What neuroscientists can and cannot learn from brain imaging

Jody Culham

Neuroscience 500
December 5, 2007

Key Questions

- What is cognitive neuroscience?
- How do PET and fMRI fit into the cognitive neuroscientist's toolbox?
- Briefly, how do PET and fMRI work? What are their strengths and weaknesses?
- What are the differences between anatomical and functional MRI?
- What can we learn from neuroimaging?
- What are the limitations of neuroimaging?
- How does the BOLD signal indirectly measure brain activity?
- What are some of the issues in relating neuronal processing to the BOLD signal?

Part I
Cognitive Neuroscience

Cognitive Neuroscience

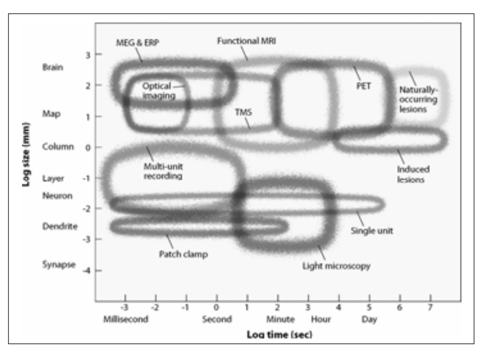
- the application of multiple techniques to study the neural basis of behavior and thought
- study of brain-mind relationship
- multidisciplinary: psychology, biology & physiology, philosophy, physics, math, computer science…
- converging techniques
- greater emphasis on humans than behavioral neuroscience in general
- greater emphasis on the brain than cognitive psychology
- term coined in late 1970s but didn't take off till advent of neuroimaging in 1980s and 1990s

The CogNeuro Toolkit

No brain needed
- Cognitive Psychology
- Computer Modelling

Brain needed
- Single Neuron Recording
- Electroencephalography (EEG)
  - Event-related Potentials (ERPs)
- Magnetoencephalography (MEG)
- Neuropsychology
- Functional Neuroimaging
  - Positron Emission Tomography (PET)
  - Functional Magnetic Resonance Imaging (fMRI)

Spatial and Temporal Resolution

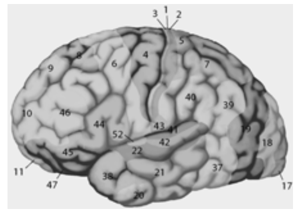


Gazzaniga, Ivry & Mangun, *Cognitive Neuroscience*

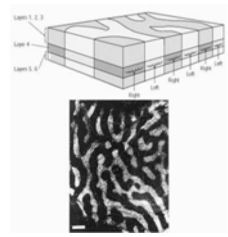
Part II
Basics of Brain Imaging

Why does brain imaging work ?

- Functional specialization is often segregated
- Neural organization is modular at many levels
- Within a functional region there can be populations that code for different features



Brodmann's areas

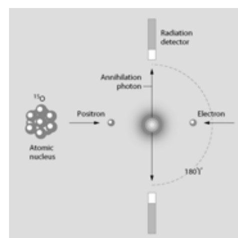


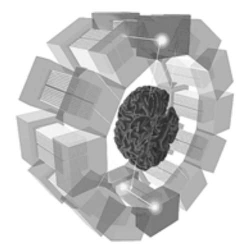
Ocular dominance columns

The Man Who Could Hear His Brain

Walter K, 1927
Whenever he opened his eyes, a gurgling sound could be heard at the back of his skull

Positron Emission Tomography (PET)





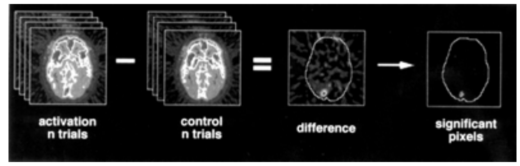
- radioactive isotopes emit positrons
- positrons collide with electrons, emitting two photons (gamma rays) in opposite directions
- detectors surrounding brain register simultaneous photons and compute likely source

PET

- Most cognitive studies are done with $H_2{}^{15}O$ labelled water via I.V. injection
- radioactive oxygen absorbed throughout body
- regions of brain with highest blood flow will have increased concentrations of radioactive oxygen
- resolution of several mm

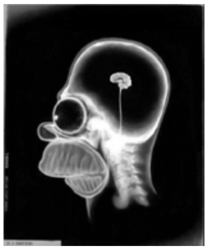
PET

- Compares regional cerebral blood flow (rCBF) between states
- A modern PET scanner integrates over 45-60 s
- Need to wait a number of half-lives before next injection



MRI vs. fMRI

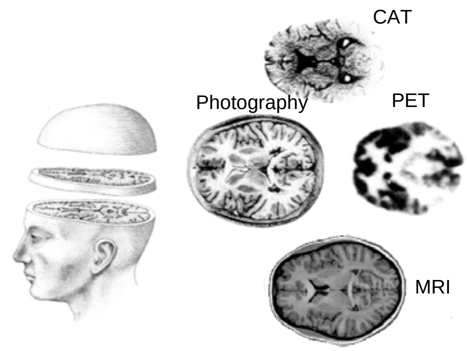
MRI studies brain anatomy.



Functional MRI (fMRI) studies brain function.

Source: Jody Culham's fMRI for Dummies web sit

Brain Imaging: Anatomy



Source: modified from Posner & Raichle, Images of Mind

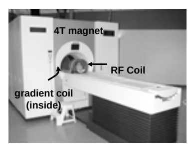
Recipe for MRI

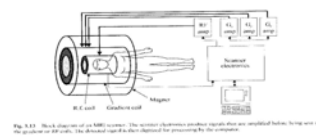
1) Put subject in big magnetic field (leave him there)
2) Transmit radio waves into subject [about 3 ms]
3) Turn off radio wave transmitter
4) Receive radio waves re-transmitted by subject
   – Manipulate re-transmission with magnetic fields during this *readout* interval [10-100 ms: MRI is not a snapshot]
5) Store measured radio wave data vs. time
   – Now go back to 2) to get some more data
6) Process raw data to reconstruct images
7) Allow subject to leave scanner (this is optional)

Source: Robert Cox's web slides

fMRI for Dummies

Necessary Equipment

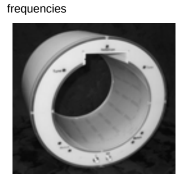




Magnet
• very strong magnetic field

Gradient Coil
• enables spatial encoding

Radio Frequency Coil
• receives and transmits radio frequencies



Source for Photos: Joe Gati

fMRI for Dummies

The Big Magnet

Very strong

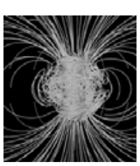
1 Tesla (T) = 10,000 Gauss

Earth's magnetic field = 0.5 Gauss

4 Tesla = 4 x 10,000 ÷ 0.5 = 80,000X Earth's magnetic field

Continuously on

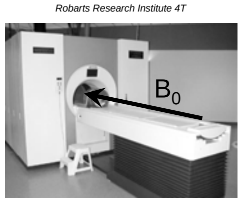
Main field = B0



Source: www.spacedaily.com

x 80,000 =

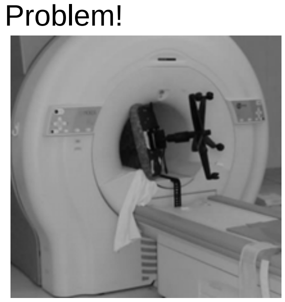
Robarts Research Institute 4T



fMRI for Dummies

Metal is a Problem!

Source: www.howstuffworks.com



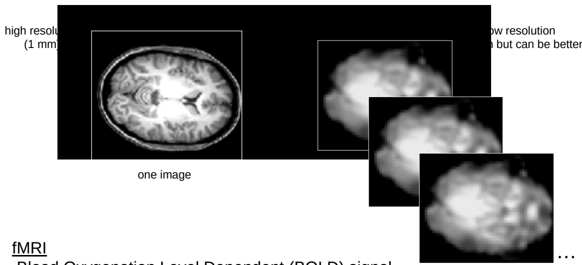
Source: http://www.simplyphysics.com/flying_objects.html

"Large ferromagnetic objects that were reported as having been drawn into the MR equipment include a defibrillator, a wheelchair, a respirator, ankle weights, an IV pole, a tool box, sand bags containing metal filings, a vacuum cleaner, and mop buckets."

-Chaljub et al., (2001) *AJR*

Source: Jody Culham's fMRI for Dummies web site

MRI vs. fMRI

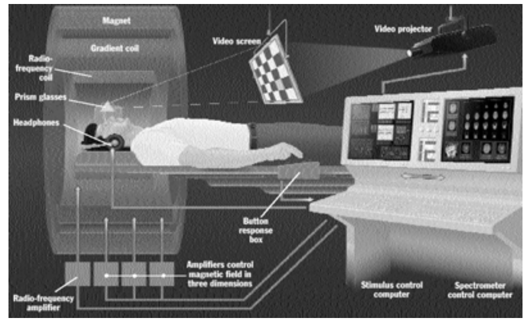


fMRI
Blood Oxygenation Level Dependent (BOLD) signal
indirect measure of neural activity

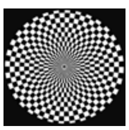
↑ neural activity ➔ ↑ blood oxygen ➔ ↑ fMRI signal

Source: Jody Culham's fMRI for Dummies web sit

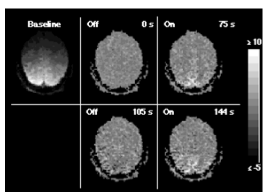
fMRI Setup



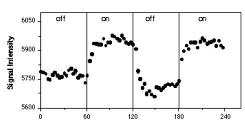
fMRI Activation



Flickering Checkerboard
OFF (60 s) - ON (60 s) -OFF (60 s) - ON (60 s) - OFF (60 s)



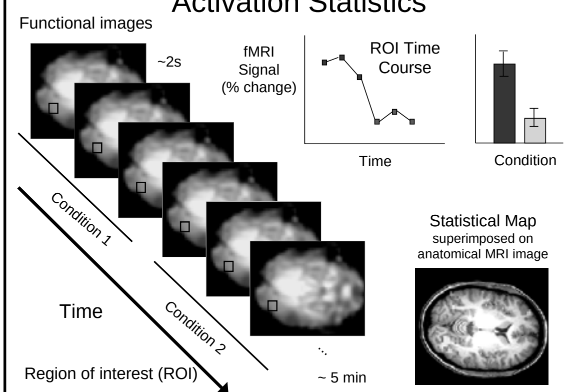
Brain Activity



Time ⇨

Source: Kwong et al., 1992

Activation Statistics



Source: Jody Culham's fMRI for Dummies web site

PET vs. fMRI

- fMRI does not require exposure to radiation
  - fMRI can be repeated
- fMRI has better spatial and temporal resolution
  - requires less averaging
  - can resolve brief single events
- MRI is becoming very common; PET is specialized
- MRI can obtain anatomical and functional images within same session

- PET can resolve some areas of the brain better
- in PET, isotopes can tagged to many possible tracers (e.g., glucose or dopamine)
- PET can provide more direct measures about metabolic processes
- PET is quiet and the signal is much less disturbed by head and body movement

Part III
What Can We Learn from Brain Imaging?

Localization

Localization for localization's sake has some value
- e.g., presurgical planning

- However, it is not especially interesting to the cognitive neuroscientist in and of itself
- Popularity of brain imaging results suggests people are inherent dualists

MOTIVATION, EMOTION, FEEDING, DRINKING — NEUROREPORT

The neural basis of romantic love

Andreas Bartels and Semir Zeki

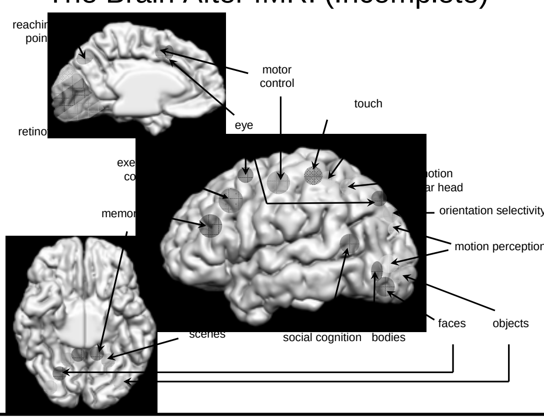
Wellcome Department of Cognitive Neurology, University College London, London WC1E 6BT, UK

The Brain Before fMRI (1957)

Polyak, in Savoy, 2001, Acta Psychologica

fMRI for Dummies

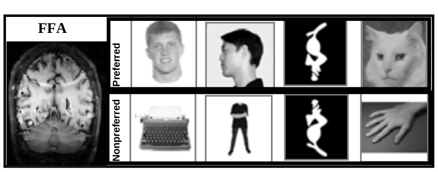
The Brain After fMRI (Incomplete)



Useful Types of Imaging Studies

- Comparisons of activation across multiple tasks or stimuli
- Characterization of a single region's responses
- Correlation between brain and behavior
- Evaluation of the role of experience
- Comparisons between species
- Exploration of uniquely human functions
- Derivation of general organizational principles

Case Study: Fusiform Face Area

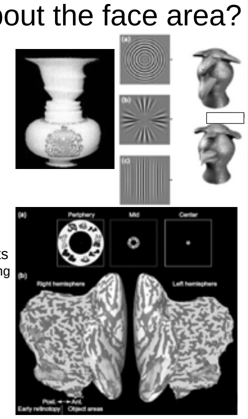


A face area in the human brain

What have we learned about the face area?

The face area is activated:
- when faces are perceived or imagined
  - → correlation between brain and behavior
- for stimuli at the fovea
  - → cues to brain organization
- by circular patterns
  - → cues/constraints for modelling
- in certain areas of the monkey brain
  - → cues to brain evolution
- for other categories of objects that subjects have extensive experience with
  - → debate regarding nature/nurture
- to some degree by other categories of objects
  - → debate regarding distributed vs. modular coding in the brain

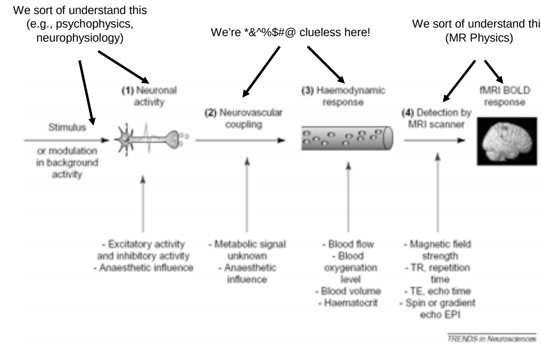
The fusiform face area may be impaired:
- in some but not all patients who have problems recognizing faces
- in people with autism
  - → understanding of brain disorders



Limitations of Neuroimaging

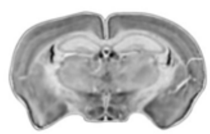
- Physical Limitations
  - spatial limitations (~1 mm)
  - temporal limitations (~50 ms to several seconds)
- Physiological Limitations
  - noise
    - head motion
    - artifacts (respiration, cardiac pulse)
  - localization of BOLD response
    - vasculature
- Current Conceptual Limitations
  - how can we analyze highly complex data sets?
    - brain networks
  - how are neural changes manifested in fMRI activation?

The Concise Summary

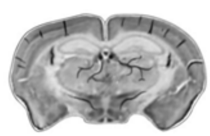


Deoxygenated Blood → Signal Loss

Oxygenated blood?
No signal loss…

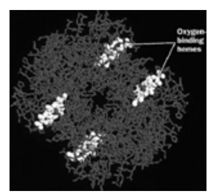


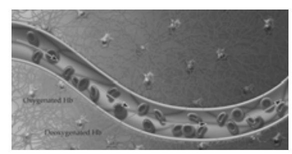
Deoxygenated blood?
Signal loss!!!



Images from Huettel, Song & McCarthy, 2004, Functional Magnetic Resonance Imaging

Hemoglobin





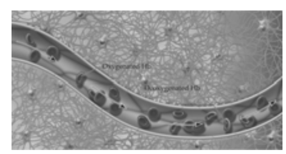
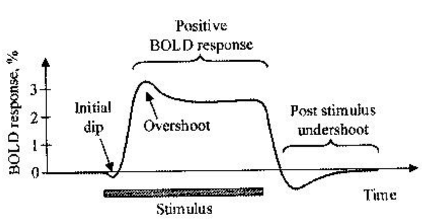
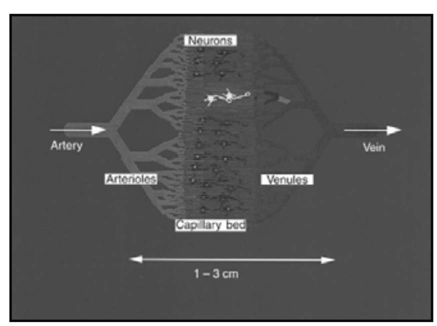


Figure Source, Huettel, Song & McCarthy, *2004, Functional Magnetic Resonance Imaging*

BOLD Time Course

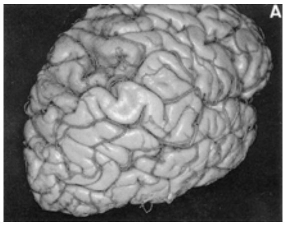


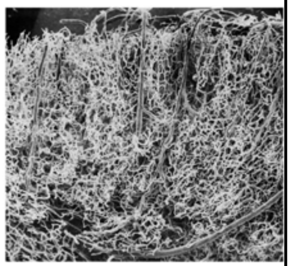
Vasculature



Source: Menon & Kim, TICS

Macro- vs. micro- vasculature





Capillary beds within the cortex.

- “brain vs. vein” debate

Neuron → BOLD?

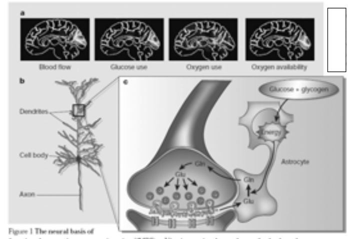
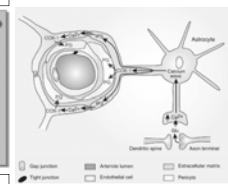


Figure 1 The neural basis of functional magnetic resonance imaging (fMRI). a, Viewing a stimulus such as a checkerboard produces marked changes in the areas of the brain that respond to visual stimuli, as seen in these positron-emission tomographic (PET) images. These changes include increases in glucose use and blood flow that are much greater than those in oxygen consumption. As a result there is an increase in the oxygen level in those areas (supply exceeds demand). PET is usually used to monitor blood flow. fMRI detects the changes in oxygen availability as a local change in the magnetic field. The resulting fMRI signal is a 'blood-oxygen-level-dependent' (BOLD) signal. b, As Logothetis et al.[3] show, these metabolic and circulatory changes are driven by electrical potentials arising from the input to, and information processing within, the dendrites of neurons. c, An attractive explanation for the BOLD signal invokes the preferential use of glycolysis in nearby non-neuronal cells (astrocytes) to handle an increase in the release of the neurotransmitter glutamate (Glu), which must be converted to glutamine (Gln) before it is returned to the neuron. Glycolysis consumes glucose to produce energy, but does not require oxygen.

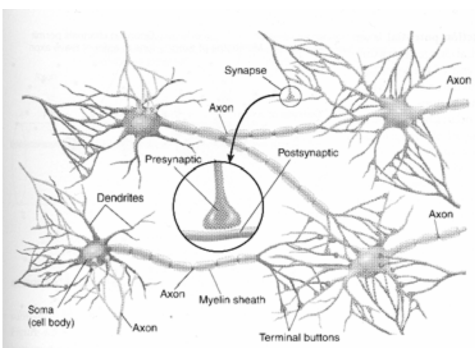
Raichle, 2001, Nature



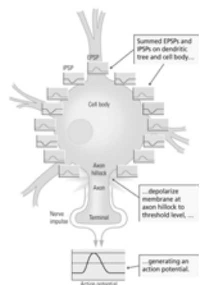
Glutamate effects on astrocytes account for about half of vasodilation

Rossi, 2006, News & Views on Takano, 2006, Nature Neuroscience

Neural Networks

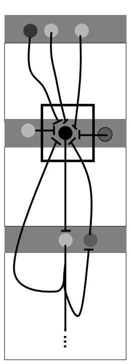


Post-Synaptic Potentials



- The inputs to a neuron (post-synaptic potentials) increase (excitatory PSPs) or decrease (inhibitory PSPs) the membrane voltage
- If the summed PSPs at the axon hillock push the voltage above the threshold, the neuron will fire an action potential

Even Simple Circuits Aren’t Simple



Lower tier area (e.g., thalamus)

Middle tier area (e.g., V1, primary visual cortex)

Higher tier area (e.g., V2, secondary visual cortex)

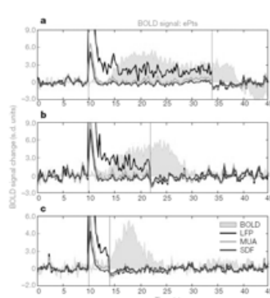
gray matter (dendrites, cell bodies & synapses)

white matter (axons)

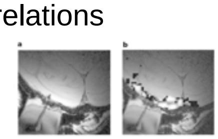
Will BOLD activation from the blue voxel reflect:

- output of the black neuron (action potentials)?
- excitatory input (green synapses)?
- inhibitory input (red synapses)?
- inputs from the same layer (which constitute ~80% of synapses)?
- feedforward projections (from lower-tier areas)?
- feedback projections (from higher-tier areas)?

BOLD Correlations



Source: Logothetis et al., 2001, *Nature*



Local Field Potentials (LFP)

- reflect post-synaptic potentials
- similar to what EEG (ERPs) and MEG measure

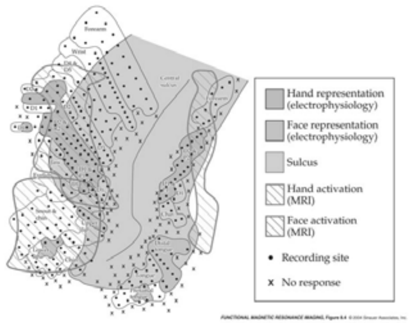
Multi-Unit Activity (MUA)

- reflects action potentials
- similar to what most electrophysiology measures

Logothetis et al. (2001)

- combined BOLD fMRI and electrophysiological recordings
- found that BOLD activity is more closely related to LFPs than MUA

Comparing Electrophysiolgy and BOLD



Data Source: Disbrow et al., 2000, *PNAS*
Figure Source, Huettel, Song & McCarthy, *Functional Magnetic Resonance Imaging*

fMRI Measures the Population Activity

- population activity depends on
  - how active the neurons are
  - how many neurons are active
- manipulations that change the activity of many neurons a little have a show bigger activation differences than manipulations that change the activation of a few neurons a lot
- fMRI may not match single neuron physiology results
  - e.g., fMRI observes attentional effects in visual cortex; neurophysiology does not

Ideas from: Scannell & Young, 1999, Proc Biol Sci

fMRI Measures the Population Activity

	Single Neuron Responses	Total Response
baseline		
broad response		
attention		
narrow response		

Subtractions

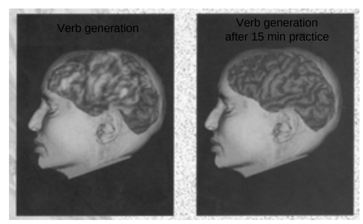
broad response - baseline

attention - baseline

narrow response - baseline

Ideas from: Scannell & Young, 1999, Proc Biol Sci

Effects of Practice



Raichle & Posner, Images of Mind cover image

Bug or feature?

- fMRI adaptation enables us to study the tuning of neurons

Readings

Required

- Bandettini, P. A. (2006). Functional magnetic resonance imaging (Chapter 9, pp. 193-236). In C. Senior, T. Russell, and M. S. Gazzaniga (Eds.), *Methods in Mind*. Cambridge MA: MIT Press.

Optional

- Culham, J. C. (2006). Functional neuroimaging: Experimental design and analysis. Book chapter in R. Cabeza & A. Kingstone (Eds.), *Handbook of Functional Neuroimaging of Cognition* (2nd ed.). Cambridge MA: MIT Press.
  - esp. pp. 59-63