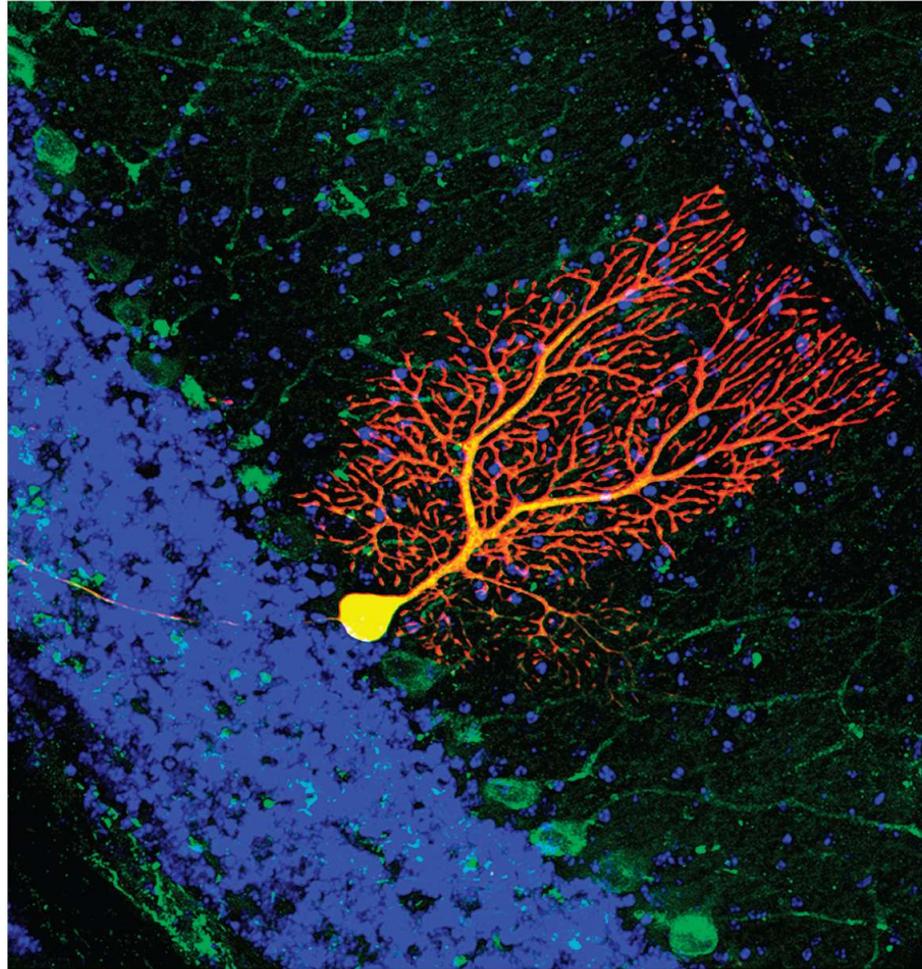


Neural Coding & Memory



Strange Factoids About Brain Function

Structurally, we have one brain, however.

Functionally, we have many brains with different “types of memories” (e.g. declarative vs procedural) and different “states of awareness” (i.e. unconscious, subconscious, and conscious). This brings into questions how we reach decisions, are able to form opinions, establish behaviors, and why we are aware! So how do we explain the following.....

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 cleaner” then your political opinions shift more toward the “political right”.

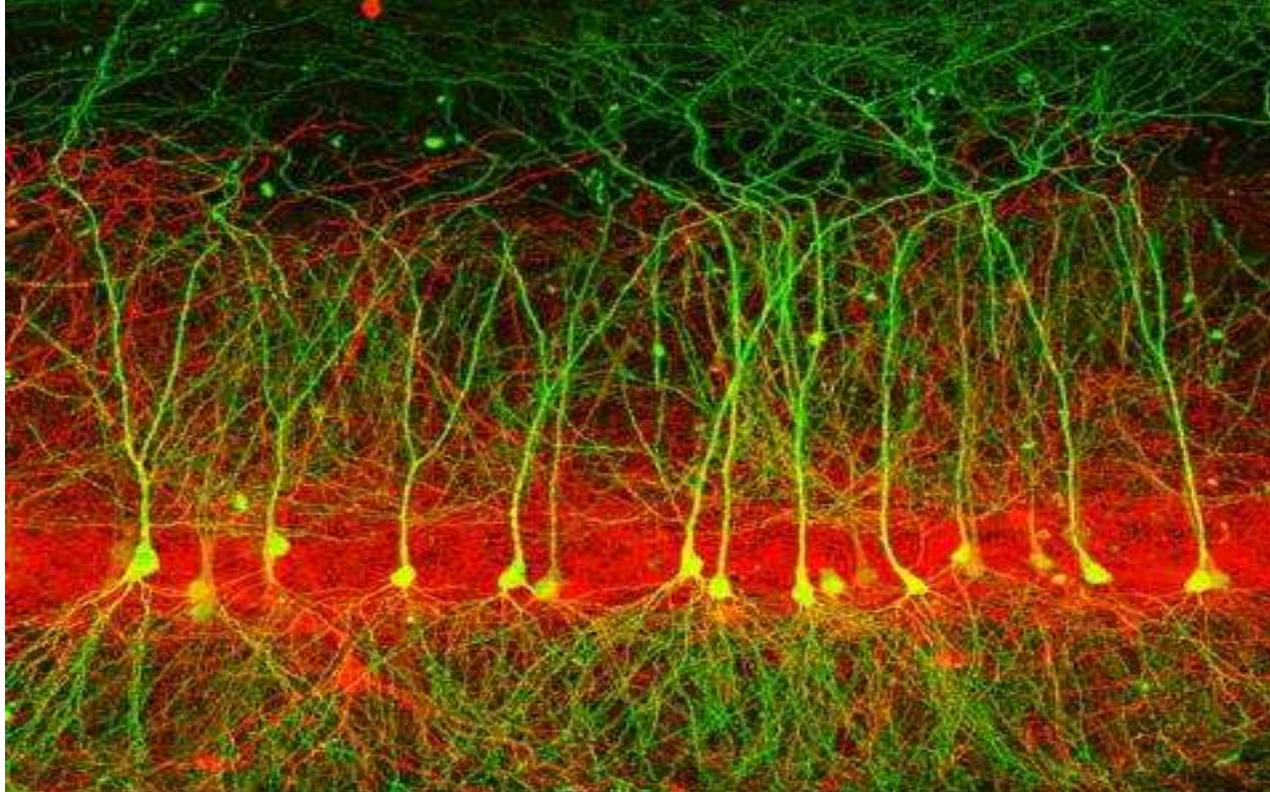
If you hold a cup of “hot coffee” then you will have a “more pleasant feeling about your mother”.

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

Neural Integration and Neural Networks

Neural integration is the ability of your neurons to process information. Neurons may store information, recall information, and integrate information. Neural networks are different patterns of connections between neurons that are responsible for these functions.

- chemical synapses are the decision making devices of the nervous system
- the more synapses a neuron has /// the greater its information-processing capabilities.
- **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



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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:

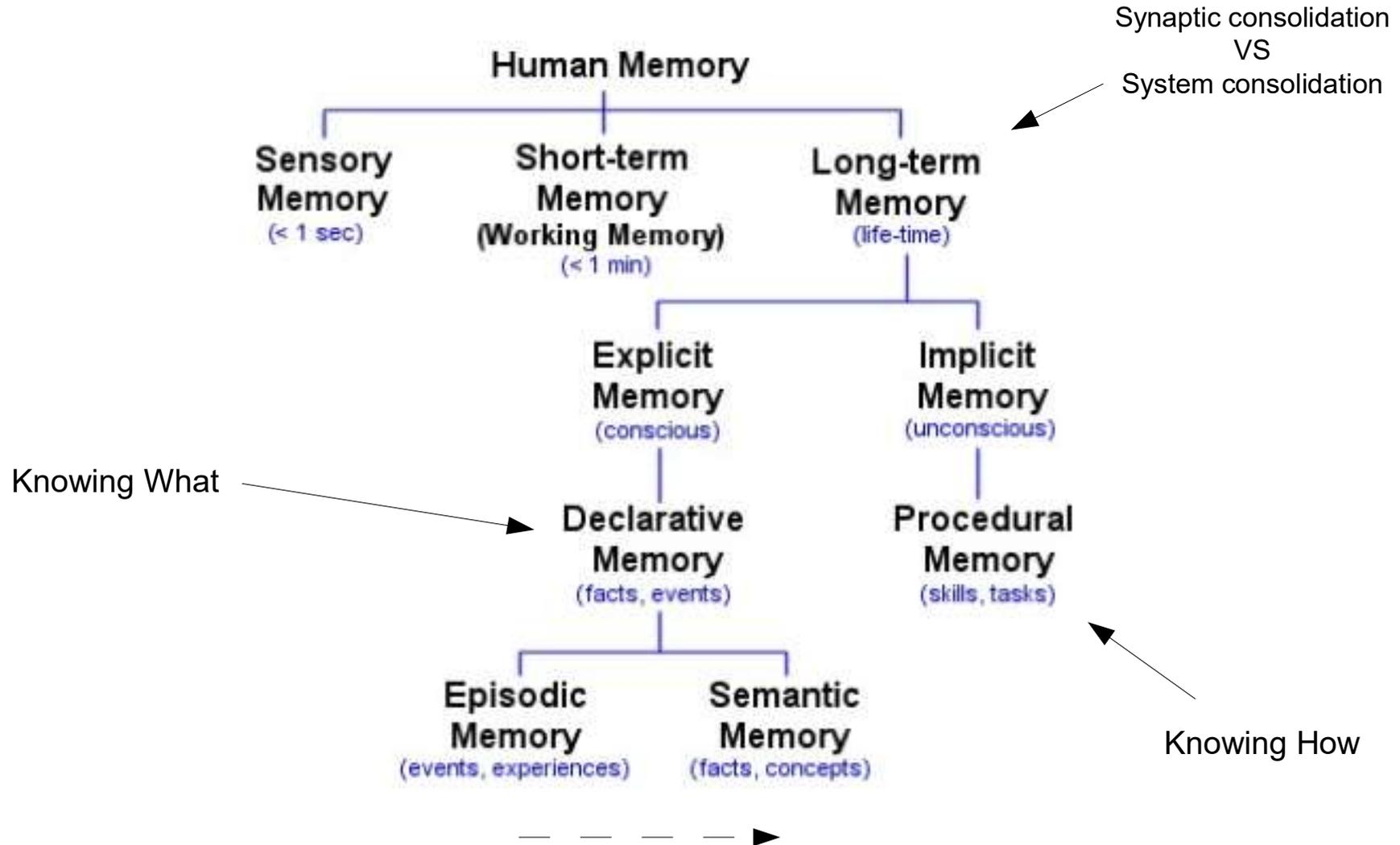
The image was produced using array tomography. This technique involves collecting thousands of ultrathin serial sections of brain tissue that was fixed and stained, imaging them with a fluorescent microscope, and aligning all of them into a 3D reconstruction using a computer. The resulting image enables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

Credit:

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

What are memories?

Are there different types of memories? How many? Why?



Memory and Synaptic Plasticity

- The physical 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 (not new neurons!)
 - **synaptic plasticity** – the ability to change physical characteristics of a synapse
 - **synaptic potentiation** - the process of increasing synaptic transmission
- Different types of memory
 - **immediate, short-** and **long-term** memory // correlate with different modes of synaptic potentiation
 - **declaritive VS procedural** (knowing what VS knowing how)

Sensory Memory

- **immediate memory** – less than a second /// the ability to have a perception of something
 - essential for brain to recognize if the stimulus is important to you
- feel for the flow of events (sense of the present)
- **Do this:** stand in place while you “slowly” turn 360 degrees with your eyes firmly fixed looking forward /// by the time you complete the turn you have forgotten what you saw at the start of the turn /// however, if there was something important to you then you will stop at that moment or return to that spot.
- This is what we sense as “**perception**”

Short-Term or Working Memory

- **short-term memory (STM)** - lasts from a few seconds (may be extended with rehearsal)
 - quickly forgotten if distracted
 - e.g. calling a phone number we just looked up
 - e.g. ability to read sentence while able to remember the beginning and ending of the sentence
 - reverberating circuits /// our memory of what just happened “echoes” in our minds for a few seconds // i.e. reverberating circuits
- Frontal lobe uses two scratch pad or post-it for short term memory /// visual and audio to facilitate short term memory
- Facilitation also called rehearsal causes 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 memory
 - **declarative** - retention of events that you can put into words
 - **procedural** - retention of motor skills
- LTM requires physical remodeling of synapses // new branching of axons or dendrites // 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 potentiation** – this occurs before LTM and is associated with pathway from hippocampus to medial temporal lobe
 - changes in receptors and other features increases transmission across “experienced” synapses
 - effect is longer-lasting

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

- molecular changes are called **long-term potentiation**
- method described
 - receptors on synaptic knobs are usually blocked by Mg^{+2} ions
 - when bind glutamate and receive tetanic stimuli, they repel Mg^{+2} and admit Ca^{+2} into the dendrite – 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 having a back and forth conversation)

Reconsolidation – after we are done with our memories, we “disassemble” the memory and return the fragments back into 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.

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. panic state) then the limbic system takes over (i.e. anxiety leads to fear leads to aggression /// the fright, flight or fight reaction)

Language

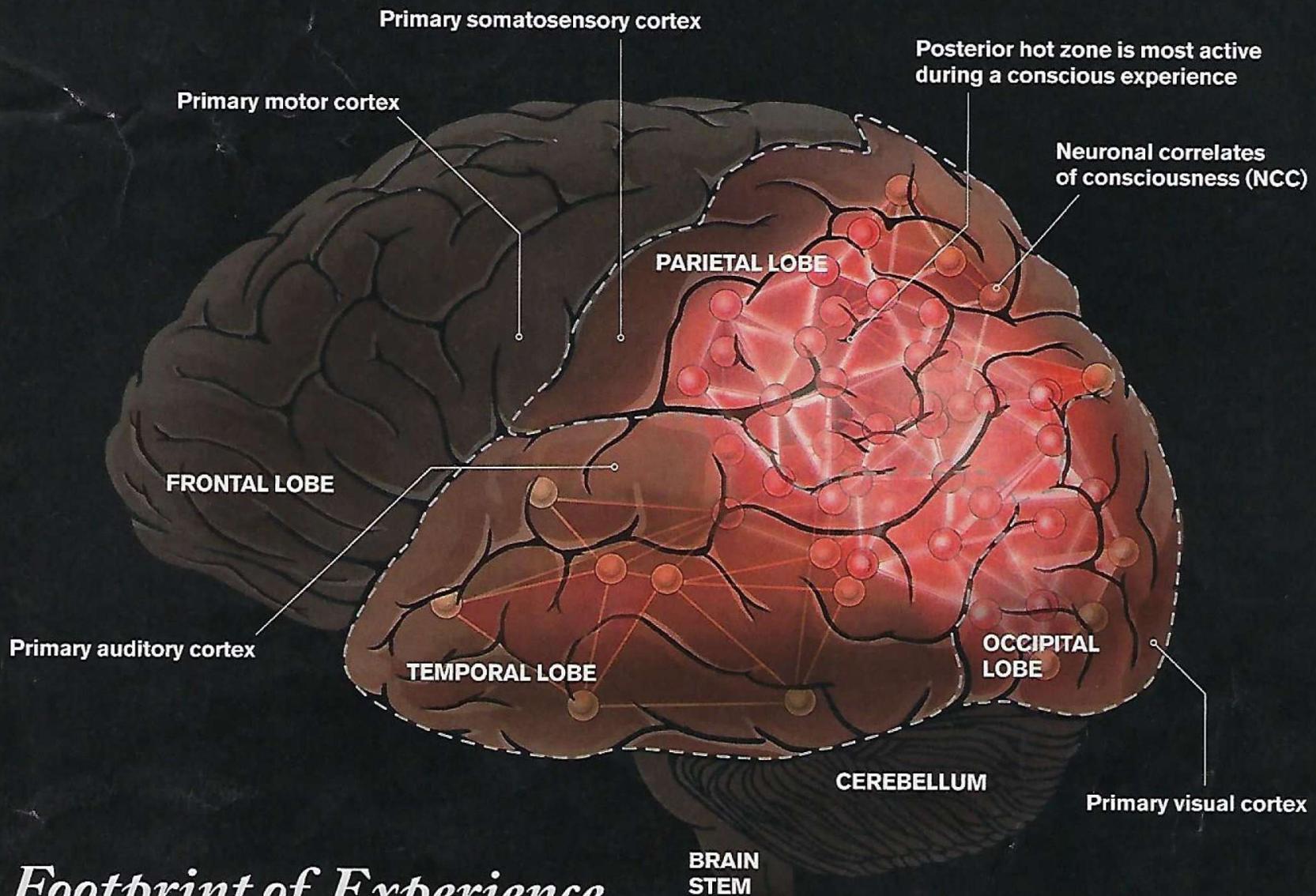
In early primate development language started with “hand gestures”.

The fox-p2 gene allowed the hyoid bone to be re-positioned lower in the pharynx which allowed homo sapiens (i.e. humans) to now make consonants and vowels (i.e. monkeys can hoot and make sound but can not form consonants and vowels)

Wernicke Areas – located in the caudal parietal lobe is the center for **receptive language** /// other areas receive stimulus and must decide if it is language (i.e. written or spoken) and if it is language then relays it to Wernicke Areas for interpretation

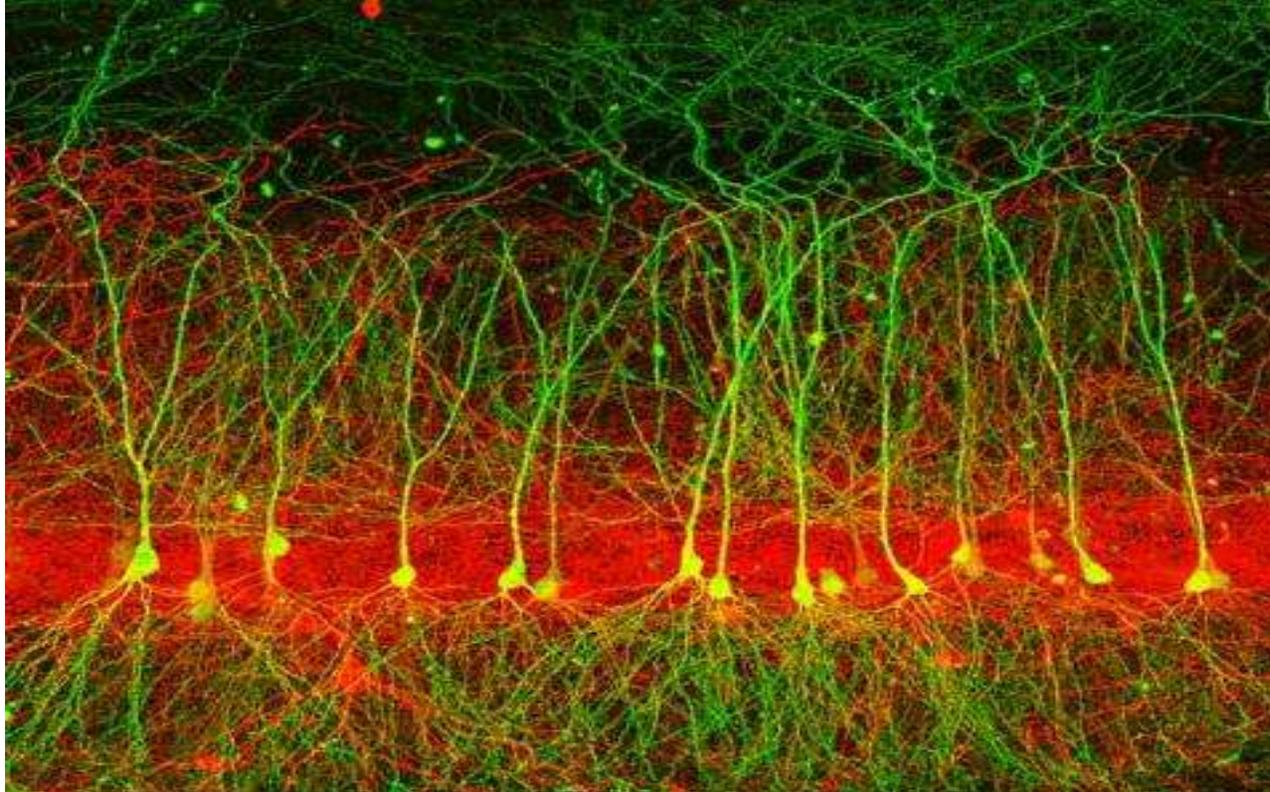
Broca Areas – located in the lower temporal lobe near the motor strip /// this is the center for **expressive language** /// this is where word syntax is constructed

Wernicke and Broca Areas are connected by a nerve tract.



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.



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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

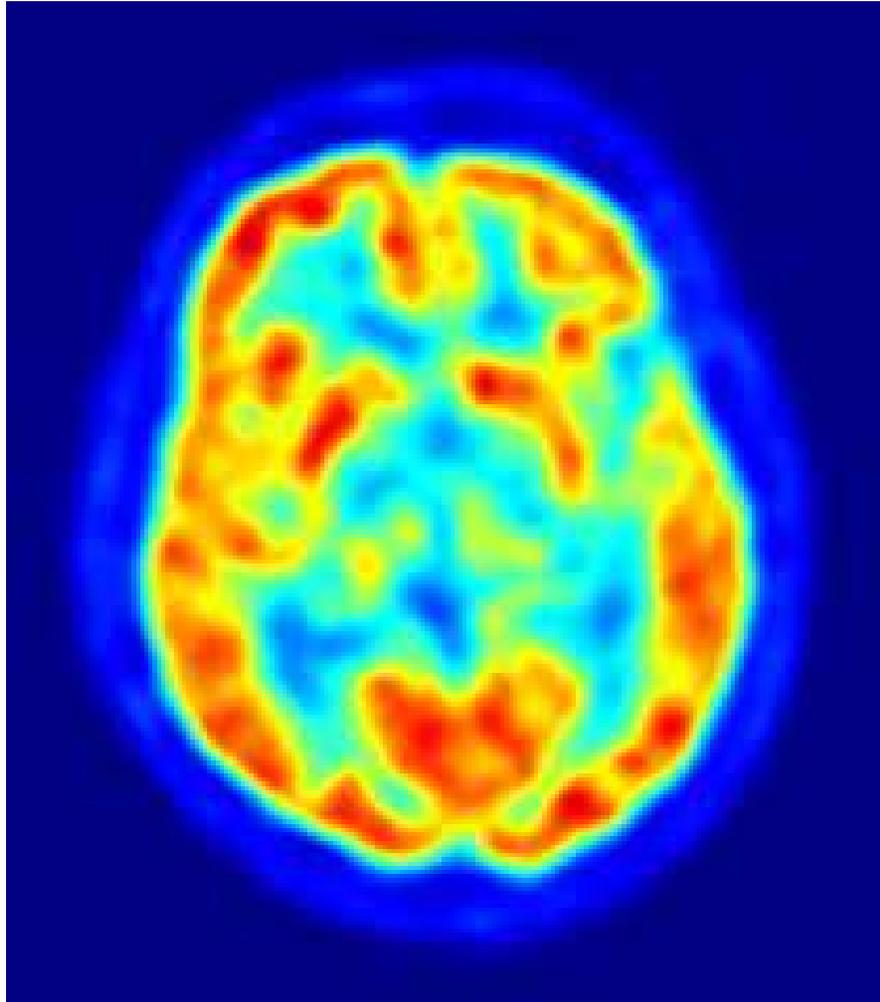
- **Positron emission tomography (PET)**
 - visualize increases in blood flow when brain areas are active
 - injection of radioactively labeled glucose
 - Metabolic active areas of brain will “light up”
 - So if you ask a patient to do something or say something during a PET Scan then the area of the 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.

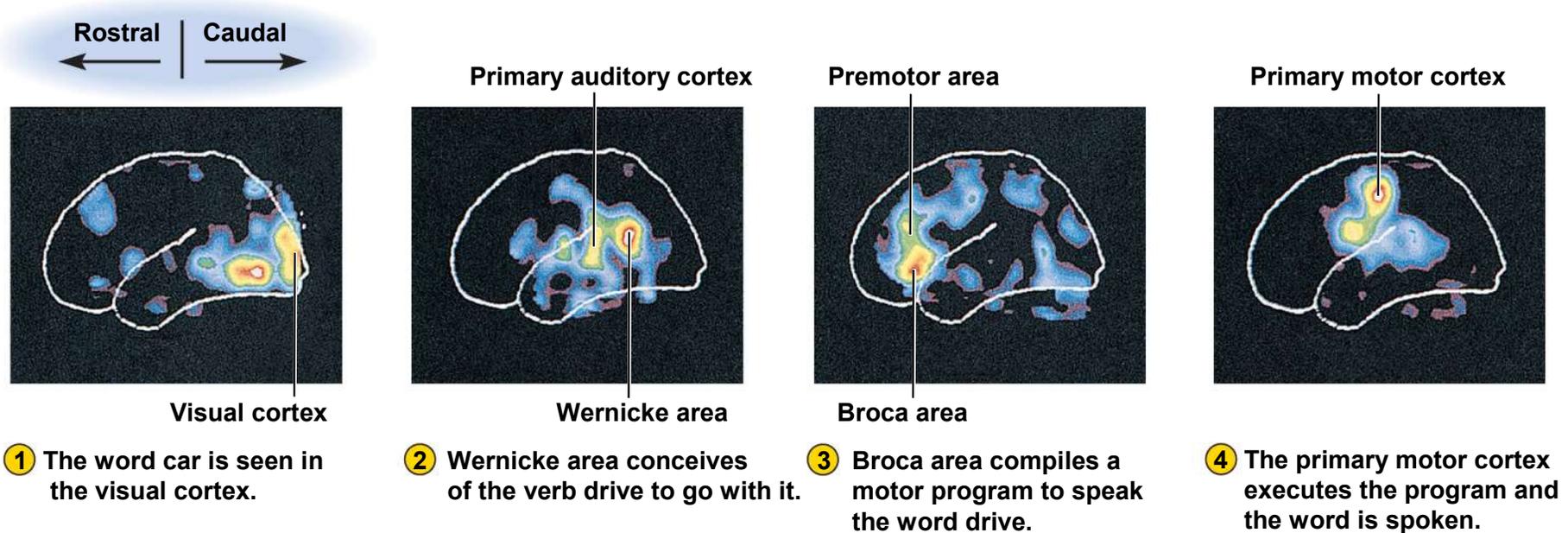
What is a Positron Emission Tomography Scan?

- 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)

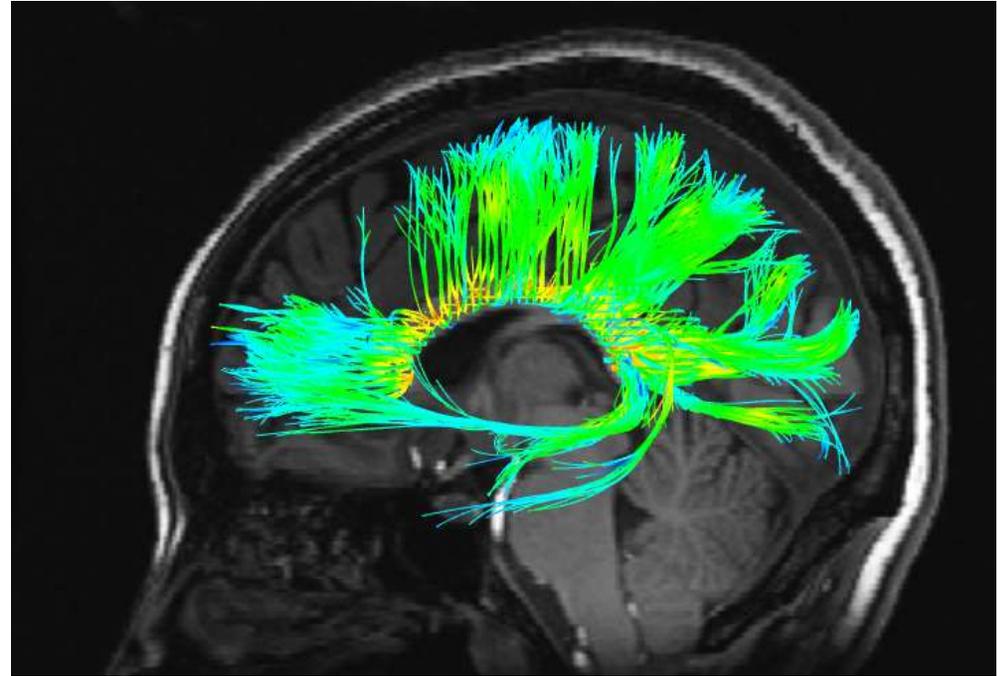
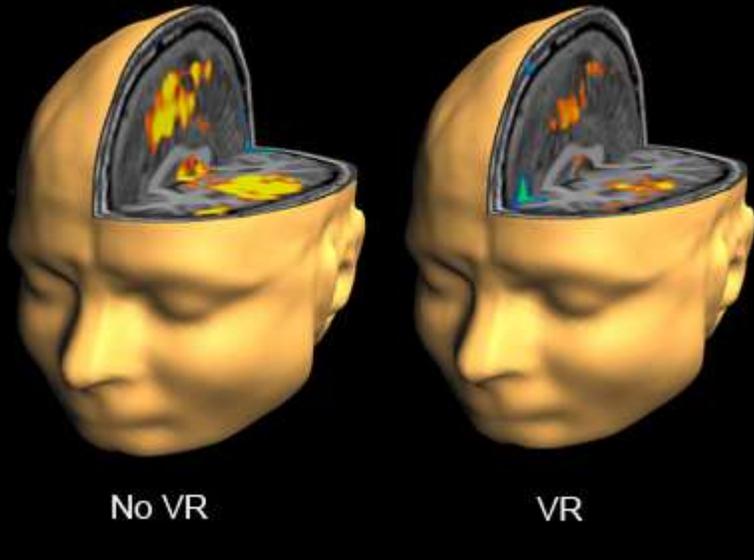
looks at increase in blood flow to an area (additional glucose is needed in active area)

magnetic properties of hemoglobin dependent on difference between oxygenated and unoxygenated
magnetic properties of hemoglobin / how much oxygen is bound to it

quick, safe and accurate method to see brain function

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. The rest of this article discusses medical-imaging x-ray CT.

CT Image

