Neurophilosophical Foundations 3

The Artifact Problem: The Epistemic Challenge

- Techniques to procure evidence alter the phenomenon about which scientists are trying to get evidence
  - Are the resulting observations merely a reflection of the alterations the investigator has made?
- Scientists confronted with observations made with new instruments are often very suspicious that they are artifacts
  - At the outset the signal is often very weak and variable--variations in the technique produce quite different responses
  - The procedures by which the instrument works are not sufficiently understood
    - We still don't know why Golgi's silver stain affects only some neurons
    - And there is considerable disagreement about the source of increased blood flow detected with fMRI
- The epistemic challenge: should the results of experimental techniques be treated as *evidence*? Are they reliable?

Clicker Question

Which of the following do scientists generally not have access to when evaluating the reliability of a new instrument?

- How well defined or determinate the results are
- The actual nature of the phenomenon being investigated
- The agreement of the results with theories regarded as plausible
- The agreement of the results with those produced by other instruments

Practical Solution to the Artifact Question

- Does the technique/instrument generate well-defined or determinate results?
  - If one isn't tracking anything, one would not expect a clear pattern in the results
- To what degree do the results from the technique/instrument agree with results generated by other means?
  - Would not expect perfect overlap since the new technique/ instrument is intended to generate new information
  - But in the domains where they overlap they should agree (or the new technique is calibrated so that it does agree)
- To what degree do the results cohere with what our theories led us to expect?
  - We believe results that seem plausible given what we think we know

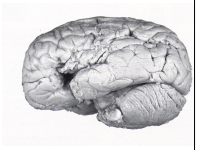
Clicker Question

What was the language deficit that Broca identified in his patient Leborgne (Tan)?

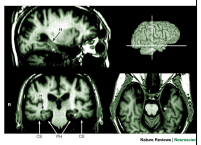
- All language abilities were lost
- Tan could not produce any vocal sounds
- Tan could not produce articulate words
- Tan could neither produce words nor understand those spoken to him

Lesion Studies: Two Examples

- Challenge 1: Knowing just what is lesioned
- Tan (Leborgne)
  - Broca met Tan late in his illness and could not examine his brain until after he died
    - By then the damage was widespread and Broca had to argue as to its likely origin



- HM (Henry G. Molaison)
  - HM suffered from serious epileptic seizures which Scoville sought to reduce by removing the hippocampus from which they seemed to originate
    - For the next 40+ years of his life HM acquired no new episodic memories
  - Although Scoville's aim was to resect the hippocampus, MR scans in 1998 indicated some of the hippocampus was initially spared (but atrophied) and nearby areas were damaged



Discussion Question

You open the hood of your car, remove something, and your car will no longer drive in reverse. You conclude that you have removed the reverse engine. How could you be wrong?

- There is a possibility that the part you removed only connects the reverse engine to the wheels
- The car may not have a reverse engine—it has only one engine whose torque is applied either in moving forward or backwards
- You might have removed the controls that activate the reverse engine, which is still perfectly functional
- Other

Lesion Studies

Challenge 2: What operations were due to the lesioned area?

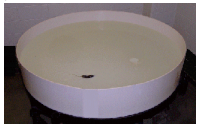
- Other areas may be secondarily altered
- Neuroplasticity may result in some "recovery" of function
- What operation involved in the lost ability is directly affected?

Tan

- Broca spoke of the faculty of articulate speech
- In the 1970s the deficit was interpreted as a deficit in syntax
- There is huge variability in patients with damage in Broca's area

HM

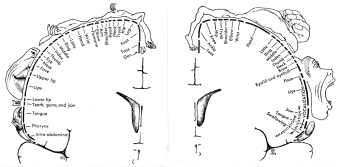
- Are episodic memories stored in the hippocampus?
- Or is the hippocampus only involved in regulating access?
- And are other functions performed by the hippocampus?



Stimulation Studies

Just as eliminating a functioning component should change behavior in a determinate manner, so should enhancing its activity by additional stimulation

- Challenge 1: What part of the brain is altered by the added stimulation?
- Challenge 2: Just what does the stimulated component contribute to the mechanism?



The sensory and motor "homunculi" identified by Penfield by using electrical stimulation. From Penfield and Rasmussen, 1950

Delgado's Bull Experiment

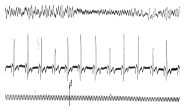
Delgado claimed he found a center that inhibited agression

Valenstein: Delgado really activated a pathway that controlled movement

Electrophysiological Recordings

Electroencephalogram (EEG): Electrodes placed on the skull detect ongoing electrical signal

- Berger (1930) distinguished large amplitude, slower waves during rest (8-12 Hz alpha rhythms) and lower-frequency, faster waves after stimulation (12-30 Hz beta rhythms)



- Subsequent discovery of both higher-frequency (>30 Hz gamma rhythms) and lower-frequency (4-7 Hz theta and 0.1-4 Hz delta rhythms) oscillations
  - Much of the focus directed at the lower-frequency rhythms associated with stages of sleep

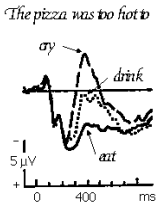
These oscillations were interesting even as researches were uncertain as to their origin

But until recently they did not seem to have much to do with cognitive activities--BUT THAT HAS CHANGED DRAMATICALLY

Evoked Response Potentials (ERPs)

By time-locking the EEG signal to the presentation of a stimulus and averaging over many trials, researchers could extract a detectable signal

- Thought to reflect the brain's processing of that stimulus
  - N400 (discovered at UCSD by Marta Kutas) thought to reflect violations of semantic expectations



ERP studies can provide high resolution information about timing of activity

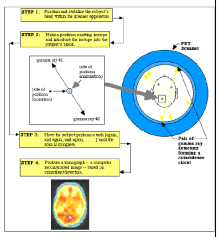
- But little information about where the signal is coming from
  - As there is no general solution to the inverse problem--inferring from what is recorded at different electrodes to the source of the signal

Single-Cell Recording

- Once the technique of inserting an electrode next to a neuron and recording its electrical behavior was developed it became the workhorse of sensory (especially visual) neuroscience
- Challenge 1: Finding the full set of stimuli that elicit response in a given neuron
- Challenge 2: Determining what that neuron is contributing to the processing of a given stimulus
- Challenge 3: Activity of individual cells may not be the relevant brain activity
  - Cannot detect what is going on in populations of cells and how timing of the responses in multiple cells might encode information

Neuroimaging: PET

- Positron emission tomography (PET)
  - Employs a radioactive compound to provide a signal
    - 2-deoxyglucose is transported to cells like glucose but not metabolized
      - Builds up in cells as they recruit glucose for energy
    - Water labeled with ^{15}O is carried by the bloodstream
      - Increasing with the increased blood flow as energy is needed



  - The products of the radioactive decay (gamma rays generated as an emitted positron collides with an electron) are detected by a scanner when they arrive simultaneously
    - Computerized tomography is used to generate a three-dimensional image from which slices in any direction can be viewed

Neuroimaging: MRI and fMRI

- Magnetic Resonance Imaging (MRI)
  - In a strong magnetic field, hydrogen nuclei align the axes of their spin
    - The energy from a radiowave pulse perturbs this alignment
    - When the pulse ends, nuclei return to the low-energy aligned state
      - And release radiowaves with a specific frequency
- Structural MRI uses the difference in frequency from atoms in grey and white matter to construct an image
- Functional MRI (fMRI) detects changes in deoxyhemoglobin resulting from changes in blood flow that *exceed* oxygen required by neurons
  - Blood oxygen level-dependent (BOLD) signal

The question of why blood flow exceeds that required to provide oxygen to neurons is still a matter of serious dispute

Clicker Question

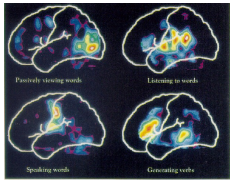
What point are Petersen and Fiez making when they comment: “A functional area of the brain is not a task area; there is no ‘tennis forehand area’ to be discovered.”

- Sporting abilities such as those used in tennis are not based in the brain
- Trying to localize functions in the brain is a mistake
- The sort of functions we should try to localize are those of language or attention
- Tasks draw upon many elementary operations, which are what are localized in the brain

Neuroimaging: Relating Signal to Cognition

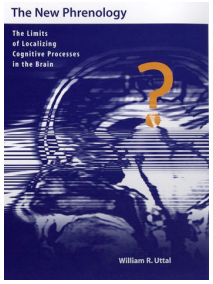
- Just as with single-cell recording, what one can infer from the results of a PET or fMRI scan depends on the input stimulus/task
- Researchers must find a means of relating inputs/task to the signal
  - During any task there will be activity throughout the brain (it is not dead when no task is presented)
- One of the most widely used strategies for relating task to detected activity is subtraction
  - An approach first developed by Donders in the 19th century for reaction time studies
    - Compare two different task conditions and subtract the time required for one from that required for the other
  - In neuroimaging, compare two tasks conditions and subtract blood flow produced by one task from that produced by another (baseline) task

Neuroimaging: The Verb-Generate Task



- Four subtraction conditions
  - Passively viewing words - resting
  - Passively listening to words - resting
  - Speaking viewed words - passively viewing words
  - Generating and speaking verb in response to viewed words - speaking viewed words
- Last subtraction resulted in increased activity in the left prefrontal cortex, anterior cingulate, right cerebellum
  - The researchers contended that the left prefrontal cortex reflected semantic processing
  - This was one of the first studies to highlight the anterior cingulate, but they and others assumed it was involved in executive control

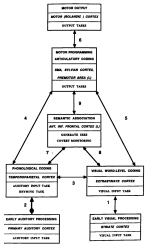
Neuroimaging: The Skeptics



- A variety of skeptics have raised doubts about the informativeness of neuroimagiing studies
  - Variability across studies: Different researchers, doing studies expected to generate the same results, show activity in different areas
    - Results reflect more the manipulations of the study than the underlying phenomenon (recall Golgi)
  - Holistically oriented critics claim that the idea of localization is built into the methodology
    - One assumes that the task is performed by a localized component and looks until one finds such
    - One may always find some area whose increased activity is statistically significant until further studies undermine the claim
    - But the search can go on forever

Neuroimaging: Answering Skeptics

- Why are neuroimagers so confident in their results?
  - The images reveal clear patterns, not just a hodgepodge of activations (although one should not be taken in by the false coloring of the resulting images)
- Results cohere with results from studies using other techniques
  - Reading activated visual areas and speaking activated motor areas
  - But generating verbs activated lateral prefrontal areas and not Wernicke's area in the temporal lobe
    - Frith et al. (1991) found activation in both Wernicke's and prefrontal areas
      - And interpreted only Wernicke's area as involved in semantic processing
      - Each group tries criticizes the interpretations of the other
- Results fit within a theoretical framework: two pathways of processing, one direct and one through semantic associations



Discussion Question

When theories and experimental evidence conflict, which should be trusted?

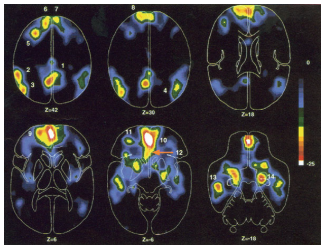
- We should always trust the evidence. Theories are evaluated by how well they conform to the evidence
- We should trust theories more than single pieces of evidence. Theories are developed to handle lots of evidence, whereas single pieces of evidence can be misleading
- It depends on how reliable the experimental technique is judged and how well supported the theories are. There are no simple rules
- Other

From Task Conditions to the Resting Brain

Early neuroimaging studies always focused on comparing two conditions—generating verbs — reading nouns

But what is the true resting state of the brain?

In the late-1990s Raichle and his colleagues began focusing on a set of brain areas that seemed to exhibit reduced activity in any task condition compared to a no-task condition



Brain areas more active in the resting state than in task conditions
(1) Junction of posterior cingulate and precuneus
(2-4) Inferior parietal cortex
(5); Left dorsolateral prefrontal cortex
(6-10, 12); Medial frontal strip that continues through the inferior anterior cingulate cortex
(11) Left inferior frontal cortex
(13) Left inferior temporal gyrus
(14) Right amygdala

From Shulman et al. (1997)

Dynamic Activity in the Default Mode Network

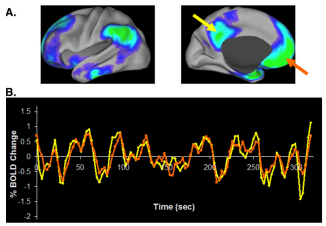
In 1995 Biswal et al. demonstrated ultra-slow oscillatory behavior in the fMRI signal—less than one cycle every 10 seconds (< 0.1 Hz)—synchronized across brain regions

Cordes et al. (2000) used functional connectivity MRI (fcMRI) to show synchronized activity in the regions active during rest, which came to be identified as the Default Model Network (DMN)

Studies in the resting state also revealed other networks anti correlated with the DMN—e.g., one active in attention demanding tasks

Challenge: What does the DMN do?

Since its activity is reduced in task conditions one cannot use the usual methods to study it



From Raichle and Schneider, 2007

Discussion Question

You have just been paid $30 to participate in a study, and have been placed in a scanner and left alone for 45 minutes (with lots of loud noises seemingly coming from the scanner) before being taken out, paid, and sent away. What would you do during those 45 minutes?

- Nothing—I wasn't given any instructions so I would just let my brain relax
- I would sit there wondering why I have to listen to this awful sound
- My mind would wander onto various topics (what to eat for dinner, what party to go to, etc.)
- I would rehearse what I learned in classes that day.

The Endogenously Active Brain

- Your brain uses about 20% of the energy consumed by your body, but the difference between the amount used in rest and in task conditions is very small (less than 5% increase)
- All of the techniques that try to find information about the brain operations involved in cognitive performance face a serious problem of dealing with noise—ongoing variation in the signal that appears random from the point of view of the task
- This “noise” may in fact be a clue to the ongoing activity of the brain as a self-organizing dynamical system
  - When the noise is analyzed, it turns out to be structured
    - It exhibits not white but pink (or brown) noise, meaning that there is correlation between activity in different brain regions
- Suggestion: Far from being a reactive system, the brain is endogenously active, exhibiting ongoing activity and generating behavior
  - Using sensory input to modulate the ongoing activity