

4. Will you assign different conditions to different subjects, or have each subject do all conditions?
5. It is not nice to keep the subject going for an hour without a break, so we usually break scans into “runs” of 3-10 minutes. How many “runs” will you include?
6. Which conditions will happen in each run (e.g., 1 condition/ run, or all conditions in each run, or what)?
7. If multiple conditions per run, will they be clumped or interleaved?
8. What rate of presentation?
9. What order of stimuli/conditions within or across runs?
10. How exactly will you analyze your data?

Decisions toward an Actual Experiment

1. What exact conditions will you run in each experiment?
   - strive for minimal pairs
2. What task will subject do in the scanner?
   - for visual experiments usually passive viewing or 1-back
   - don't have diff tasks for diff stimuli
3. Will you have "baseline" conditions? Of what? Why?
   - for vision, staring at a cross (no eye movements)
   - useful to have a baseline of minimal visual processing
   - 1% response to faces and .5% response to objects is diff from
     - 2% for faces and 1.5 to objects
     - but these cannot be distinguished without baseline
   - one the other hand baseline is not really baseline

9.13 The Human Brain

Spring 2019