An Introduction to Modern Methods of Brain Exploration with a Focus on Functional Magnetic Resonance Imaging (fMRI)

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My Background

- B.S in Engineering Science and Mechanics, University of Tennessee
- M.S. & PhD. in Bioengineering, University of Pittsburgh
  - Heart rate variability in Sudden Infant Death Syndrome (SIDs)
  - Neurosignal processing and prediction
- Post-doctoral Research Fellow in Child and Adolescent Psychiatry
- Faculty in Pharmaceutical Sciences, Radiology and Bioengineering, University of Pittsburgh
- Senior Research Fellow, University of Pittsburgh Medical Center

Course Overview

- Brief introduction to Neuroscience
- Introduction to the nervous system
- Brain anatomy
- Mapping function to structure
- Anatomical and functional neuroimaging
- Magnetic Resonance Imaging

Course Overview (continued)

- Functional MRI
  - How it works - the BOLD signal
  - Design of experiments, data processing
  - Modeling the data
  - Statistical problems in fMRI
  - Mini-lab session
  - Safety in MRI
  - Functional connectivity & resting state fMRI
  - Diffusion Tensor Imaging
  - Specific Applications

Course Expectations

- Basic overview of concepts (sometimes complex with equations)

- Gain a basic understanding of:
  - The brain and nervous system
  - Basic imaging techniques (especially MRI and fMRI)
  - Extensions of these techniques (diffusion imaging, resting state)
  - Applications of these techniques

- Please don’t be afraid to ask questions or stop me if you don’t understand

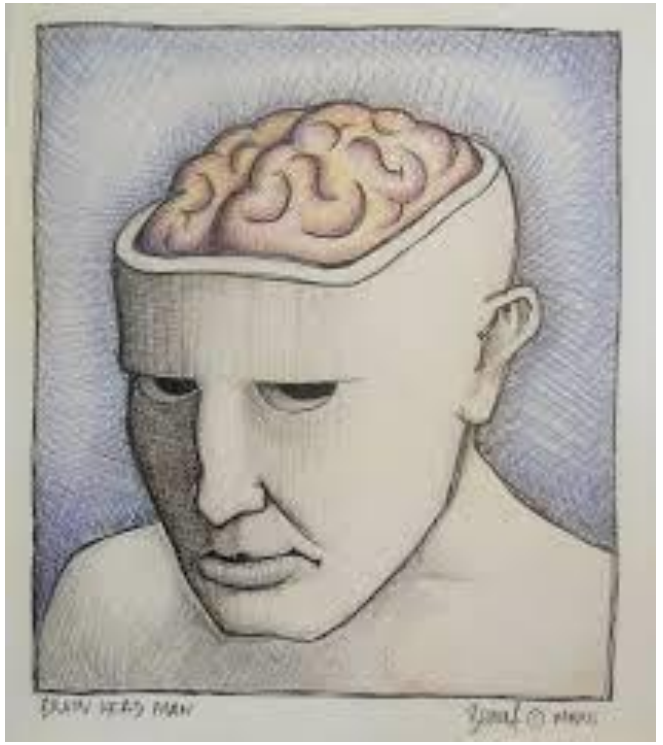
- Quiz at the end

Basic Etiquette

- Please turn your cell phones to vibrate
- If you need to talk, please step out of the room

Why Study the Brain?

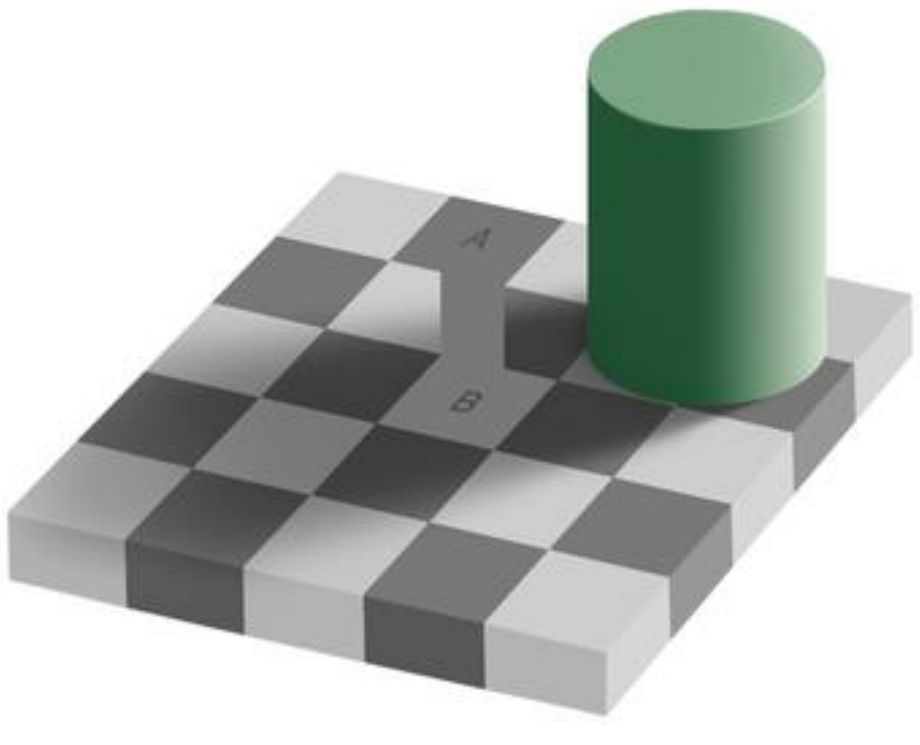
- One of the greatest mysterious of our time
- Brain is thought to be responsible for
  - Thoughts, perception and behaviors
  - Integration of sensory information
  - Movements, balance, coordination
  - Storage and retrieval of memories
  - Learning and adaptation
  - Emotions and fear
  - Rest and sleep
- We have very little understanding of how it works!!



Let’s start out with some perception experiments……

Adelson's Same Color Illusion - perception

Look at the drawing below. Which square is darker, square A or square B?

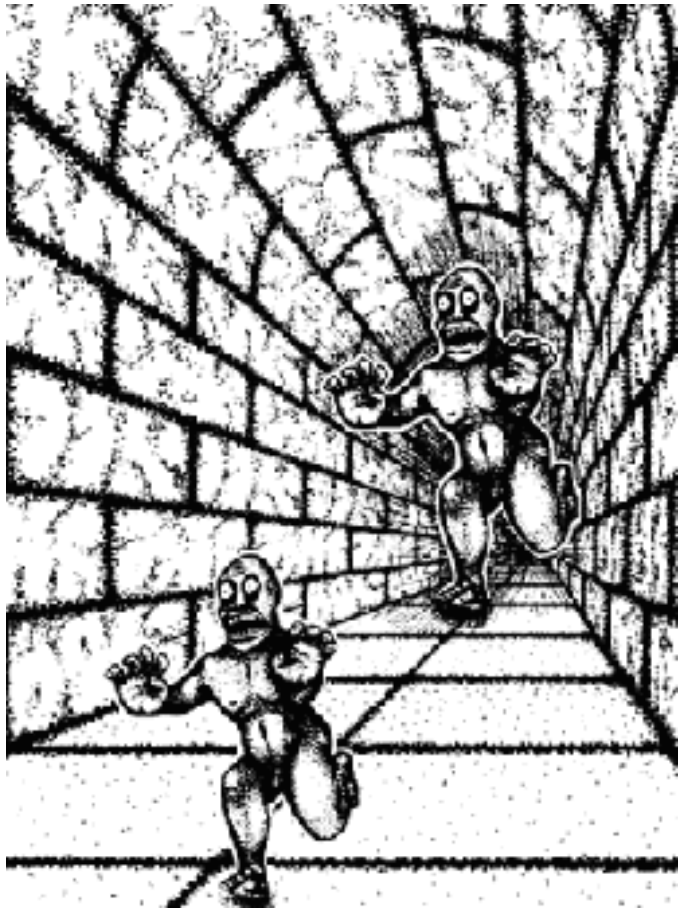


Color Illusion

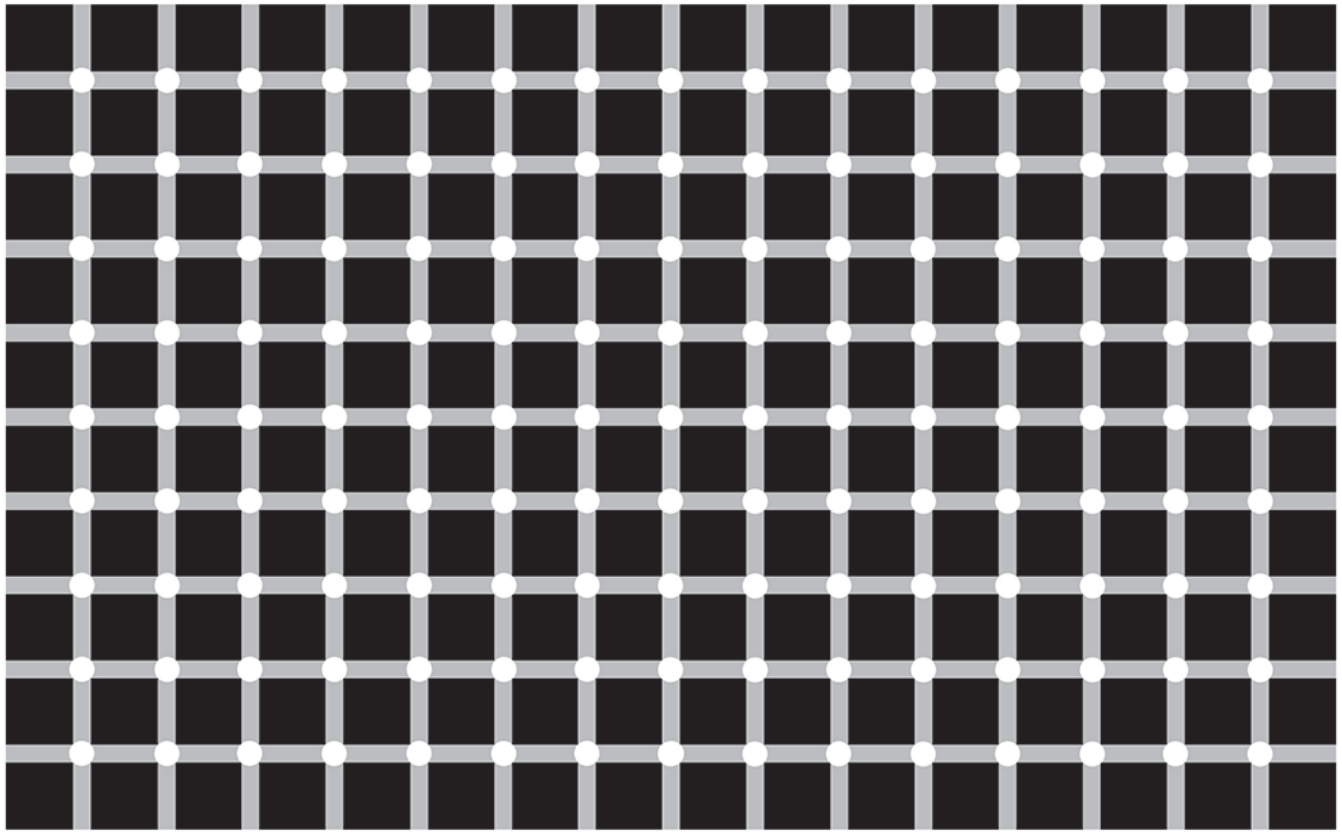
- Even when we know the colors are the same, they still appear different
- We expect the cylinder to cast a shadow
- Brain is seeing something different from our eyes

Which monster is larger?

To most people, the one in the background seems larger, though in fact they are exactly the same size. Your brain is interpreting depth cues.



Count the black dots between the squares.

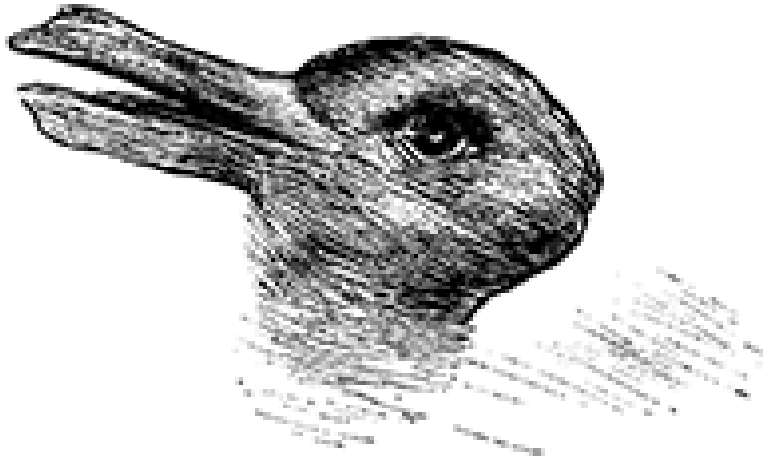


Count the black dots

- There are no black dots
- Visual system processes edges of objects, edges help to define and understand an image
- Visual “artifacts” when looking away from the center of the receptive field

Hidden Animals

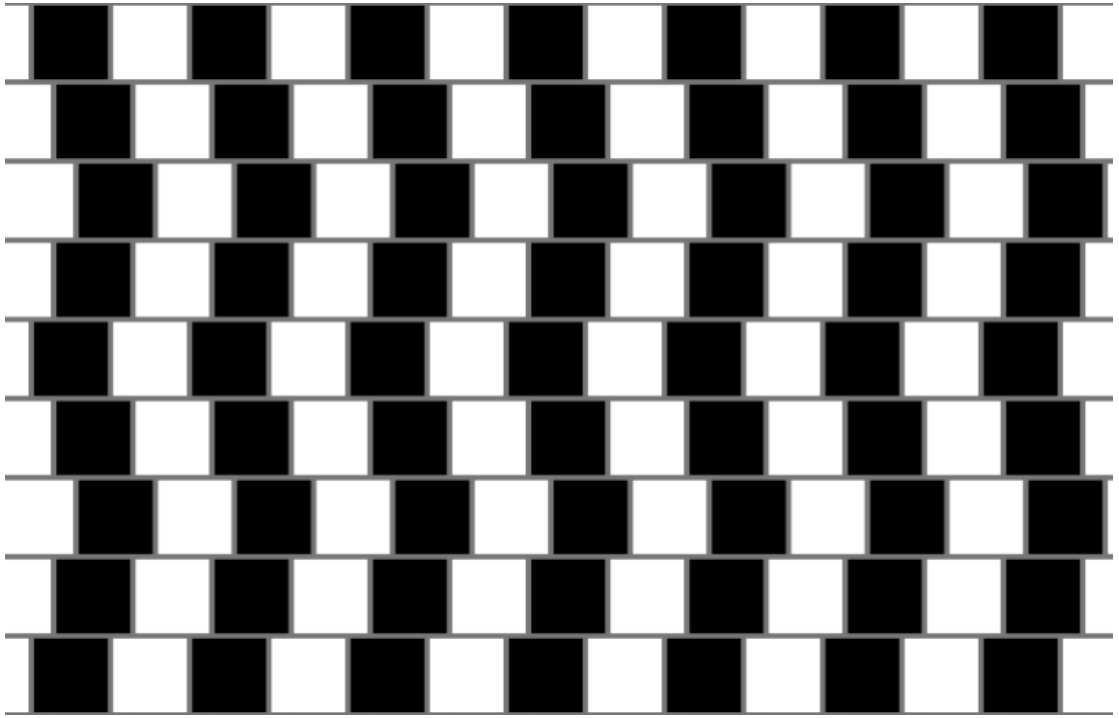
Horse or frog?



Rabbit or duck?

Café Wall Illusion

- Lines are actually parallel.
- Squares are slightly offset, so lines look sloped.
- Our brains have expectations of how the lines have to flow on what we see.



https://www.aivoke.com/news/5-things-to-know-about-perception/

Perception

- We perceive a 3D world in spite of seeing a 2D image in each eye
- The relative position difference between each eye (binocular disparity) provides a cue for the brain's computation of distance
- The brain is constantly taking in sensory information and constructing our perception of the world around us

Human Brain Facts by the Numbers

http://bebrainfit.com/human-brain-facts/

The typical brain is about 2% of a body's weight but uses 20% of its total energy and oxygen intake.

Your brain is 73% water. It takes only 2% dehydration to affect your attention, memory and other cognitive skills.

Your brain weighs about 3 pounds. Of that, the dry weight is 60% fat, making your brain the fattiest organ.

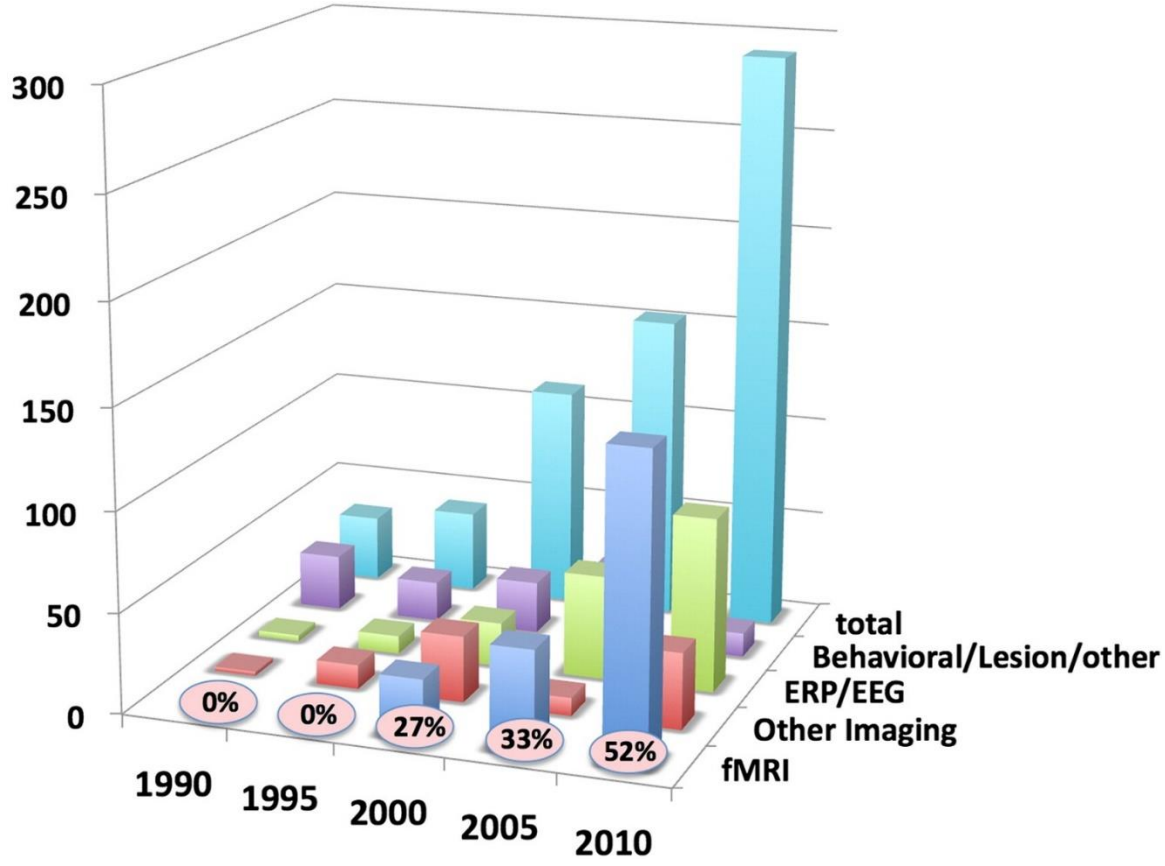
No one knows for sure, but the latest estimate is that our brains contain roughly 86 billion neurons.

Each neuron connects with, on average, 40,000 synapses.

A piece of brain tissue the size of a grain of sand contains 100,000 neurons and 1 billion synapses all communicating with each other.

Human Brain Research

- Number of studies on the brain have advanced greatly with the advancement of methods.
- Anatomical and functional neuroimaging techniques have advanced greatly over the past 50 years.
- Now possible to study the living, functioning brain in a non-invasive manner.



Distribution of technologies used in papers published in the *Journal of Cognitive Neuroscience* between 1990 and 2010. From: Rosen & Savoy, NeuroImage Volume 62, Issue 2, 15 August 2012, Pages 1316–1324, 20 YEARS OF fMRI

Brief History of Neuroscience

- Evidence of records of the nervous system in 1700BC
- 600 B.C. Indian physician Sushruta describes nervous system diseases in the *Sushruta Samhita*
- Hippocrates (460-379BC) discusses epilepsy as a disturbance of the brain
- Hippocrates and Plato believe the brain is the “seat” of mental process
- Aristotle believes the heart is the seat of mental process (brain cools the heart)

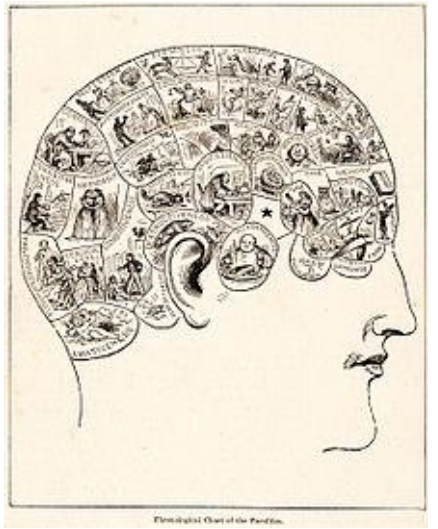
Brain Surgery in Ancient India

- Estimated to be 4300 years old
- From Harappan Civilization site
- Discovered by Archaeological Survey of India (ASI)
- Evidence of Trephination (drilling holes in damaged skull to remove shattered bones and blood pools)
- Evidence of healing after the injury (successful surgery!)

http://www.hitxp.com/articles/science-technology/worlds-oldest-brain-surgery-india/

Age of Enlightenment (1700-1800s)

- Nervous system is electrical in nature
- Where is the “mind”
- Franz Joseph Gall / Johann Spurzheim
  - Cerebral localization to study brain function
  - Phrenology “the only true science of mind” (1810-1840)
  - Anatomically divided the brain into 35 functional “brain organs”
    - Each responsible for intellectual or emotional faculty
    - Shape of brain = shape of skull
    - More tissue in an area of the skull meant more of that attribute



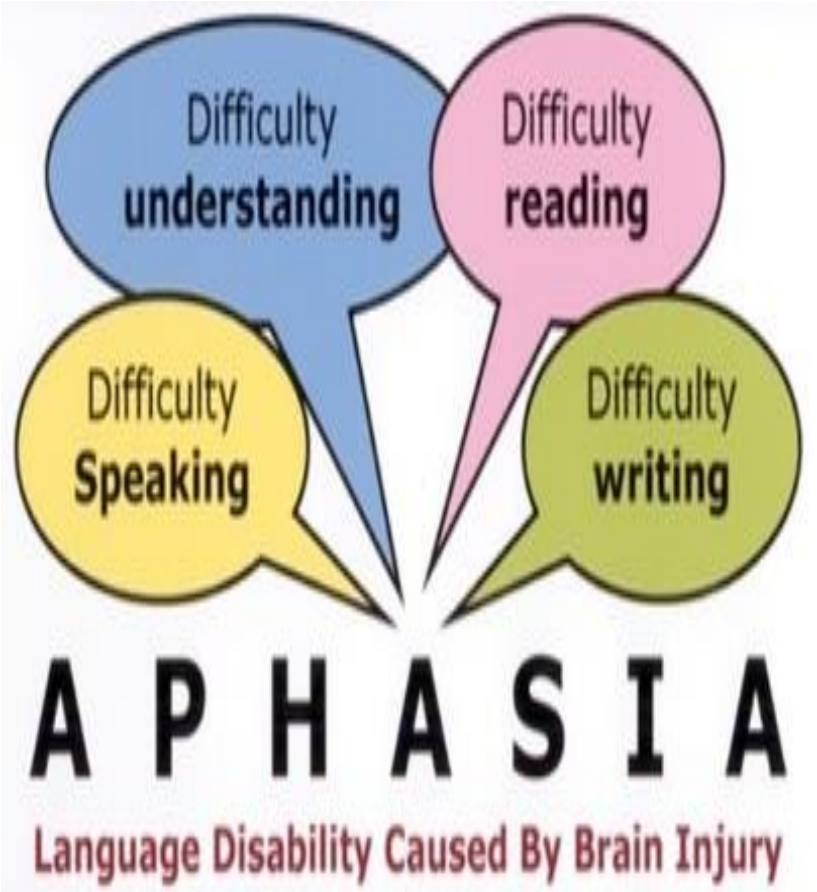
Phrenology Region Examples

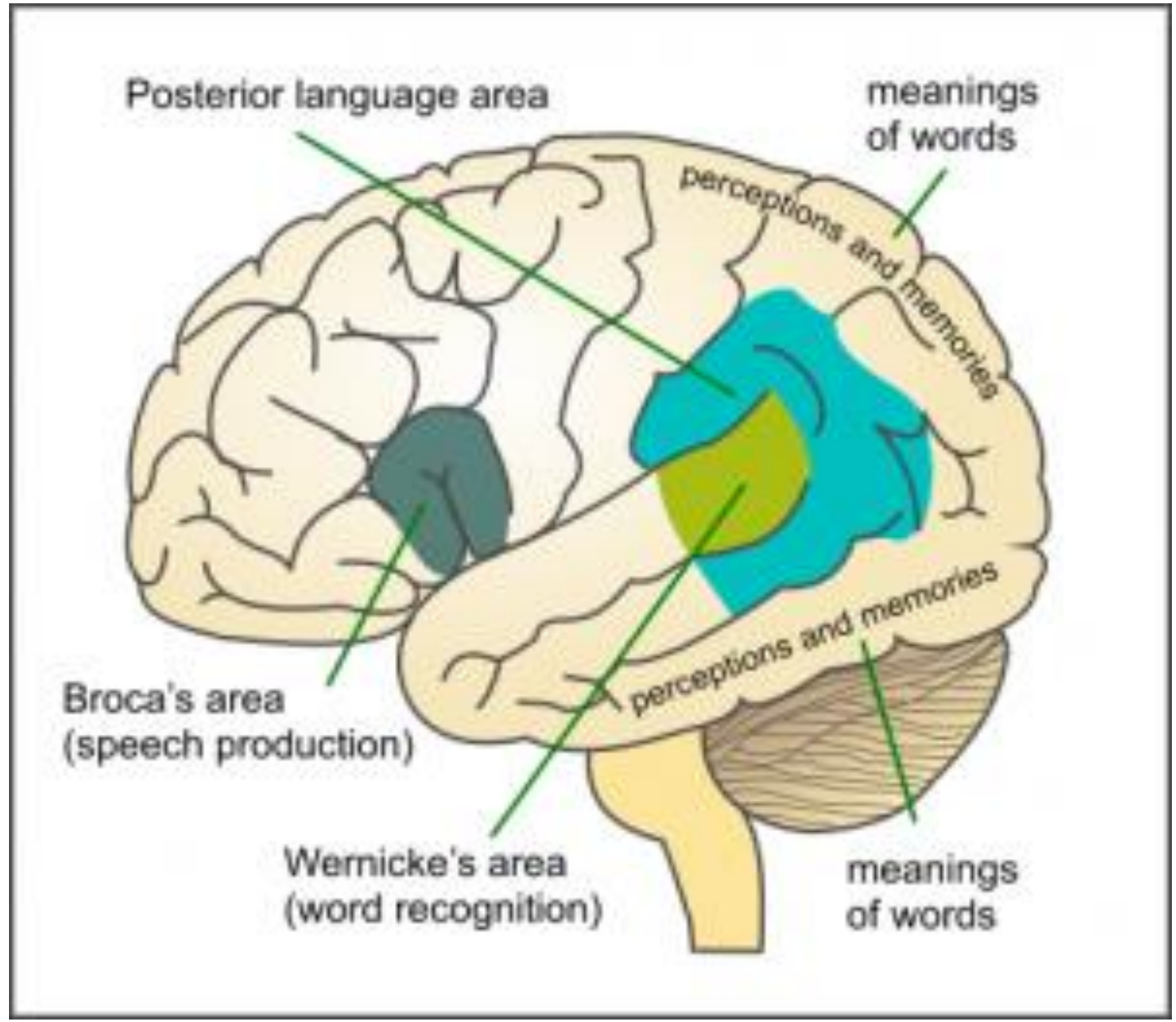
From: "Phrenology, the History of Brain Localization"
By: Renato M.E. Sabbatini, PhD
In: Brain & Mind, March 1997.

1	**Amativeness**	Physical Love
2	**Philoprogenitiveness Parental Love**	A particular feeling which watches over and provides for helpless offspring, or parental love
3	**Adhesiveness Friendship**	A feeling or attraction to become friendly with other persons, or to increase social contacts
4	**Combativeness**	The disposition to quarrel and fight
5	**Destructiveness**	The propensity to destroy
6	**Secretiveness**	The propensity to conceal, predisposes the individual to cunning and slyness
7	**Acquisitiveness**	The propensity to acquire
8	**Self-Esteem**	This sentiment gives us a great opinion of ourselves, constituing self-love
9	**Approbativeness**	This faculty seeks the approbation of others. It makes us attentive to the opinion entertained by others of ourselves
10	**Cautiousness**	This organ incites us to take precautions
11	**Individuality**	This faculty contributes to the recognition of the existence of individual beings, and facilitates the embodiment of several elements into one

Functional Localization

- Mapping brain function to brain structure
- Broca (1824-1880) – Lesions in a stroke patient led to lack of speech (spontaneous speech and motor speech control) but not lack of understanding of spoken language
- Wernicke (1848-1905) - stroke patient could still speak with connected words but lacked ability to understand the meaning spoken words and sentences





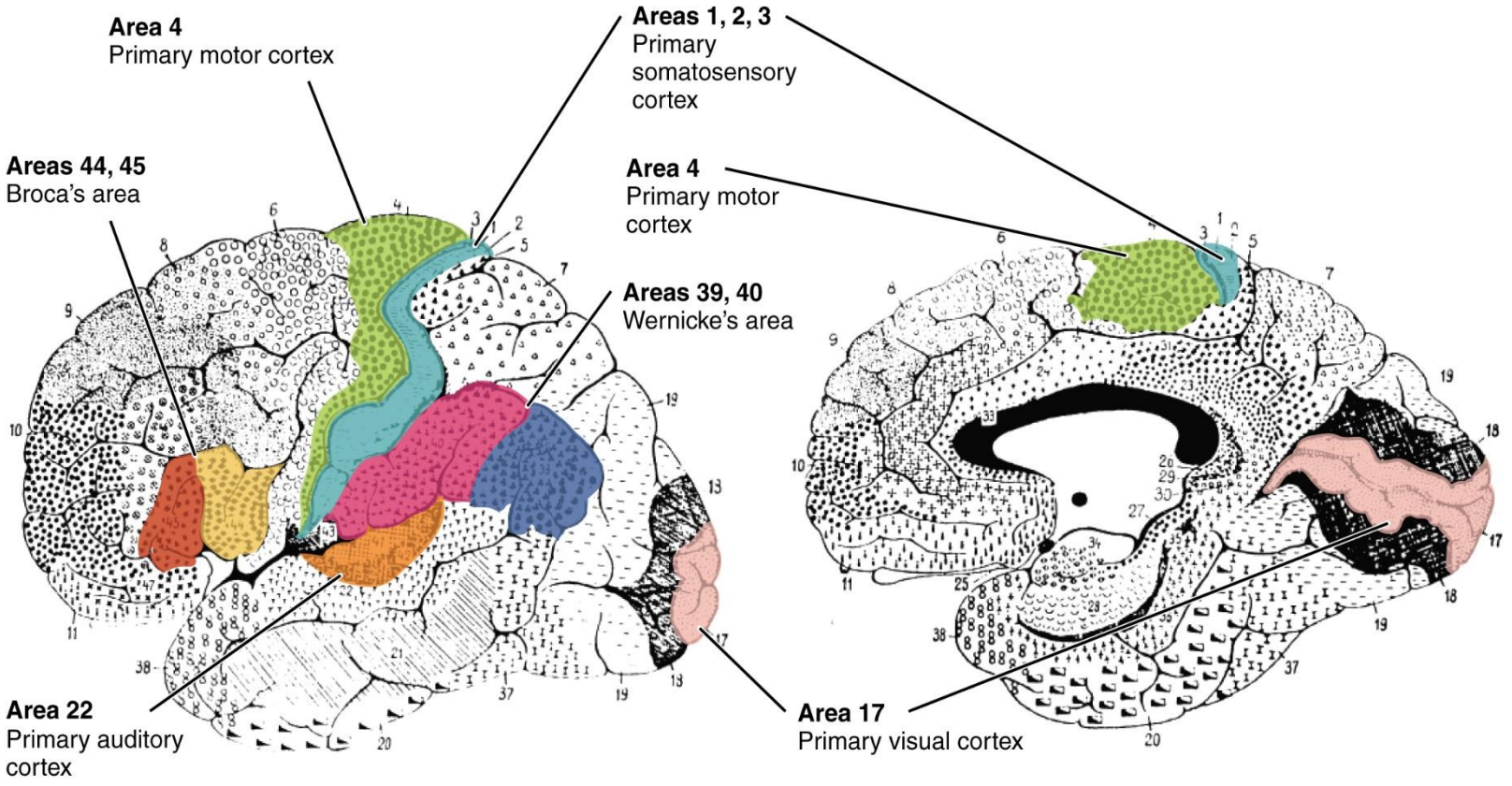
http://www.speakwithit.org/aphasia/

Examples:

- Broca's aphasia: Video
- Wernicke's aphasia: Video

Brodmann (1868-1918) – Functional segmentation

- Divided brain into 52 distinct functional areas based on cellular organization



Brodmann's cytotechtonic map (1909): Lateral surface

Brodmann's cytotechtonic map (1909): Medial surface

How did people study the brain before imaging techniques were available?

Early Methods to Study the Brain

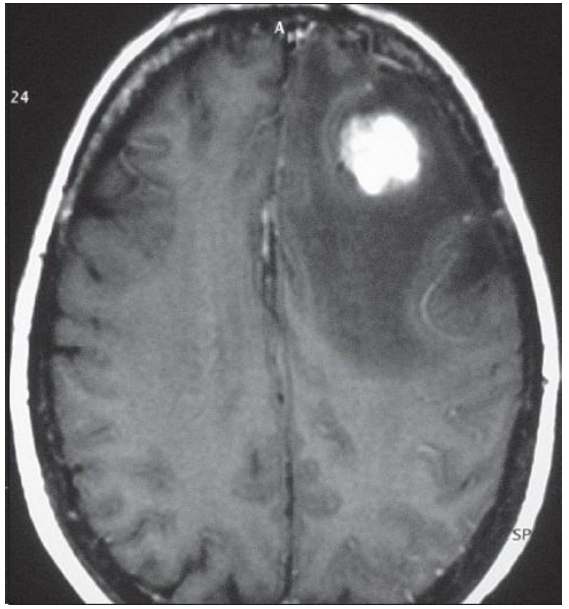
- Animal brains/ Animal models
  - Don’t have to use live humans
  - Limitations on functional experiments
  - Brains are very different than humans
  - How well does this translate to humans?

Early Methods to Study the Brain

- Post-mortem Dissection
  - Don’t have to use live humans
  - Samples are limited
  - No opportunities for functional experiments

Early Methods to Study the Brain

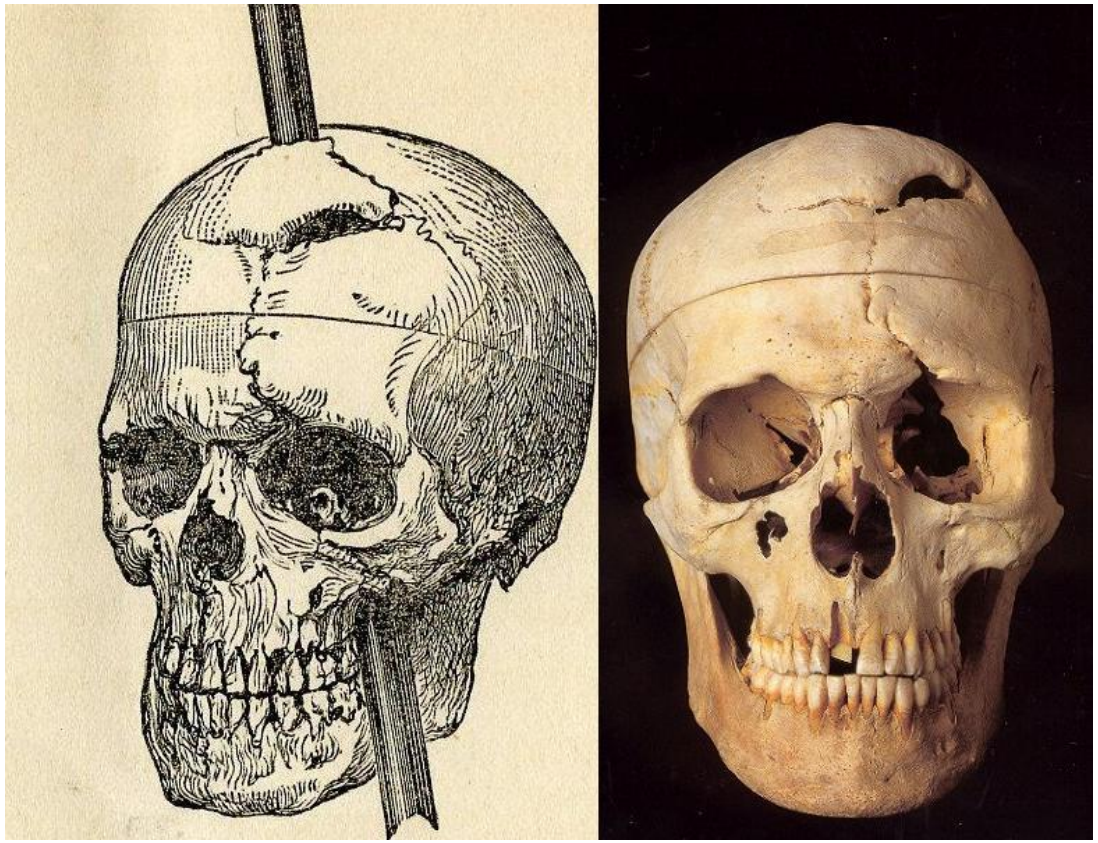
- Disease, Accident, Surgery
  - Removal of tumor or injury to brain
  - Lesion created to reduce the effects of epilepsy
  - Strokes
- Associate loss of function to the location of the injury or lesion
- 1880s – Angelo Mosso measured redistribution of blood during intellectual tasks using pressure waves in the head in subjects with skull deficiencies (blood flow changes)
- Studies of opportunity only



Phineas Gage – famous brain injury

The Accident

On September 13, 1848, twenty-five-year-old Phineas Gage was working with a blasting crew when he was in an accident that drove a tamping iron through his head. The rod entered through the left cheekbone, past his eye, and out the top of his head. He survived the trauma, but exhibited significant behavioral changes.



http://www.slideshare.net/jennab99/phineas-gage-48366289

Phineas Gage – famous brain injury

- Big part of his left frontal lobe destroyed
- Large changes in personality and behavior
- Prior to the accident, he was well-liked, skillful, the “most efficient and capable foreman”
- After the accident: “fitful, irreverent, profane”, impatient, lacks restraint
- “No longer Gage”
- Deduced that complex functions, decision-making, social cognition are largely dependent on frontal lobes

Technology was limited…. but….

- Newer methods emerged:
  - X-ray (1895), radiography – brain is mostly soft tissue, difficult to see
  - Electroencephalography (EEG) – to measure electrical activity from the brain (1924, Sir Hans Berger)
  - Computer-based brain scans (1970s) – CAT, CT scans
  - Positron Emission Tomography (PET) 1973 – measures metabolic functions
  - Magnetoencephalography (1968) – magnetic activity from the brain
  - Magnetic Resonance Imaging (1970s) – ability to see soft tissue
  - Functional MRI (1990) – ability to see blood flow changes during functioning

Next topics:

- We will talk about imaging methods much more later
- First we will talk about the brain from the levels of:

Lecture 2 - Action potentials and communication between neurons

Lecture 3 - Brain lobes and other neuroanatomy

Lecture 4 - Functional systems