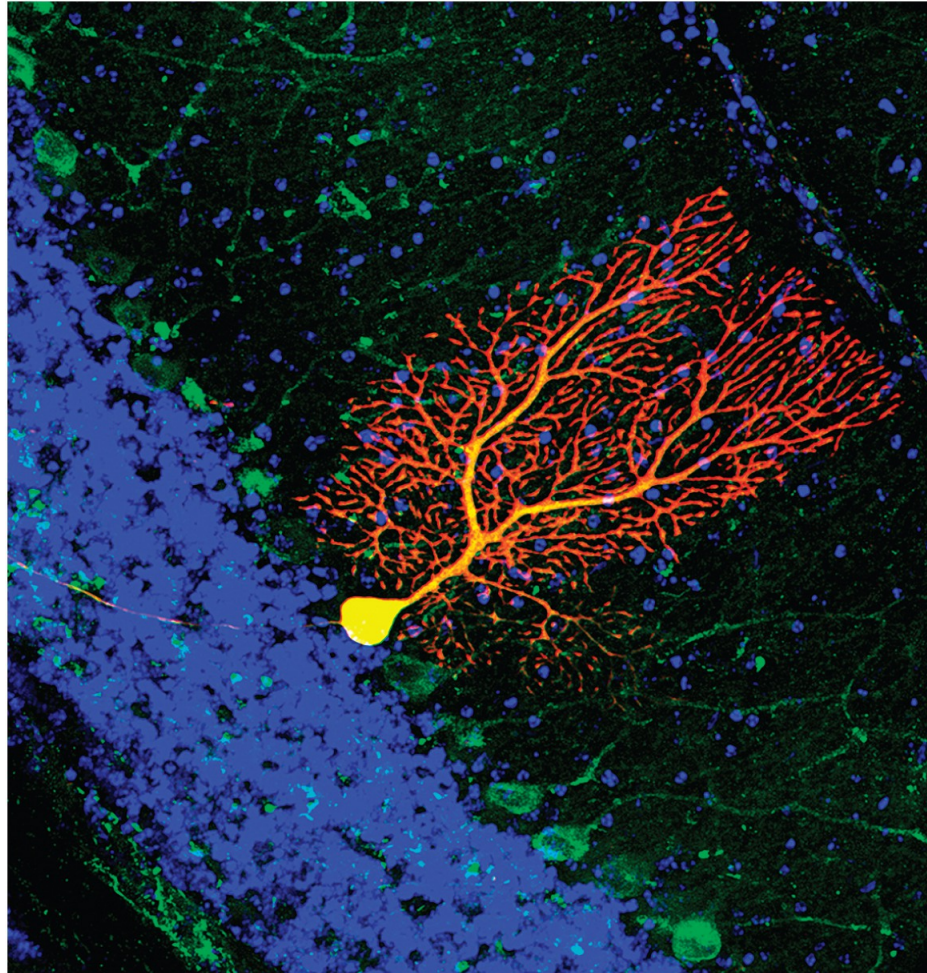


Neural Coding & Memory



Do We Have One Brain?

Structurally, we have one brain, however.

Functionally, it seems like we have many different brains.

Each “functional processor” controls different sensations, integrate information differently, may form different types of memories, and project responses that occur in different states of consciousness.

Our brain is like a computer that run different types of “applications” while in different “states of awareness” (i.e. unconscious vs conscious vs subconscious). Many believe the invention of the computer was simply a reflection of our brain's structure and function.

This begs us to ask, what does it mean to be us? How do we make decisions, form opinions or create patterns of behaviors? Neuroscience is finding answers to some of these questions. Each new discovery creates more new questions.

How do we explain how the brain works?

Strange Factoids About the Brain

If there is a “foul smell” in the room then you are more likely to make a “harsh decision”.

If you sit near a container of “hand sanitizer” then your political opinions will shift more toward the “political right”.

If you hold a cup of “hot coffee” then you will have a “more pleasant feeling about your mother”.

If a woman's iris is dilated then men will find her more “desirable”.

Eye witness testimony is the most unreliable evidence in a court proceeding.

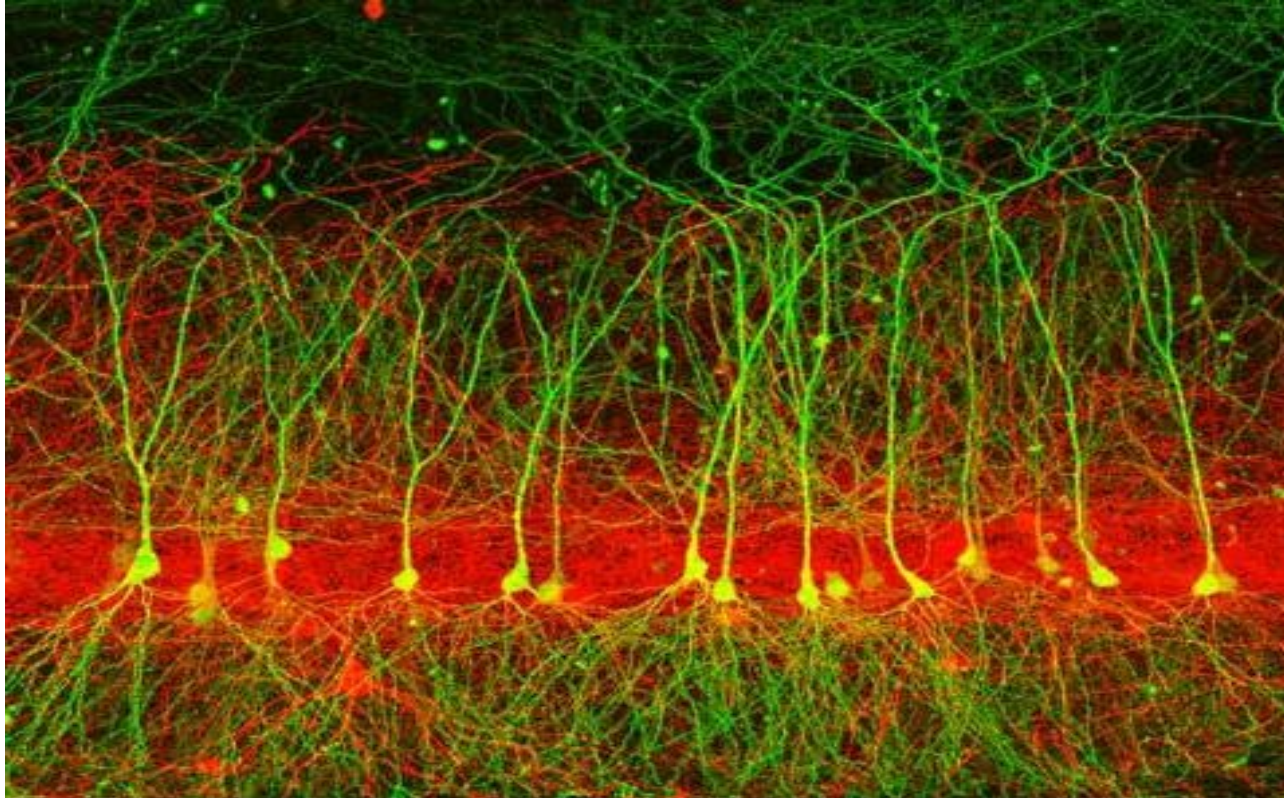
Neural Networks and Neural Integration



Neural networks are different patterns of connections between neurons. These nerve structures are responsible for the brain's functions.

Neural integration is the ability of neural networks to process sensory information. Neural networks are able to encode and store sensory information. We may recall this information, use this information to make decisions, project a motor response, and then return the information to where it is was stored. (In the process, the original memory maybe slightly changed). This explains why our memory of events may change over time!

- chemical synapses are the decision making devises of these neural networks // we can change the number of synapses over time // synaptic pruning
- the more synapses a neuron has /// the greater its information-processing capacity
- As we learn the number of synapses and dendrites increase (not the number of neurons)
- **pyramidal cells** in cerebral cortex have about 40,000 synaptic contacts with other neurons
- **cerebral cortex** (main information-processing tissue of your brain) has an estimated 100 trillion (10^{14}) synapses



hhmi - www.BioInteractive.com

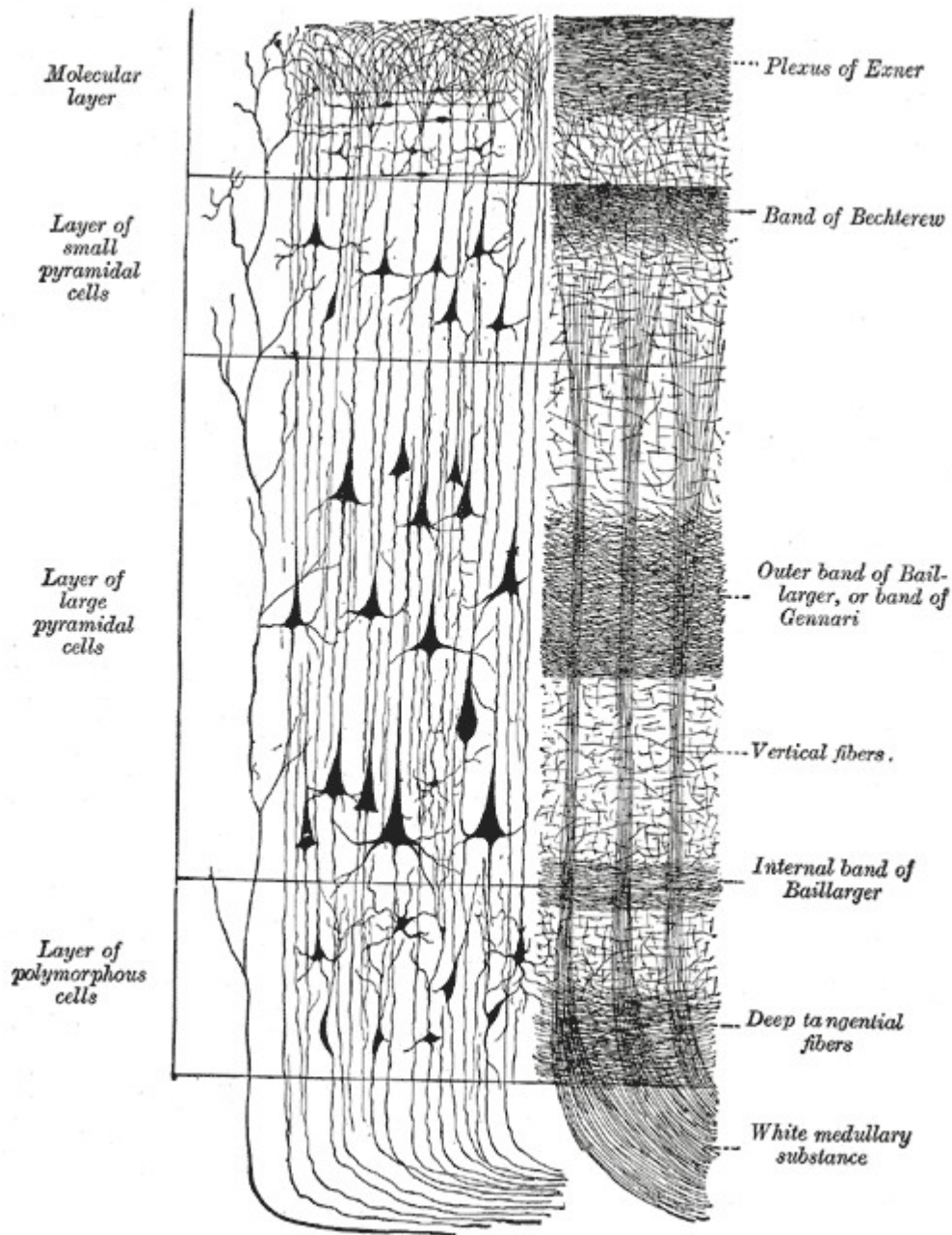
The key to understanding how our brains work lies in determining how each nerve cell or neuron continuously integrates the information it receives from other neurons via connections called synapses. For example, each pyramidal neuron (colored green) can receive tens of thousands of synapses from neurons belonging to several different brain regions. Interneurons (colored red) form local connections onto pyramidal neurons to form specific microcircuits. By using a combination of approaches including electrophysiology, microscopy, molecular biology and computer modeling, scientists are able to approach the complex puzzle of understanding how the 100 billion neurons in our brains make us who we are.

Technical Details:

The image was produced using array tomography. This technique involves collecting thousands of ultrathin serial sections of brain tissue that was fixed and stained, imaging them with a fluorescent microscope, and aligning all of them into a 3D reconstruction using a computer. The resulting image enables the detailed patterns of connectivity to be mapped between fluorescently-labeled neurons.

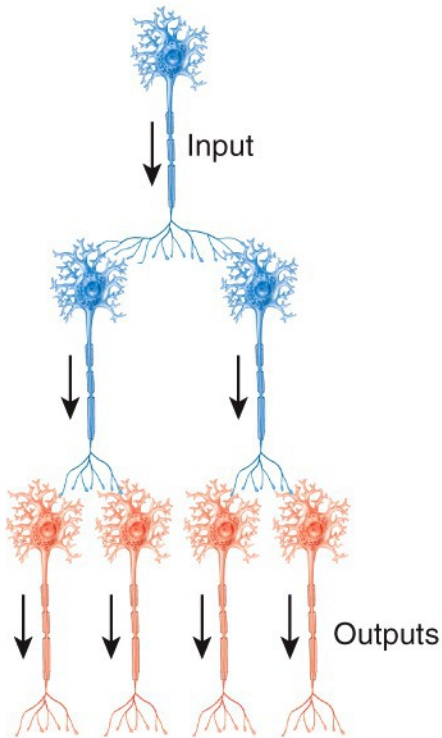
Credit:

Erik Bloss, PhD and Nelson Spruston, PhD., HHMI, Janelia Research Campus

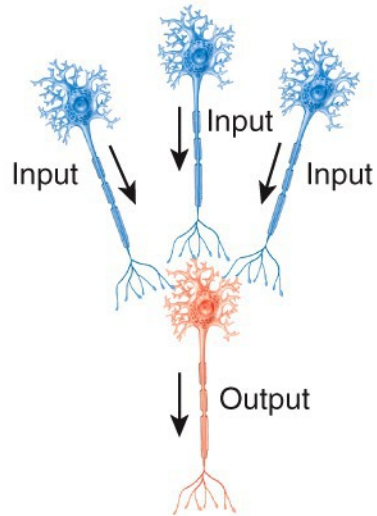


First 4 mm beneath the meninges membrane.

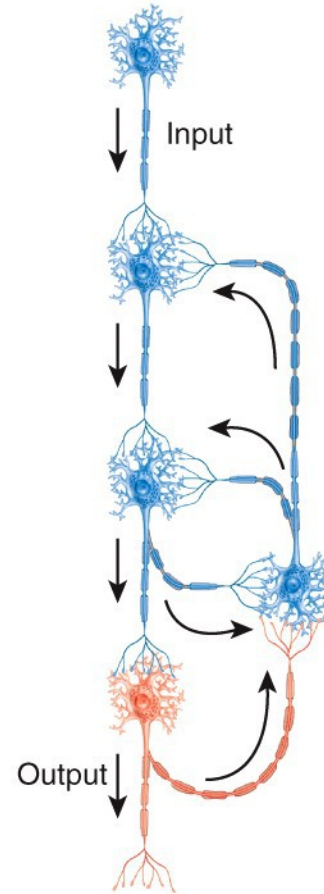
Possible Neural Network Patterns (Information Processing)



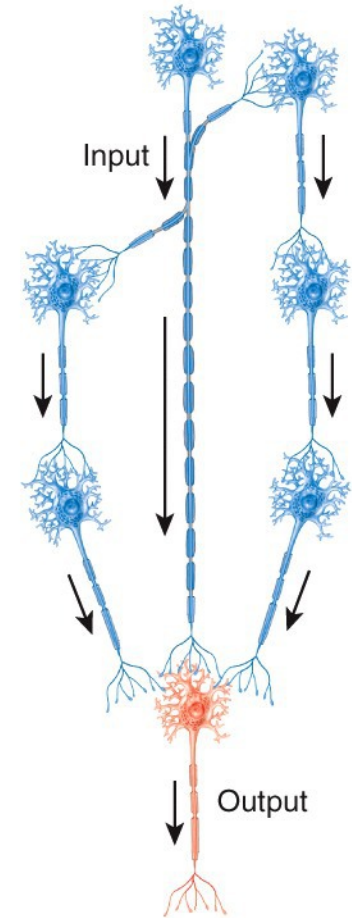
(a) Diverging circuit



(b) Converging circuit



(c) Reverberating circuit



(d) Parallel after-discharge circuit

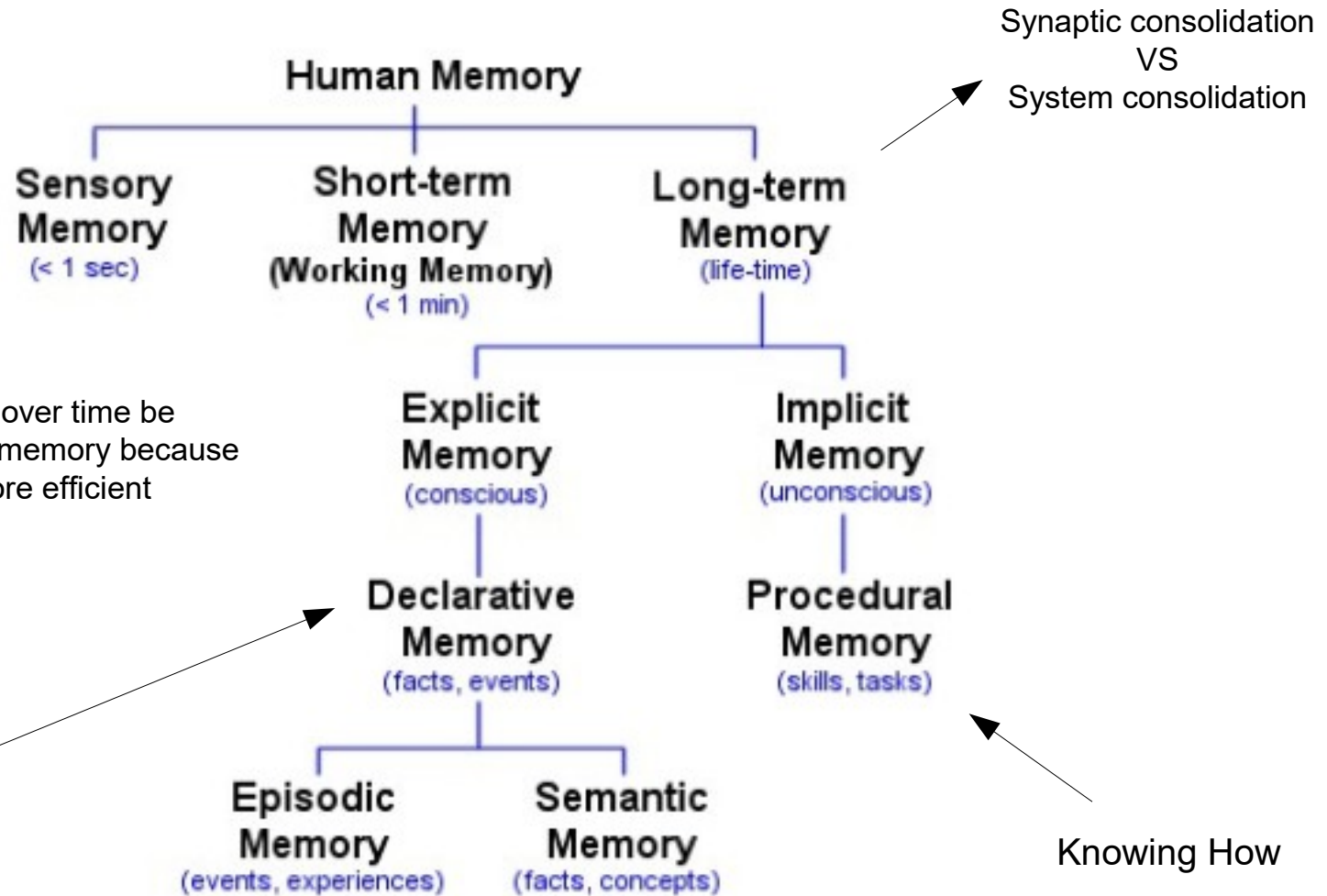
Memory and Synaptic Plasticity

- The structural basis of memory is a pathway through the brain called a **memory trace or engram**
 - along this pathway, new synapses are created or existing synapses modified to make transmission easier
 - **synaptic plasticity** – the ability to change physical characteristics of a synapse
 - **synaptic exaptation** - the process of increasing synaptic transmission
- Different types of memories
 - **Immediate**
 - **Short-term**
 - **long-term memory** (correlate with different modes of synaptic potentiation)
 - **declarative VS procedural** (knowing what VS knowing how)
- Cognition - examples of cognition include paying attention to something in the environment, learning something new, making decisions, processing language, sensing and perceiving environmental stimuli, solving problems, and using memory.



What are memories?

How many types of memories do we have?



Synaptic consolidation
VS
System consolidation

Explicit memory may over time be changed into implicit memory because implicit memory is more efficient

Knowing What

Knowing How

(over time episodic memories degrade into semantic memories)

Sensory Memory



- **immediate memory** – less than a second /// the ability to have a perception of something
 - essential for brain to recognize to determine if the stimulus is important to you
 - A feeling for the flow of events (sense of the present)
- **Try this:** stand in place while you “slowly” turn 360 degrees with your eyes fixed firmly looking forward /// by the time you turn 20 degrees you have already forgotten what you just saw /// however, if there was something your brain deemed important then you will stop or return to that spot.
- When was the last time this happened to you? Today?
- Immediate memory is what we sense as a “**perception**”

Short-Term or Working Memory



- **Short-term memory (STM)** - lasts from a few seconds (may be extended with rehearsal)
 - quickly forgotten if distracted
 - the ability to call a phone number we just looked up
 - the ability to read sentence while able to remember the beginning when you get to the end of the sentence
 - these are reverberating circuits /// our memory of what just happened “echoes” in our minds for a few seconds // the “reverberating circuits”
- The frontal lobe uses the equivalent of “two scratch pads or post-it pads” for short term memory /// **visual and audio** to facilitate short term memory
- Facilitation (also called **rehearsal**) will cause this type of memory to last longer
 - **tetanic stimulation** – rapid arrival of repetitive signals at a synapse // causes Ca^{2+} accumulation and postsynaptic cell more likely to fire

Long-Term Memory



- **Long-term potentiation** – this occurs before we create long term memories and is associated with pathway from hippocampus to medial temporal lobe
 - changes in receptors and other features that increases transmission across the “experienced synapse” /// results in **synaptic consolidation**
- Long term memory - this requires physical remodeling of synapses // new branching of axons or dendrites // also known as **system consolidation**
 - requires new protein synthesis at synapse // memories are moved from medial temporal lobe to disparate parts of the neocortex – these are forever memories
- Long-term memory
 - **Explicit or Declarative knowledge** - retention of events that you can put into words (Knowing what) // hippocampus – medial temporal lobe
 - **Implicit or Procedural knowledge** - retention of motor skills (Knowing how) // amygdala – cerebellum – basal ganglia - reflex arcs

Long-Term Memory Associated with New Protein Synthesis at the Synapse

- molecular structural changes within the synapse are called **long-term potentiation**
- method described
 - receptors on synaptic knobs are usually blocked by Mg^{+2} ions
 - when receptors bind glutamate they receive tetanic stimuli, result to repel Mg^{+2} and admit Ca^{+2} into the synaptic knob – Ca^{+2} acts as second messenger
 - more synaptic knob receptors are produced
 - synthesizes proteins involved in synapse remodeling
 - releases nitric oxide that triggers more neurotransmitter release at presynaptic neuron

About Memory



Fundamentally, memory acquisition occurs at the synapse

Learning occurs with **Synaptic Consolidation** /// a process that occurs when signals are passed over a synapse /// with repeated signaling over the same synapse we see an increase in the amount of neurotransmitter released and an increase in the sensitivity of the receptors on the post synaptic membrane. // rehearsal therefore makes the memory pathway stronger

Synaptic consolidation – this occurs in the medial temporal lobe (hippocampus dependent)

System consolidation – this occurs when memory is moved from the medial temporal lobe and redistributed throughout the neocortex – this is our lifetime memories – this process may take decades // memory then becomes hippocampus independent

Memory Retrieval – when we recall a memory we “reconstruct the memory” in our working memory (in the frontal lobe) // working memory is “short term” memory which only lasts for minutes – therefore we use “**auditory and visual scratch pads**” to hold thoughts (e.g. think about what happens while you are having a back and forth conversation)

Reconsolidation – after we are done with the information in our working memory, we “disassemble” the memory and return the fragments to where they are stored in the neocortex

Declarative Memory VS Procedural Memory

When we learn something new we process the new memory using one of two pathways which are associated with different brain structures.

One memory form is about learning facts and is a type of memory called declarative memory. This is “knowing what”.

Another memory form is about learning skills (e.g. playing piano) and this is called procedural memory.

Declarative memory is processed through the hippocampus and the newly formed declarative memory is stored in the medial temporal lobe as “synaptic consolidation”. // This memory will later be distributed into the general neocortex as “systemic consolidation” (i.e. this may take decades to complete)

Procedural memory is processed through the amygdala, basal nuclei, and cerebellum.

Normally, these different memory centers are completely integrated, however. You can have an accident that eliminates declarative memory but retains procedural memory.

What is the function of the medial orbital frontal lobe?

The **medial orbital frontal lobe** is an area in the frontal lobe directly above the eyes orbits.

This tissue **makes our decision**. In our conscious state, we need to make a never ending stream of decision as we move through time.

If the frontal lobe is the site of our working memory then the medial orbital frontal lobe provides the raw data for our working memory.

The medial orbital frontal lobe does two things: **First**, the MOFL will make decisions about an action based on a reward-punishment analysis. Then the MOFL sends this action plan to the frontal lobe where the action is executed

Secondly, the medial orbital frontal lobe will remember the decision made and after the execution of the action the MOFL will review the outcome to see if the decision met the analysis criteria – this is how we learn from our experiences!

What is the relationship between the frontal lobe and the limbic system?

The frontal lobe is our conscious brain. This is where our “working thoughts” occur.

The limbic system is where our subconscious judgment values and remembrances of emotional events are stored as pleasant or unpleasant events.

The frontal lobe is our slow brain and the limbic system system is our fast brain. Explain

These two areas are richly interconnected with nerve tracts. Therefore, the limbic system can influence frontal lobe function.

More importantly, if under stress the frontal lobe stops working (i.e. as in a panic state) . Now the limbic system takes over (i.e. anxiety leads to fear which then leads to aggression /// it is the cause of the fright, flight or fight reaction)

Language

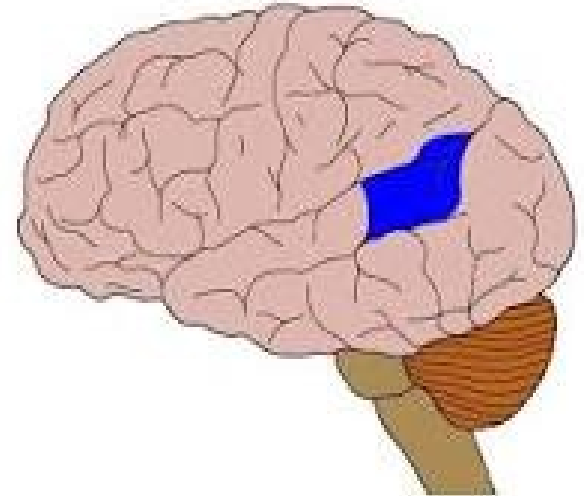
Language in early primates started as “hand gestures”.

The fox-pro-2 gene allowed the hyoid bone to be re-positioned lower in the pharynx which allowed homo sapiens (i.e. humans) to make consonants and vowels (i.e. monkeys can hoot and make sound but can not form consonants and vowels because their hyoid bone is placed higher in the pharynx)

Wernicke Areas is located in the posterior section of the superior temporal gyrus (STG) in the left cerebral hemisphere. This area encircles the auditory cortex on the lateral sulcus (the part of the brain where the temporal lobe and parietal lobe meet).

This is the receptive language center. /// other areas receive sound or symbolic stimulus and must decide if it is language. If it is language then the stimulus is passed to Wernicke Areas for interpretation

Note – language maybe written or spoken.



Language

Broca's Area is the expressive language center. It is where the grammar of our language is located

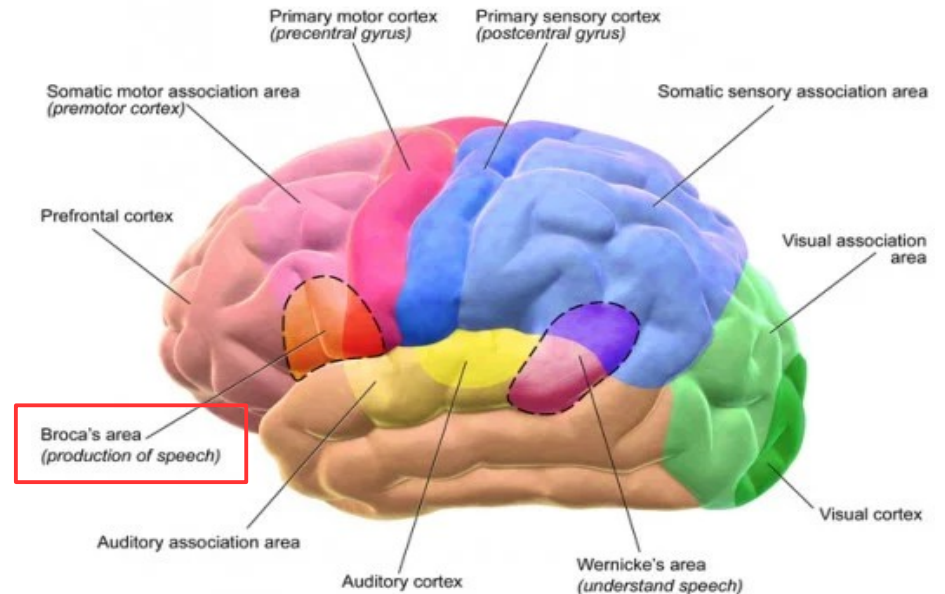
It is a region in the frontal lobe of the dominant hemisphere, on the left side of the brain with functional link to motor strip skeletal muscles used in speech production and respiratory centers.

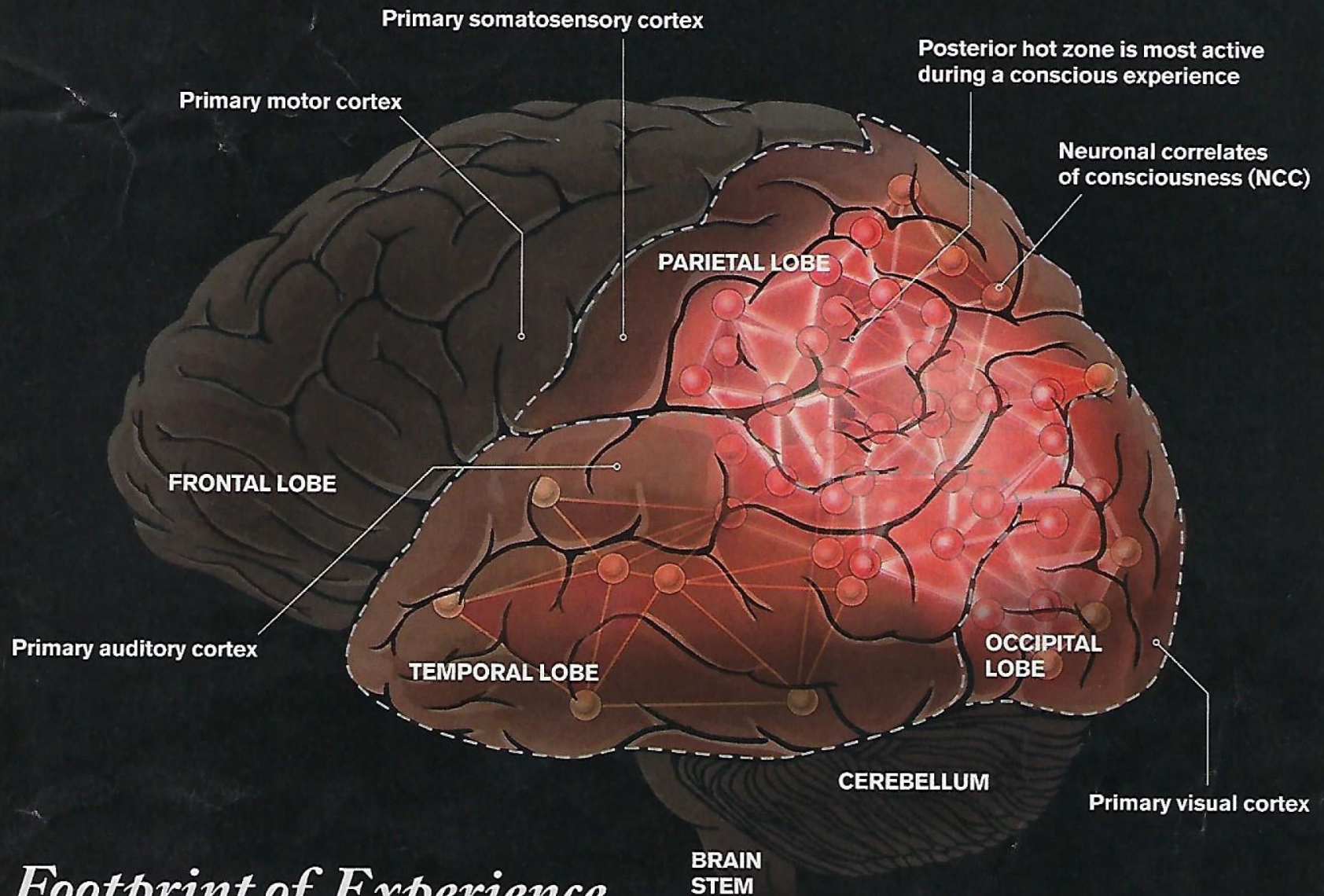
Note the location of the primary motor cortex to Broca's Area.

What is the spacial relationship between Broca's Area and Wernicke's Area?

How do do the two areas communicate? (arcuate fasciculus)

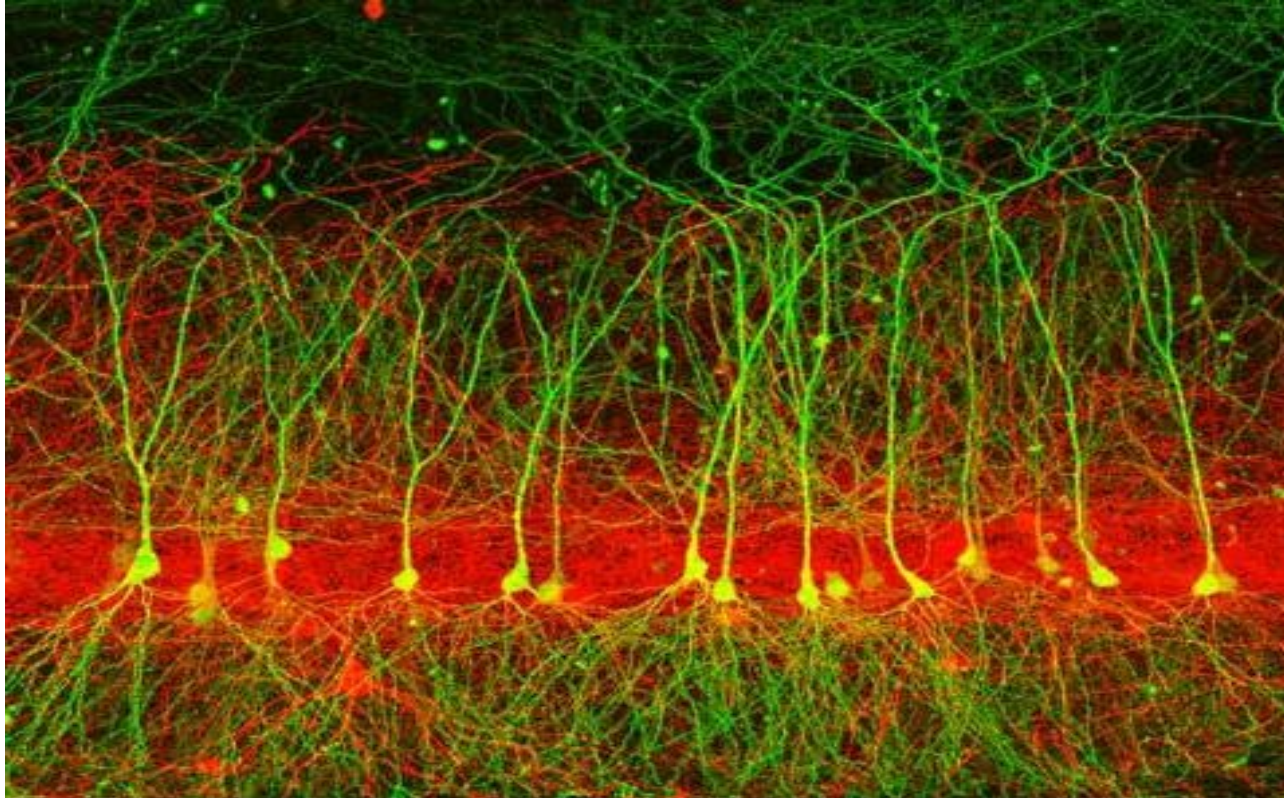
Motor and Sensory Regions of the Cerebral Cortex





Footprint of Experience

Conscious awareness is closely associated with the cerebral cortex, an intricately folded and connected sheet of nervous tissue. Each experience corresponds to a specific set of neural activities, called the neuronal correlates of consciousness (NCC), in a posterior hot zone of the brain that consists of the parietal, occipital and temporal lobes of the cerebral cortex. Complexity of the neural excitations after a magnetic pulse yields a measure of the degree to which a person is conscious.



hhmi - www.BioInteractive.com

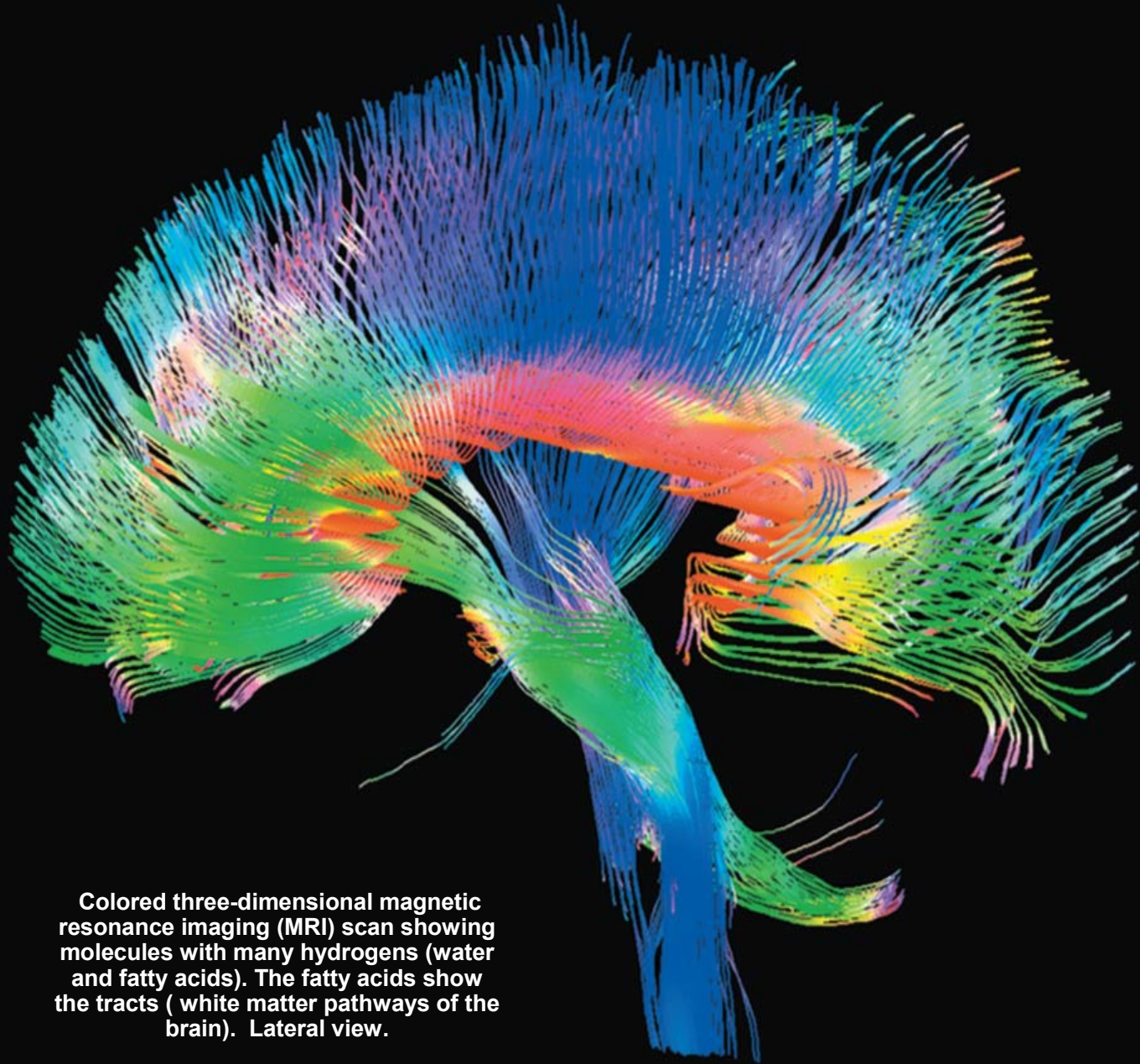
The key to understanding how our brains work lies in determining how each nerve cell or neuron continuously integrates the information it receives from other neurons via connections called synapses. For example, each pyramidal neuron (colored green) can receive tens of thousands of synapses from neurons belonging to several different brain regions. Interneurons (colored red) form local connections onto pyramidal neurons to form specific microcircuits. By using a combination of approaches including electrophysiology, microscopy, molecular biology and computer modeling, scientists are able to approach the complex puzzle of understanding how the 100 billion neurons in our brains make us who we are.

Technical Details:

The image was produced using array tomography. This technique involves collecting thousands of ultrathin serial sections of brain tissue that was fixed and stained, imaging them with a fluorescent microscope, and aligning all of them into a 3D reconstruction using a computer. The resulting image enables the detailed patterns of connectivity to be mapped between fluorescently-labeled neurons.

Credit:

Erik Bloss, PhD and Nelson Spruston, PhD., HHMI, Janelia Research Campus



Colored three-dimensional magnetic resonance imaging (MRI) scan showing molecules with many hydrogens (water and fatty acids). The fatty acids show the tracts (white matter pathways of the brain). Lateral view.

Images of the Mind

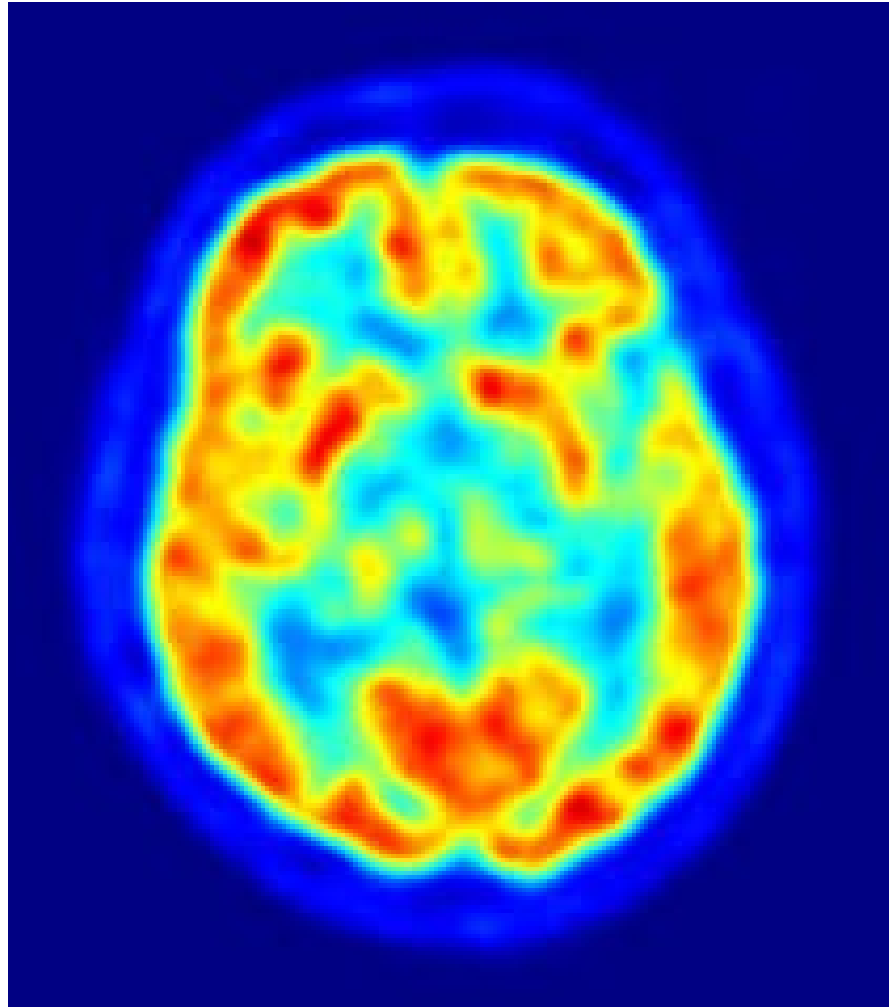
- **Positron emission tomography (PET)**
 - visualize increases in blood flow when brain areas are active
 - injection of radioactively labeled glucose
 - Metabolic active areas of brain will “light up”
 - So if you ask a patient to do something or say something during a PET Scan then the area of the brain processing the command will increase metabolism to process the request and it will “light up” as more glucose flow into this area

New non-invasive technologies allow neuroscientist to study both the structure and function of a living brain. CT, PET, and fMRI are now the new images of the brain.

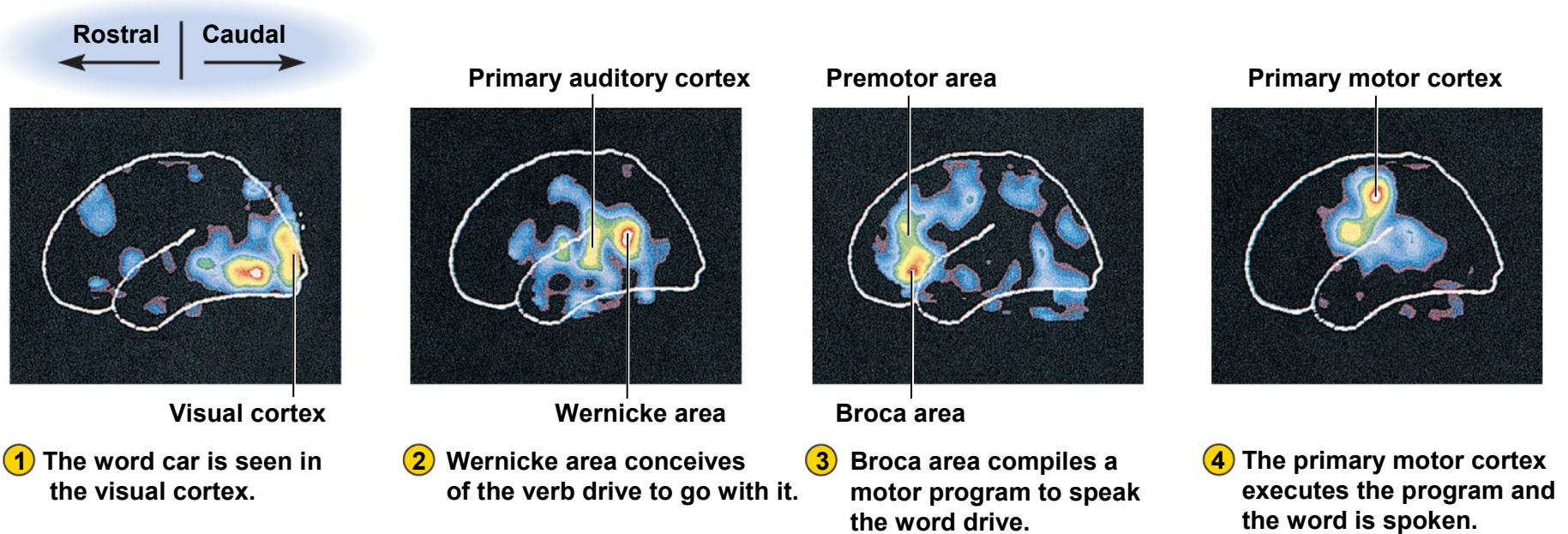
What is a Positron Emission Tomography Scan?

- A PET scan uses radiation, or nuclear medicine imaging, to produce 3-dimensional, color images of the functional processes within the human body. PET stands for positron emission tomography.
- The machine detects pairs of gamma rays that are emitted indirectly by a tracer (positron-emitting radionuclide), which is placed in the body on a biologically active molecule (e.g. glucose). The images are reconstructed by computer analysis.
- Modern machines often use a Computer Tomography X-ray scan which is performed on a patient at the same time in the same machine.

PET Image



PET Scans and Language Task



What is fMRI?

- Functional magnetic resonance imaging or functional MRI (fMRI) is a functional neuroimaging procedure using MRI technology that measures brain activity by detecting associated changes in blood flow. This technique relies on the fact that cerebral blood flow and neuronal activation are coupled. When an area of the brain is in use, blood flow to that region also increases.
- The primary form of fMRI uses the blood-oxygen-level-dependent (BOLD) contrast, discovered by Seiji Ogawa. This is a type of specialized brain and body scan used to map neural activity in the brain or spinal cord of humans or other animals by imaging the change in blood flow (hemodynamic response) related to energy use by brain cells. Since the early 1990s, fMRI has come to dominate brain mapping research because it does not require people to undergo shots, surgery, or to ingest substances, or be exposed to radiation, etc. Other methods of obtaining contrast are arterial spin labeling and diffusion MRI.
- The procedure is similar to MRI but uses the change in magnetization between oxygen-rich and oxygen-poor blood as its basic measure. This measure is frequently corrupted by noise from various sources and hence statistical procedures are used to extract the underlying signal. The resulting brain activation can be presented graphically by color-coding the strength of activation across the brain or the specific region studied. The technique can localize activity to within millimeters but, using standard techniques, no better than within a window of a few seconds

Images of the Mind

Functional magnetic resonance imaging (fMRI)

Looks at increase in blood flow to an area (additional glucose is needed in active area)

Magnetic properties of hemoglobin dependent on differences between the oxygenated and unoxygenated magnetic properties of hemoglobin

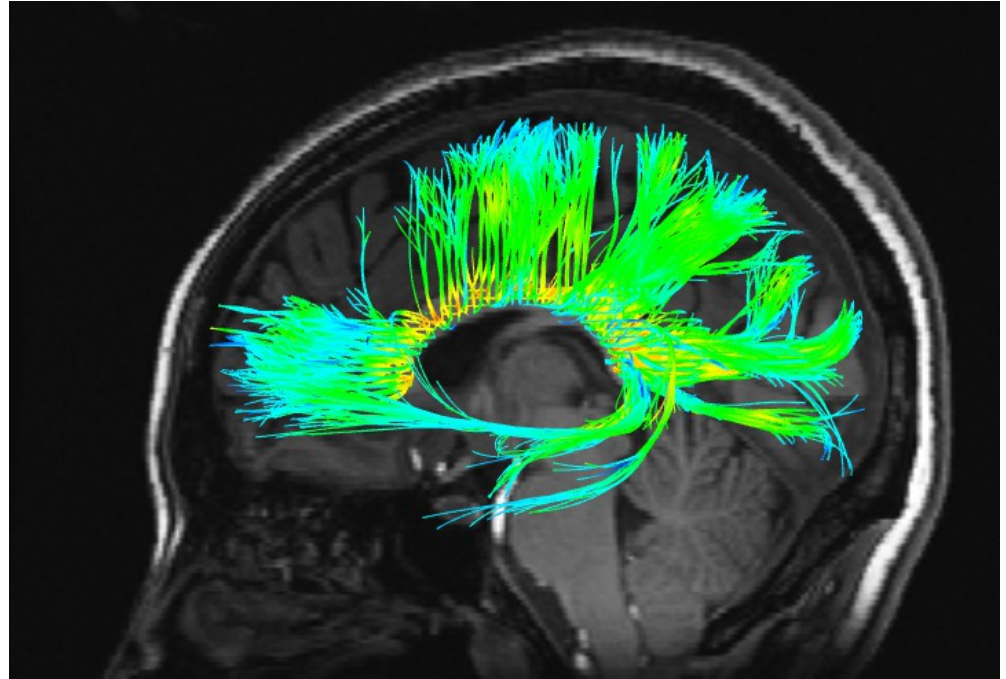
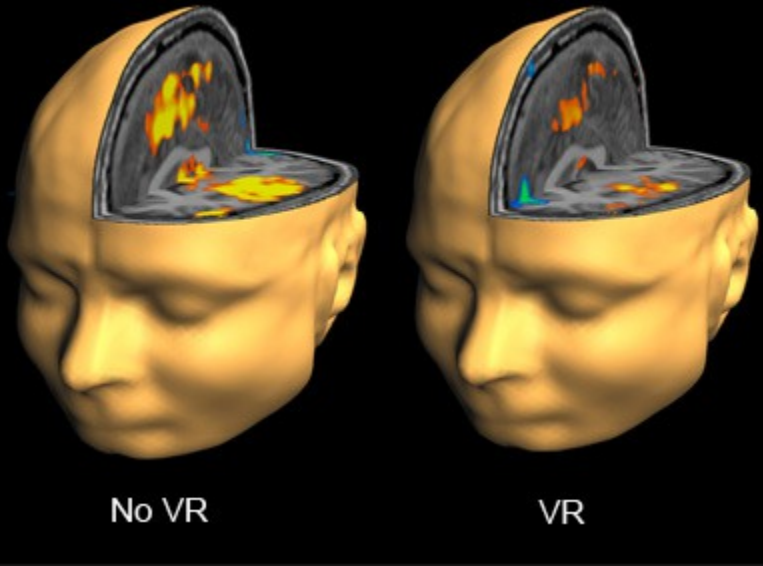
Oxygen bound to hemoglobin produces a “magnetic image” different than unbound hemoglobin // creates “contrast”

Quick, safe and accurate method to see brain function

Does not use ionizing radiation!

fMRI

Pain Related Brain Activity is reduced during VR



What is CT Imaging?

- X-ray computed tomography (x-ray CT or CT) is a technology that uses computer-processed x-rays to produce tomographic images (virtual 'slices') of specific areas of the scanned object
- Allowing the user to see inside without cutting.
- Digital geometry processing is used to generate a three-dimensional image of the inside of an object from a large series of two-dimensional radiographic images taken around a single axis of rotation.
- Medical imaging is the most common application of x-ray CT. Its cross-sectional images are used for diagnostic and therapeutic purposes in various medical disciplines.

CT Image

