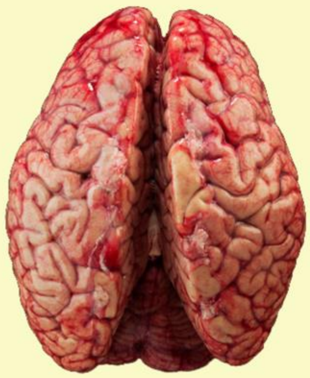
Brain and Mind



The Brain—is wider than the Sky—
For—put them side by side—
The one the other will include
With ease—and You—beside—

The Brain is deeper than the sea—
For—hold them—Blue to Blue—
The one the other will absorb—
As Sponges—Buckets—do—

The Brain is just the weight of God—
For—Lift them—Pound for Pound—
And they will differ—if they do—
As Syllable from Sound—

Emily Dickinson, 1863
(read by Becky Miller)

Welcome to the LIFE course on Brain and Mind! The human brain only weighs about 3 pounds (1400 gm). Yet it contains about 80 billion neurons. With over 10 trillion connections between them. In some way, we know not yet how, it embodies all our thinking and makes it possible for us to find meaning in the sounds we hear. And one day understand the universe.

Emily Dickinson's poem is every bit as complex as the brain – it also has a surface structure and a deep meaning. And many unanswered questions. What is the weight of God? It likely has to do with the meaning of the word 'weight,' which includes ideas of importance and of meaning. The divinity creates a universe in which sound occurs but only the brain can understand some sounds as syllables.

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The Anatomy Lesson of Doctor Deijman
Rembrandt van Rijn, 1656

You should know a little about me. I am old like you. I have a medical background but I have not practiced for almost thirty years and I would not trust my own health advice. I have studied hearing. It is therefore perhaps fitting that I now have a hearing loss and hearing aids. Since I have also studied cognition. I am now waiting for dementia to catch up with me.

The illustration on this slide is the Anatomy Lesson of Dr. Deijman (pronunciation: dee-eye-man). It is only a fragment of a larger painting that was severely damaged in a fire. The professor demonstrates the membranes surrounding the brain of the thief Joris Fontejn, who had been executed by hanging.

The original painting showed the professor dissecting the brain and an assembly of students observing. The fellow on the left is a simple assistant. He is holding the calvarium – the top of the skull that has been removed. I am not an expert in many of the topics I shall be presenting. I am an attendant lord, one that will do to start you thinking but one that may not have all the answers.

I am happy to entertain questions, though I may need the help of the class liaison in understanding them. Forgive me if I sometimes answer a different question from the one you asked, Even so the answer might still be interesting.
I would be happy to receive emails, and I will try to answer emailed questions. However, do not expect an immediate reply. It may take a day or two.

The LIFE Institute has just started a webpage. This will allow you to download the course notes. The LIFE page will require you to log in.
http://coursepages4life.ca/

I also have a webpage. Though initially started for other reasons, it will also allow you to download course notes. If one site is down the other might work.
http://creatureandcreator.ca/?page_id=1330

Brain and Mind: Course Outline

1. Introduction. Brain anatomy. Stroke. Neurons. Excitation. Action potentials. Synaptic transmission.. Body sensations. Braille.

2. Moving to the Music. Muscles. Stretch reflexes. Basal ganglia. Cerebellum. Parkinson's Disease. Balance. Hearing. Speech and music.

3. Sensation and Perception. Taste and smell. Hunger and satiety. Vision. Visual fields. Motion. Recognizing faces and objects. Illusions.

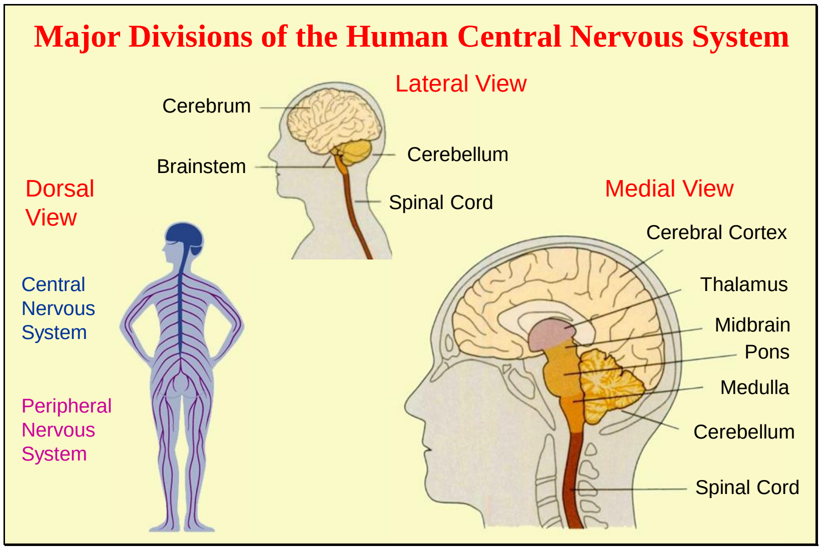
4. Consciousness. Sleep, meditation, coma, epilepsy. Locked-in syndrome. Attention. Consciousness. Theory of mind. Split-brain studies – interpreter.

5. Learning and Memory. Synaptic changes. Motor skills. Priming. Episodic vs semantic memory. Amnesia. Alzheimer's Disease.

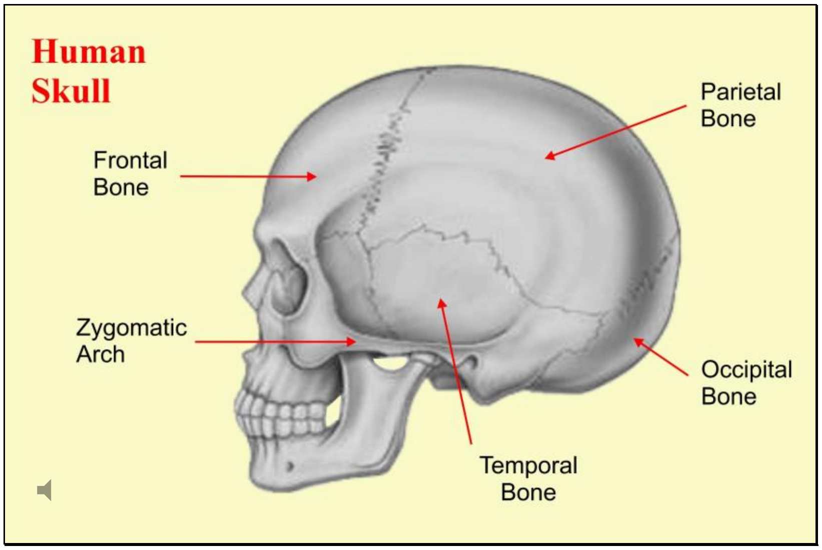
6. Language and Emotion. Language. Humans vs chimps. Aphasia. Dyslexia. Basic emotions. Autonomic Nervous System. Love and Hate. Music.

7. Thought and Will. Executive functions. Psychopathy. Brain networks (attention and default). Determinism. Free will.

8. Madness and Wisdom. Psychiatric diagnosis. Anxiety. Schizophrenia. Depression. Addiction. Maturation of brain. Mental speed. Ageing. Wisdom.



To understand how the brain works we need to learn a little anatomy.
It takes effort to learn the names but we must know where things are before we figure out what they do or how they do it.
The nervous system is (like Gaul) in three parts divided – the brain, spinal cord and peripheral nervous system. The brain and spinal cord are the central nervous system. The peripheral nervous system is divided into the somatic (skin and muscles) and the autonomic (internal organs, blood vessels)
The brain itself also has three main parts – cerebrum, cerebellum (big brain and little brain) and the brainstem.
And the brain stem has three parts – midbrain, pons, medulla
The God of Evolution was partial to the number three.

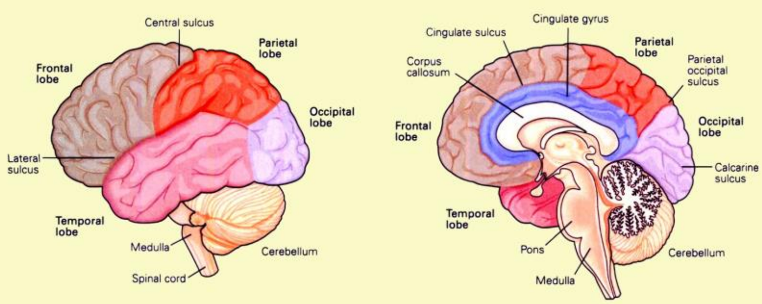


Alas, poor Yorick! I knew him, Horatio, a fellow of infinite jest, of most excellent fancy. He hath borne me on his back a thousand times, and now, how abhorred in my imagination it is! My gorge rises at it. Here hung those lips that I have kissed I know not how oft. —Where be your gibes now? Your gambols? Your songs? Your flashes of merriment that were wont to set the table on a roar? Not one now to mock your own grinning? Quite chapfallen?

Consider the skull:
The skull is the brain's container. Knowing the bones is helpful to knowing the underlying parts of the brain. Frontal is obvious. Parietal means wall. Occipital is back of the head. Temporal is difficult to understand – it has senses of time and religion.

Now get you to my lady's chamber and tell her, let her paint an inch thick, to this favor she must come. Make her laugh at that.

Lobes of the Human Cerebral Cortex

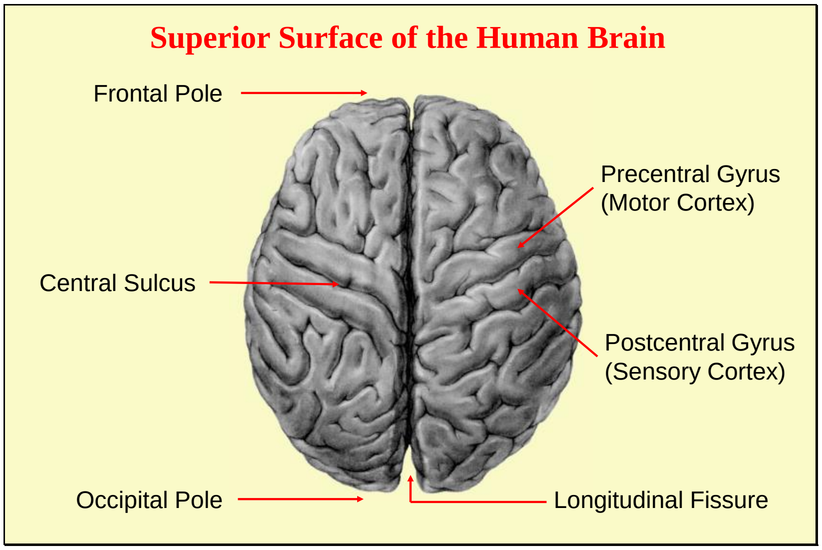


Frontal: control of movement; motivation; planning; imagination
Temporal: memory; hearing; object perception; emotions
Parietal: body sensation; attention; spatial perception
Occipital: vision
Limbic: emotions; memory

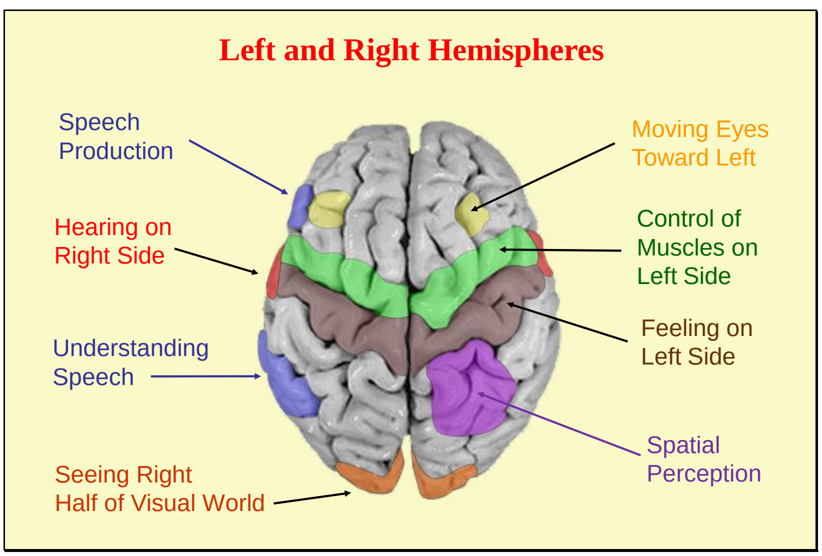
Most of the lobes of the cerebrum are named after the bones which overlie them.
The left figure is the brain viewed from the left. The right figure shows the right half of the brain after it has been cut into two halves. The cut separates the two hemispheres of the cerebrum by sectioning the corpus callosum.

The limbic lobe is the part of the brain that borders the brainstem.

The cerebral cortex ("covering" or "bark") over most of the cerebral hemispheres is neocortex (new style cortex). This deals with perception, thought and action. Some parts of the limbic system such as the hippocampus are old style. They deal with memory and emotions.

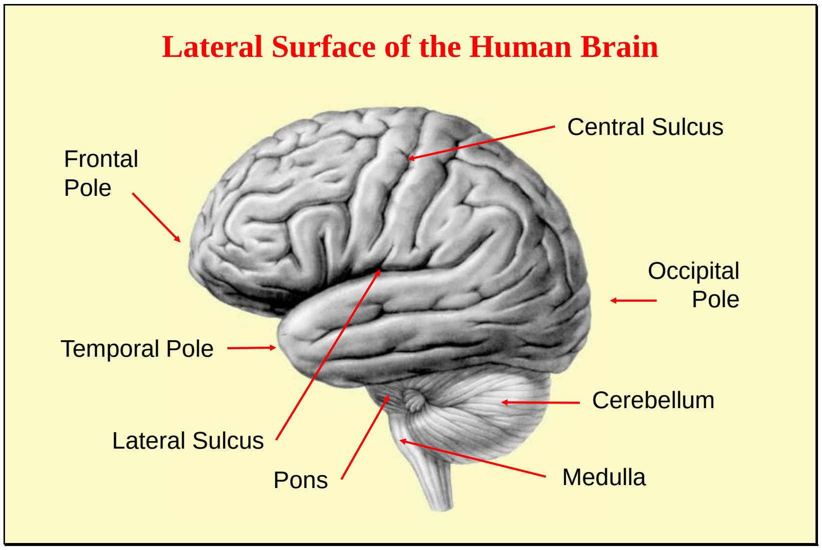


First thing to note is that there are two hemispheres, one for each side of the body. Philosophers among you may wish to consider why two? Symmetry seems to be a characteristic of the universe – from subatomic particles to human brains.
The convex regions of the cortical convolutions are called "gyri." These are separated from each other by 'sulci' (furrows).
From the top, the main landmarks are the longitudinal fissure and the central sulcus.
Sensory and motor cortex are behind and in front of the central sulcus, respectively.

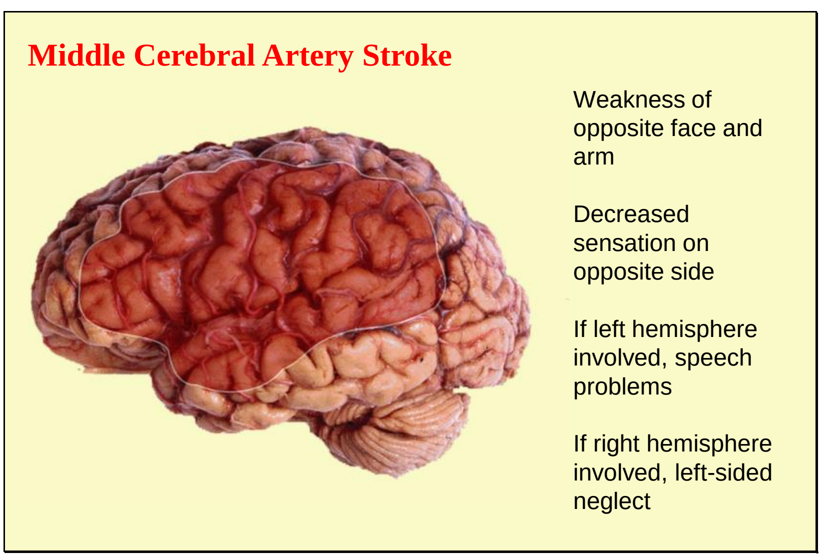


The brain in colors: a functional view of the top of the brain.
Sensation: seeing, hearing, bodily feeling
Perception: space, speech
Motor: body, eyes, speech.

Note that there are two sides to the brain with the right brain controlling the left side of the body and vice versa.
Note that speech (blue) is left sided (except in a small percentage of left-handed people).



From the side the main landmarks are the central sulcus and lateral sulcus.
We can also see the cerebellum nestled underneath the occipital lobes
And the brainstem that connects the cerebrum to the spinal cord.
With the pons (the bridge to the cerebellum) and the medulla (in the middle between the brain and spinal cord)



The most common stroke involves the middle cerebral artery – this can be caused by thrombosis of the internal carotid, or an embolus from the heart or internal carotid into the middle cerebral artery.
This artery supplies the lateral aspect of the cerebral cortex. Such a stroke causes weakness and decreased sensation in the opposite face and arm, often with some sparing of the leg. If the left hemisphere is involved speech is affected and if the right hemisphere is involved attention is affected.

Transient Ischemic Attack ("Mini-Stroke")

Embolus plugs artery, stopping blood flow

Embolus breaks apart and blood flow is restored

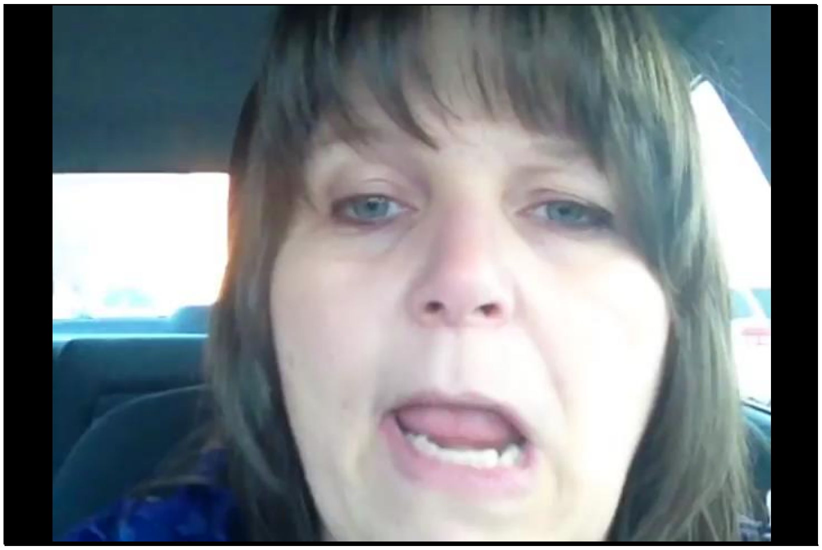
Symptoms: Ischemia in distribution of internal carotid causes weakness on one side of the body (especially face and arm) and speech problems if left hemisphere involved. Ischemia in vertebro-basilar distribution causes vertigo, double vision and visual loss.

Sometimes an embolus blocks an artery causing symptoms and later breaks up with resolution of the symptoms. This is a transient ischemic attack. These are extremely important to recognize as they may be a forerunner of a full-blown stroke.

Treatment of Stroke

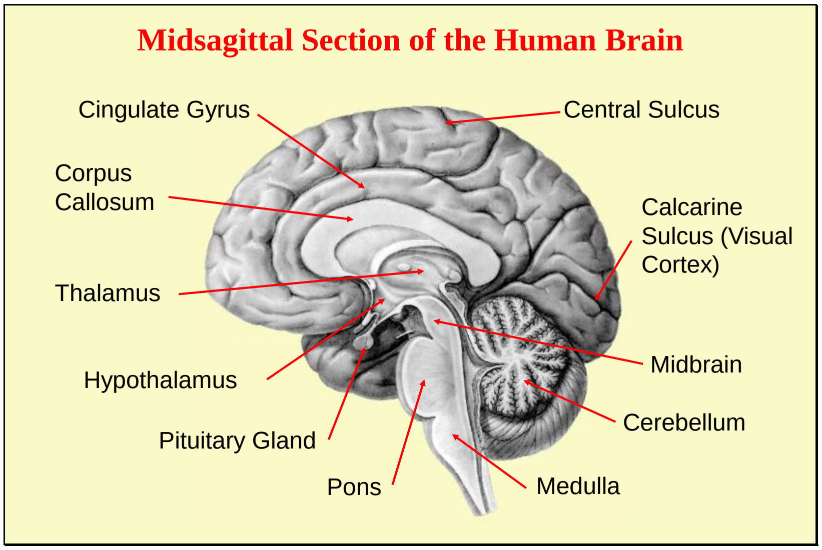
Treatment must be initiated rapidly to prevent or attenuate brain damage. Treatment of ischemic stroke consists of drugs that dissolve the clot and/or surgical removal of the clot with an arterial catheter. Treatment of hemorrhagic stroke is to stop the bleeding (e.g. clipping an aneurysm).

Nowadays there are treatments for stroke – these involve dissolving the clot with anticoagulants or radio-surgical removal of the clot. It is essential that treatment be started rapidly.
The acronym FAST is an easy way to remember the most common signs of a stroke – facial drooping, arm weakness, slurred speech. It is important to get medical help as quickly as possible if any of these signs occur.



Stacey Yepes
This video shows a transient ischemic attack in process.
https://www.youtube.com/watch?v=D7YYWVNG4jA

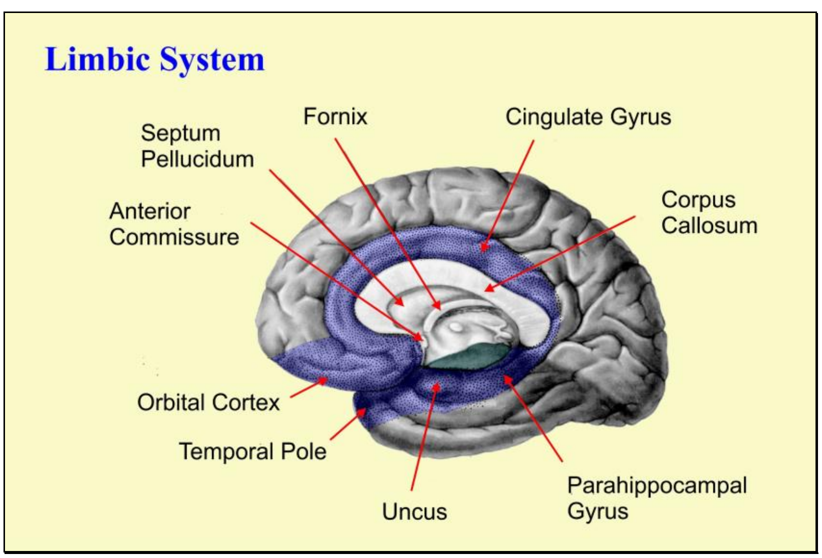
Her speech is slurred because of the facial weakness. She has no language problem because the ischemia is on the right side of the brain. Speech is controlled through the left hemisphere.



Sagittal comes from the way we shoot arrows.

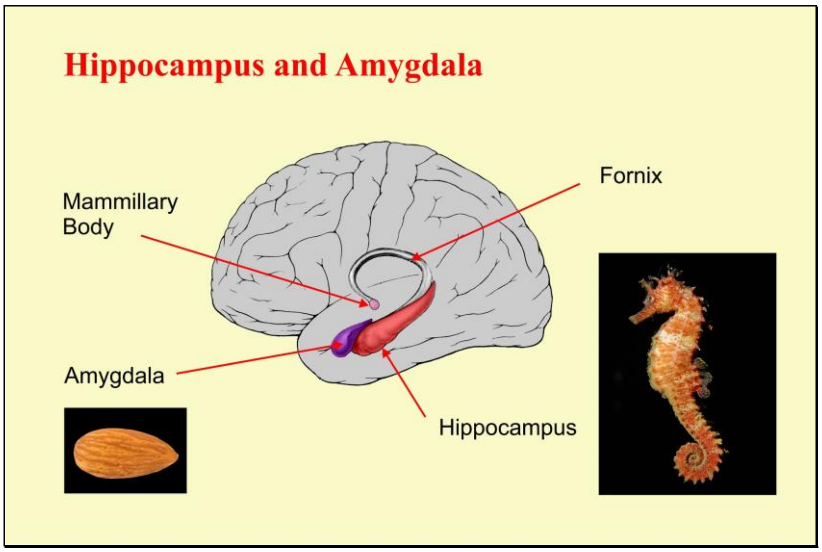
Major landmark is the corpus callosum – the set of fibers that link the two hemispheres. These are the fibers that are cut in split-brain surgery.
The cingulate gyrus is the "girdle" between cortex and the brain's central core (brain stem and thalamus)
At the back of the brain is the visual cortex – the calcarine sulcus is named after the cock's spur.

Brainstem consists of medulla, pons and midbrain.
At the top of the brainstem is the thalamus. Underneath and in front of the thalamus is the hypothalamus. Thalamus means bedroom or bed. Why the thalamus is called this unknown. Yet almost everything goes through the thalamus – just like the bed is the basis of human existence.



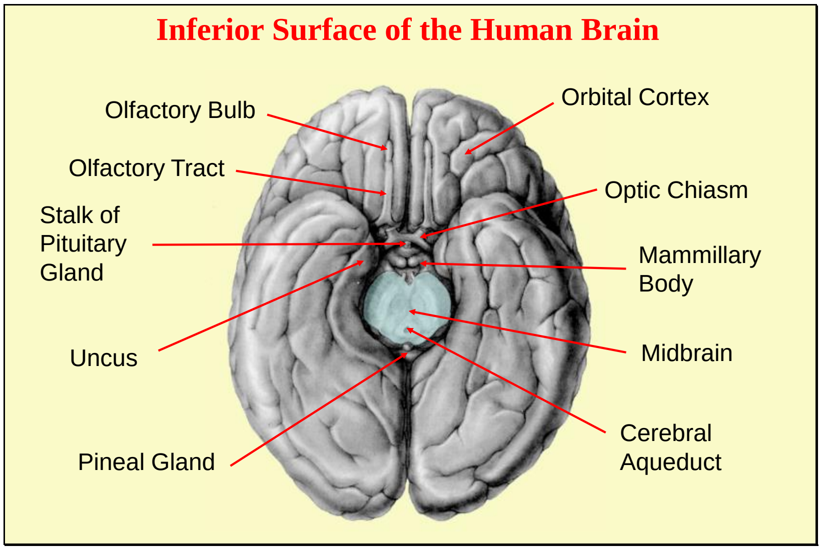
When we remove the brainstem (light blue cut), we can clearly see the limbic system encircling the central core of the brain. The limbic system is important for memory and emotion.

The cingulate gyrus we have already seen. Now revealed is the parahippocampal gyrus inside of which is the hippocampus.
Other parts of the limbic system are the temporal pole containing the amygdala and the orbital cortex of the frontal lobe. The orbital cortex was where the icepick entered the brain in the frontal lobectomy made popular by Walter Freeman.



The amygdala (almond) is involved in emotions.
The other important area that is adjacent to the lateral ventricle is the hippocampus (sea horse). You can see the uncus at the neck of the seahorse and the fornix coiled up in its tail.

The hippocampus is in the medial wall of the lateral ventricle whereas the tail of the caudate is in the lateral wall
The main outflow from the hippocampus goes through the fornix to the mammillary body in the thalamus
The hippocampus is essential for encoding and recalling memories.

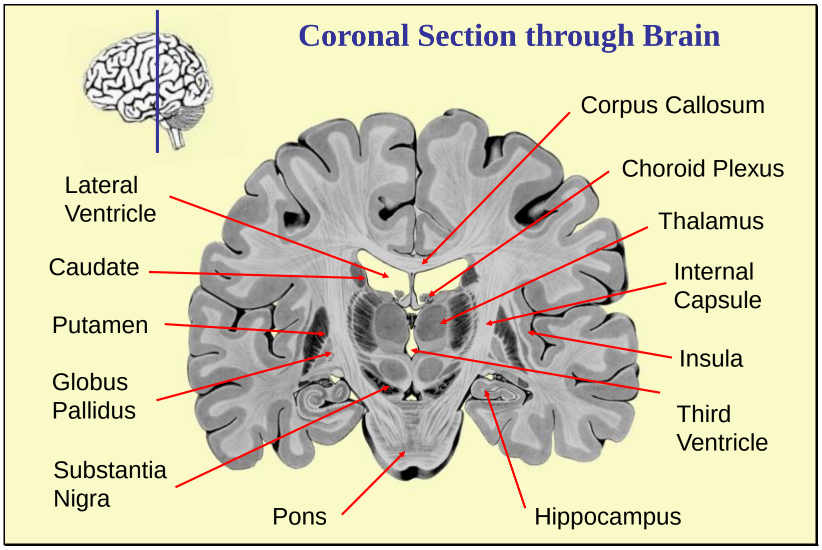


The uncus is better seen from the bottom of the brain. The lower part of the brainstem has been removed with a cut (light blue) through the midbrain.

We can see the olfactory nerves lying on the orbital surface of the brain (so-called because it is above the eyeballs). The olfactory nerves are the only sensory nerves that go directly to the cortex without passing through the thalamus. They connect to the limbic system. As we shall see they are important to memory and emotion. Smell is a powerful trigger for both.

There are two glands on this view of the brain, the pineal at the back of the thalamus and the pituitary at the bottom of the hypothalamus. On this illustration only the stalk of the pituitary is visible. In front of the pituitary is the optic chiasm where some fibers from the right eye go to the left brain and vice versa.

Behind the pituitary are the mammillary bodies (named after the nipples) – where the fornix ends up.

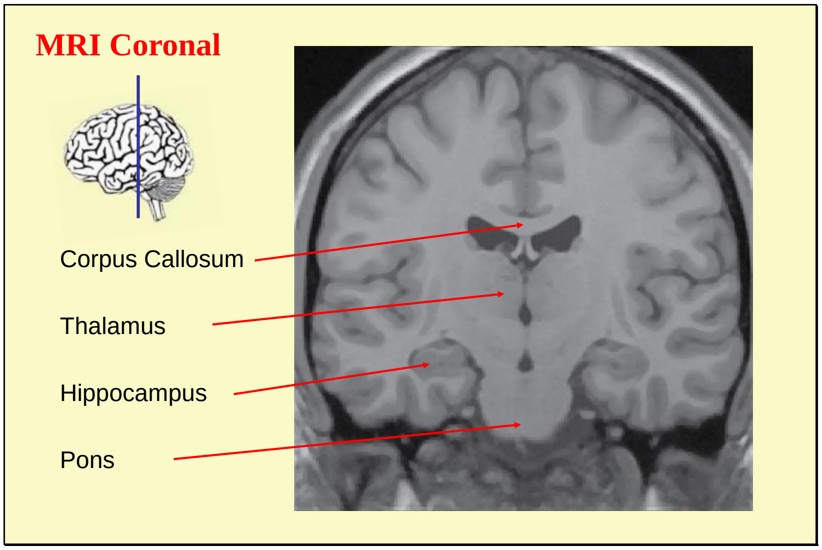


We have looked at the brain from the outside.
Now we shall try to see the inside of the brain using in a slice through the brain. This is the way in which the brain is viewed using magnetic resonance imaging.
There is a lot to see in this illustration, so we shall go slowly.

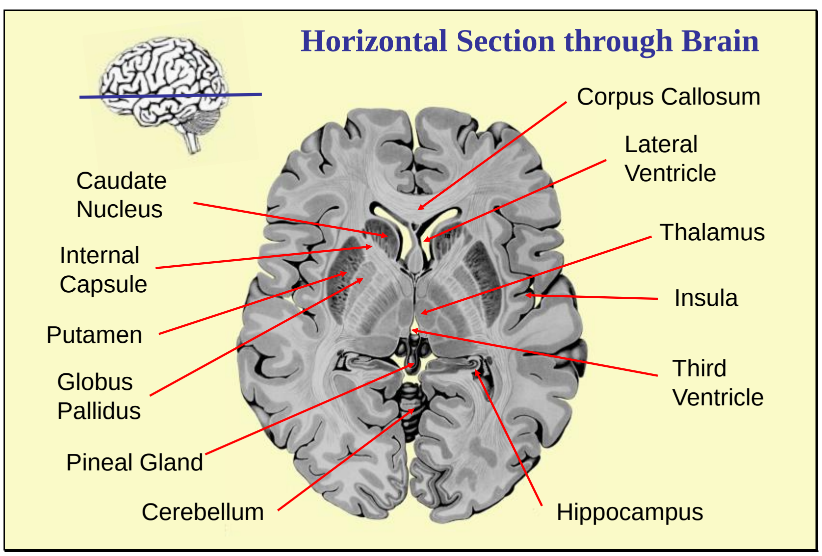
We first identify the bodies of the lateral ventricles, and then the inferior horn of the lateral ventricles in the temporal lobe. These ventricle curl around to form a c-shape
Above the body of the lateral ventricle is the corpus callosum that connects the two cerebral hemispheres. Within the ventricles are the choroid plexuses which secrete cerebrospinal fluid. Remember those regions which are close to the lateral ventricles – the caudate nucleus (lateral wall) and the hippocampus (medial wall in the temporal lobe).

The internal capsule is the pathway that connects the cortex to the thalamus and brainstem. It separates the thalamus from the basal ganglia – the putamen on the outside (that which is pruned) and the paler globus pallidus inside.

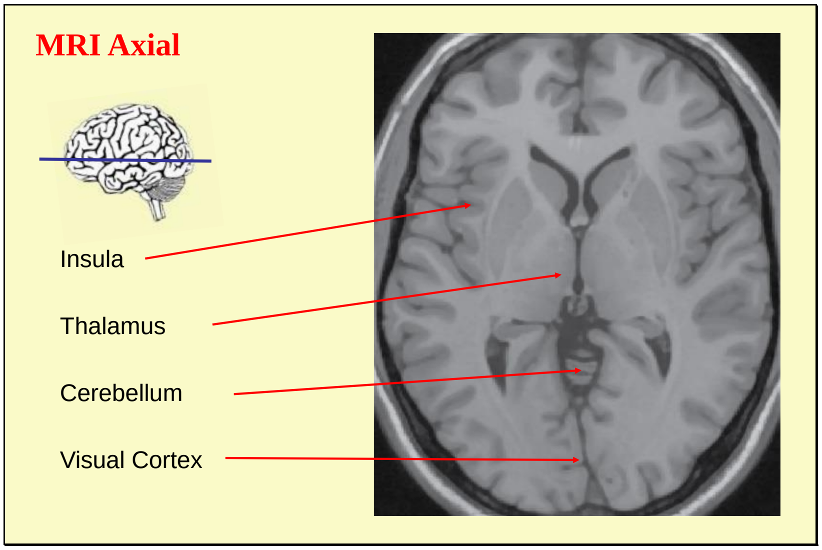
In the brainstem we can see both the midbrain and the pons (at the level of the cerebellum)
And in the midbrain (between thalamus and pons) is the substantia nigra – black substance. This is the region that is primarily affected by Parkinson's Disease. It connects to the basal ganglia and is involved in motor control.



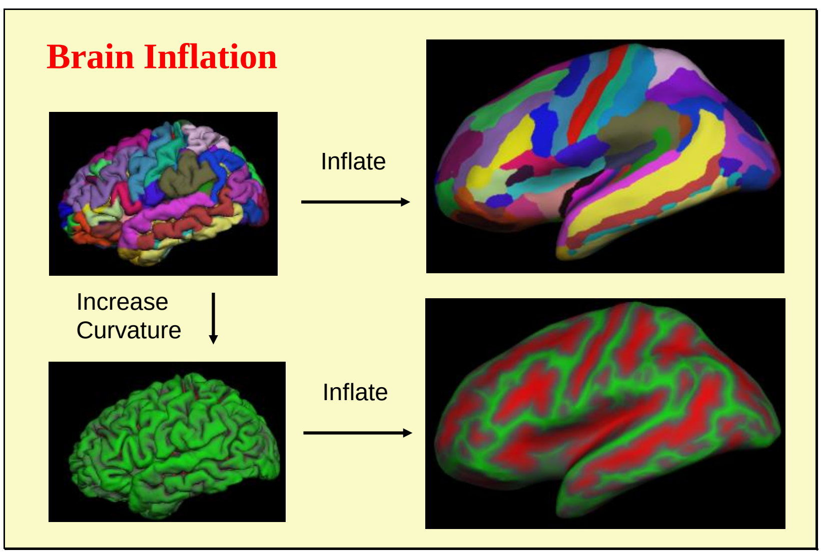
This is an actual slice through a living brain obtained by magnetic resonance imaging.
The hippocampus lies in the inferior horn of the lateral ventricle
The body of the lateral ventricle with the corpus callosum above.



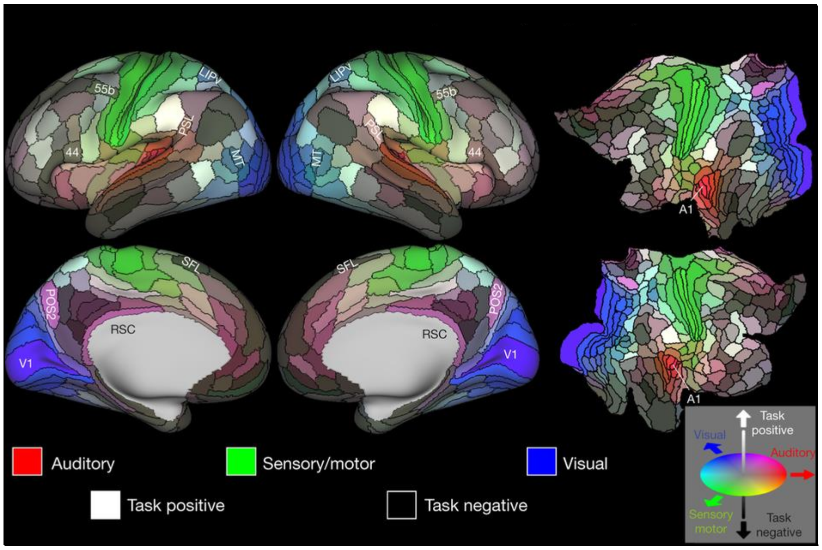
This is a horizontal section of the brain.
This section shows us the regions deep in the cerebral hemispheres. The thalamus, the basal ganglia – consisting of the globus pallidus. the putamen and the caudate nuclei. These are important for the control of movement.
We can just see the top of the cerebellum between the occipital lobes



This is an axial or horizontal section of the MRI of a living brain
Note how the cortical surface of the insula is within the lateral sulcus
At the center is the thalamus.
At the back of the brain is the visual cortex on the medial surface of the occipital lobe



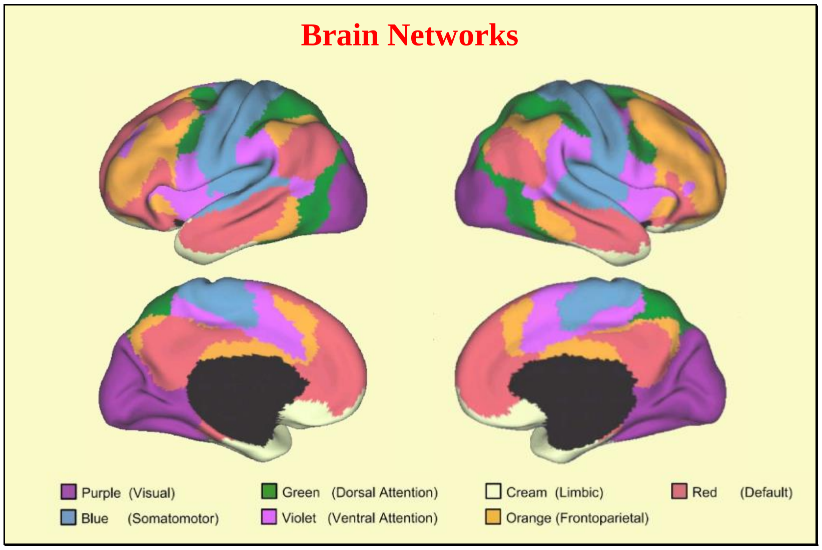
This slide shows some of the manipulations we can apply to a brain image obtained by MRI. Pumping up the brain allows us to see the cortex within the sulci.
By deflating (or increasing the surface curvature) we can accentuate the gyri (green). The brain can then be inflated so that sulci (red) are shown on the surface.



Using these techniques on a large number of brain images obtained during different tasks (listening to sounds, looking at faces, solving problems, etc.) has allowed neuroscientists to identify 180 separate areas in each hemisphere of the brain. Each of these regions participates in a different brain function.

This illustration from a paper by Glasser and colleagues in summer 2016 organizes these areas in relation to the different sensations. the left and middle figures show the inflated brain images for the left and right hemispheres. The upper view is from the side and the lower view shows the medial surface.
The images on the right show the flattened brain (left above, right below) – this is as though he ballooned brain had burst.

The areas are coded by their relation to the main sensory systems. The darker areas show secondary cortices which are active in processing information from these systems. The lighter regions of the cortex represent areas that are more active when the brain is doing nothing (task-negative). The big white area in the medial sections is where the brainstem connects to the cerebrum.

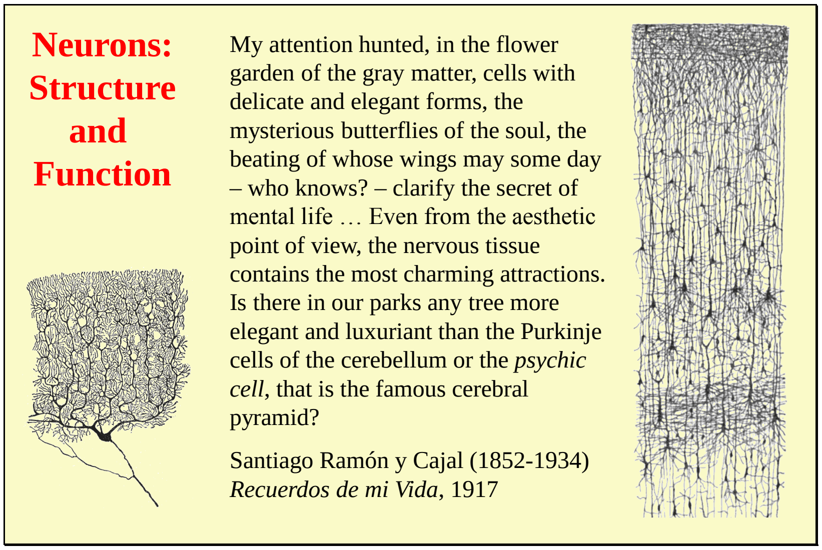


So far we have been dividing the brain up into separate regions.
However, the brain is much more connected than divided.
This recent figure from Yeo et al, 2007 shows the various ways that different areas of the brain work together in 'networks.' It is a little like the paintings of the Tachism movement in France.

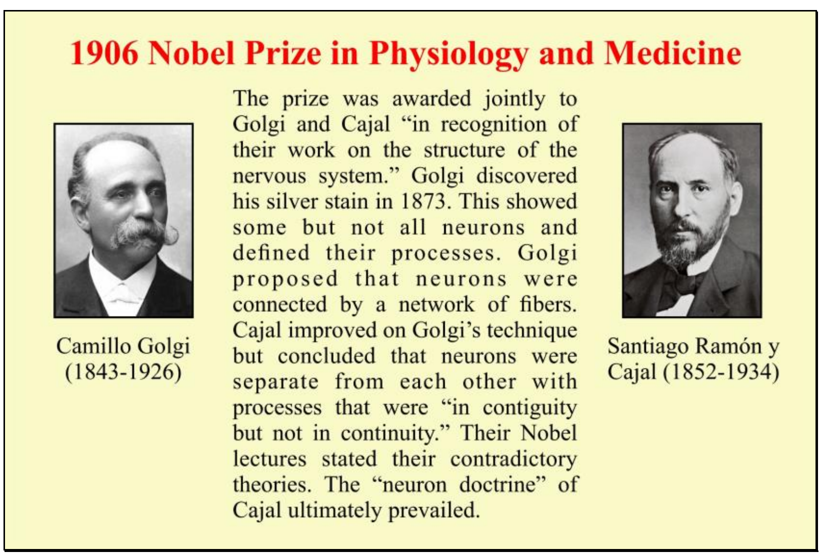
Black shows where the hemispheres are connected to the brainstem.

The colored regions represent different "networks"
One major network is mainly related to seeing the world (purple). Another is related to bodily sensation and movement (blue). Others are related to attention.
Some areas of the brain are mainly active when we are "doing nothing." These are connected together in the "default network (red). They are perhaps active in memory, imagination, reverie, etc.

This abstract view of the brain shows function rather than anatomy.
We shall return to these networks in later sessions.



The preceding slides considered the brain in its normal (macro) size. Over the next few slides we shall consider its fine structure as seen through the microscope.
The brain contains neurons and glia. The functions of the brain in terms of information-processing depend mainly on the neurons. The glia provide structural and metabolic support.
The quotation on the slide is from the great Spanish neuro-anatomist Cajal. He made thousands of beautiful drawings of the microscopic anatomy of the brain's neurons – that he lovingly called the "butterflies of the soul." The illustrations are two of his most famous drawings – one of a Purkinje cell in the cerebellum, and the other of the pyramidal cells in the cerebral cortex.



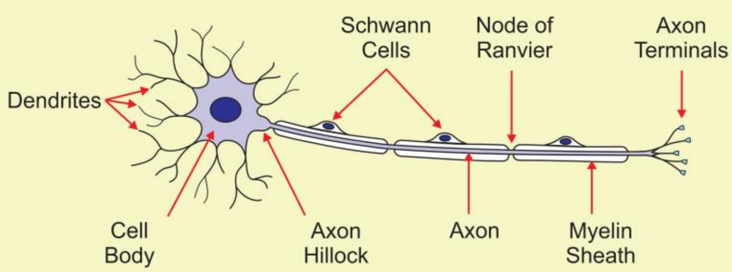
In order to see the neurons, Cajal used a silver stain invented by the Italian anatomist Golgi. The stain is intriguing since it stains only a small proportion of neurons in a section, but stains them completely so that all their connections become visible. A few individual neurons are shown in exquisite detail whereas the others are invisible.

Golgi and Cajal shared the Noble Prize in Physiology and Medicine in 1906.
In their acceptance speeches, they presented completely different views of the nervous system. They certainly did not win the peace prize ☺
Golgi proposed that the brain was a vast network of connected fibers and that the neurons existed mainly to support and maintain this network. This was the “reticular theory.”
Cajal proposed that the network of fibers was composed of multiple thin extensions of the neurons. Each neuron and its fibrillary extensions was separate from those of other neurons. The neuron was just like any other cell in the sense that it was self-contained. This was the “neuron doctrine.”

Cajal was quite acerbic in his Nobel Lecture:
“True, it would be very convenient and very economical from the point of view of analytical effort if all the nerve centres were made up of a continuous intermediary network between the motor nerves and the sensitive and sensory nerves. Unfortunately, nature seems unaware of our intellectual need for convenience and unity, and very often takes delight in complication and diversity.”

Over the ensuing years it became clear that Cajal was right. Neurons are self-contained, but make multiple contacts with each other through “synapses.” These junctions were postulated by Sherrington, could not be directly observed until electron microscopy. Nevertheless neurons do work together as functional networks. These networks are composed of separate neurons that interact with each other.

Typical Neuron



The dendrites receive information from other neurons. This input is integrated. If a threshold is reached, excitation occurs at the axon hillock and an electrical impulse travels along the axon. The myelin sheath increases the speed of the impulse. At the axon terminals information is transferred to another neuron or to a muscle.

This shows the main parts of a neuron. The neuron used in this example is an alpha motor neuron that sends its axon out of the spinal cord to terminate in a muscle. This neuron makes the muscle contract.

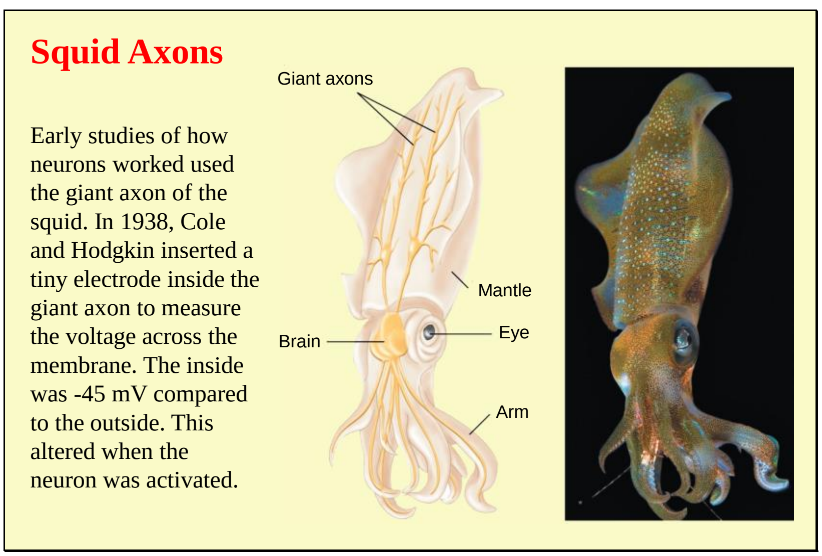
The flow of information in a neuron is from dendrite to axon. Dendrites receive and axons transmit information: D R A T

The neuron maintains an electrical potential over its membrane. The inside is negative relative to the outside. This is called polarization.
The neuron is excitable – it generates an action potential when it is activated. It conducts this action potential down the axon. At the synapse it transmits excitation or inhibition to another neuron through a synapse or to a muscle through the neuromuscular junction.

Four steps: polarization, excitation, conduction, transmission.

The axon hillock is the location where an electrical impulse is generated.
This axon is wrapped in a myelin sheath that is formed by Schwann cells. (If the neuron were in the central nervous system the myelin sheath would be made by oligodendroglia.) Myelin is white – thus the regions of the brain where there are mainly fibers are white whereas the regions where there are mainly cell-bodies are grey. You can remember this from Hercule Poirot who exercised the “little gray cells” of his cerebral cortex.

The nodes of Ranvier are spaces between the areas covered by myelin – these are locations where the electrical impulse travelling down the axon can be regenerated.
The axon of this peripheral nerve fiber terminates in a muscle (at a neuromuscular junction). If the axon were in the central nervous system, it would terminate on another neuron at a synapse.

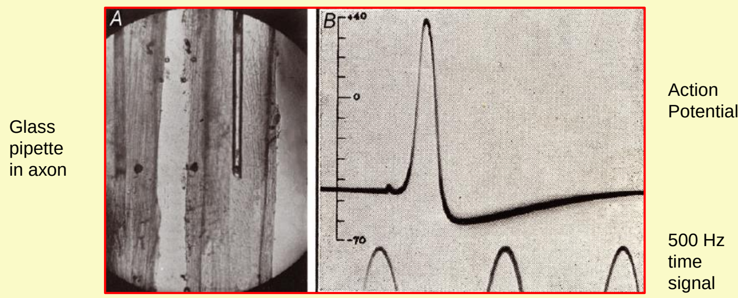


Polarization, excitation, conduction, transmission.
The inside of a neuron is negative – polarization.
The excitability of neurons was first understood in experiments with the squid.
In order to activate the mantle for jet propulsion, the squid has a giant axon. The typical diameter of this axon is about 0.5 mm. Axons with large diameters conduct more rapidly than thin axons.

The two giant axons in the squid activate all the muscle fibers in the squid mantle – their almost synchronous contraction causes rapid jet propulsion as water is squeezed out of the mantle. (Note that even small squids have giant axons – the physiologists did not have to capture a giant squid. ☺)

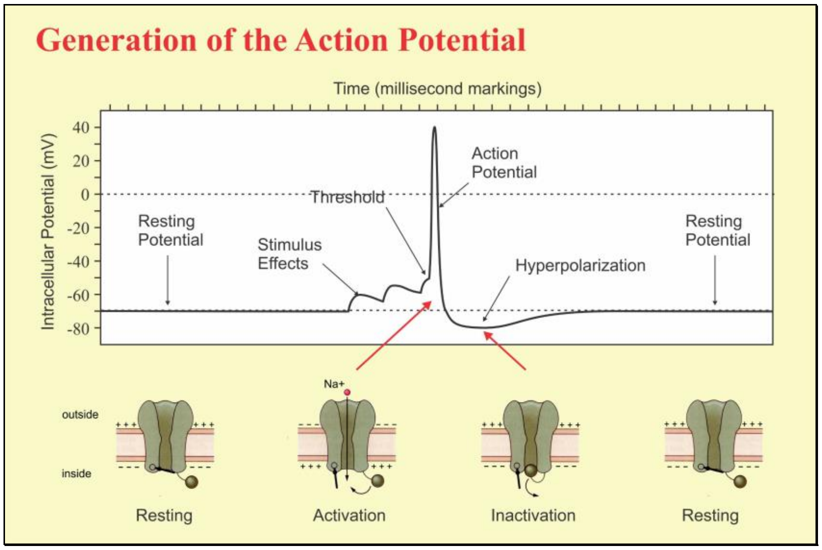
Action Potentials

In 1939, Hodgkin and Huxley found that when the giant axon was activated the nerve potential did not just go away. Rather it "overshot" so that the inside actually became positive rather than negative. In 1952, they demonstrated that this was caused by changes in the membrane's permeability to ions. They received the Nobel Prize in 1963 together with Eccles (who studied the synapse).



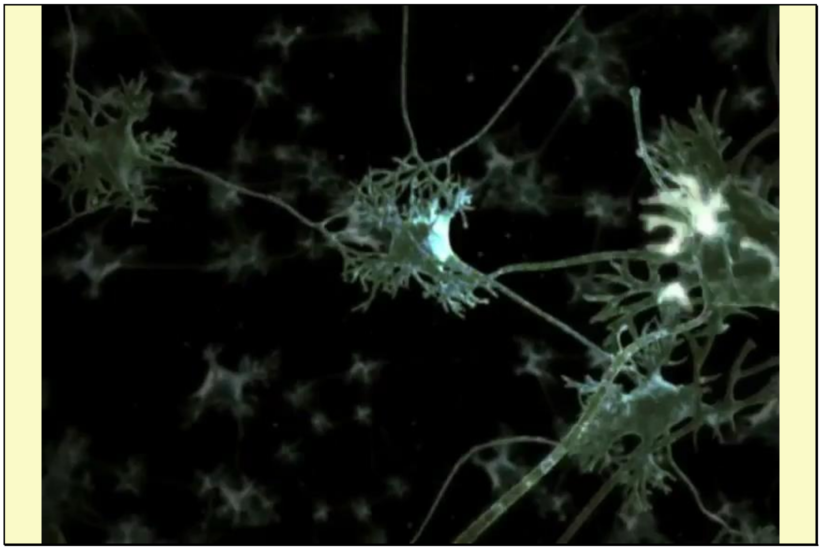
Hodgkin and Huxley were able to place a thin glass pipette within the squid giant axon. The left side of the illustration shows the pipette in the axon – a fancy mirror arrangement allows both top and side views.
The first thing determined about the giant axon was that it was electrically negative on the inside.

Further studies showed that when the axon was activated it reversed the potential across the membrane. This was therefore not just a loss of the resting potential but rather an active process of ion-exchange.
Alan Hodgkin had worked on radar during WWII. Andrew Huxley came from a very famous family – he was the grandson of Thomas Huxley, the tenacious supporter of Darwin ("Darwin's bulldog"), and the half-brother of Aldous Huxley who wrote *Brave New World*.

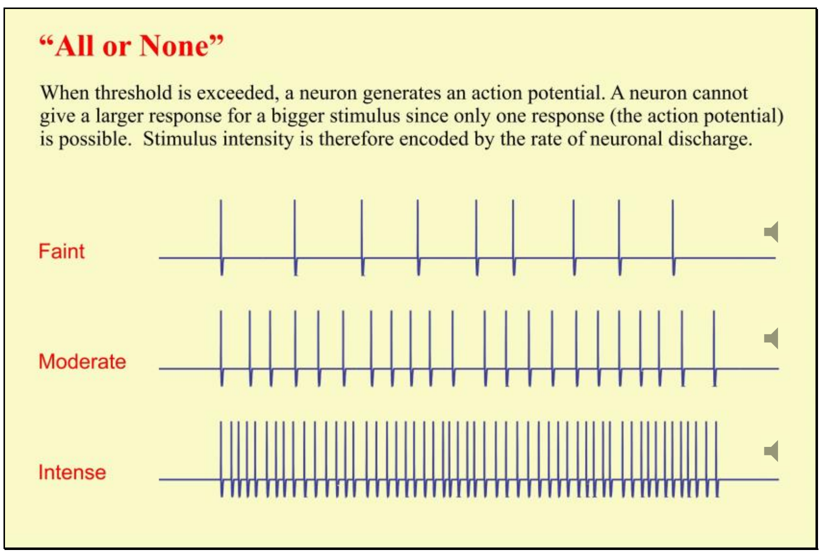


If we make electrical measurements during the excitation process this is what we record. We are recording from inside the cell. At rest this is negative relative to the outside.
As the neuron is stimulated, it reaches a threshold level and an action potential is generated..
The bottom of the slide shows how this happens. A sodium channel in the membrane opens
When threshold is reached the channel reconfigures itself to let sodium ions pour into the cell.
The membrane potential goes away – depolarization. It even briefly becomes positive on the inside.
Inactivation occurs and the neuron is no longer permeable to sodium ions. Then special ion pumps remove all the excess sodium that entered the cell and then some – causing the membrane to become briefly even more negative on the inside – hyperpolarized.
The hyperpolarization lasts for several milliseconds. Because it requires a greater stimulus to overcome the hyperpolarization, it is difficult for the neuron to fire more rapidly than several hundred times a second,

I have just shown the changes that occur in the voltage-dependent sodium channel when an action potential is generated. The actual changes in the membrane during the action potential are more complex. Other ion-channels are also affected. Each changes according to a slightly different time course.
Life is always more complicated than teacher lets on ☺



This animation showing the conduction of the nerve impulse is from *The Human Brain Book* by Carter. Ions flood into the axon to cause the action potential.



The action potential either occurs or it does not – it is "all or none." This characteristic of the neuronal response was discovered by Edgar Adrian just before the first World War. Adrian shared the Nobel Prize with Sherrington in 1932.
The neuron therefore cannot give a bigger action potential for a bigger stimulus.
The only way to indicate that a stimulus is more intense is for the neuron to fire more rapidly: 10/s 25/s 65/s
What happens is that an intense stimulus causes sufficient ongoing depolarization to overcome the hyperpolarization that follows an action potential.

Neurophysiologists often listen to their recordings – that way they can quickly hear how rapidly the neuron is responding.

Note that all neurons behave this way. A neuron coming from the eye will generate a series of action potentials when stimulated by light. The brighter the light the faster the rate of discharge. A neuron coming from the ear will have the same kinds of discharges. The louder the sound the faster the discharges.

The central nervous system knows what type of stimulus it is from where it is coming from – the "labelled line." This idea was different from the old "doctrine of specific nerve energies" which proposed that each perceptual system used a specific type of energy. The new understanding was that the nature of perception is defined by the pathway over which the sensory information is carried. The information was always carried in the same electrical way.
The brain knows
what the stimulus is by which neurons are active – "labelled line"
how intense the stimulus is by the frequency of discharge – "rate coding."

Synapses and Neural Networks

…we are led to think that the tip of a twig of the [axon's] arborescence is not continuous with but merely in contact with the substance of the dendrite or cell body on which it impinges. Such a connection of one nerve cell with another might be called a *synapsis*.

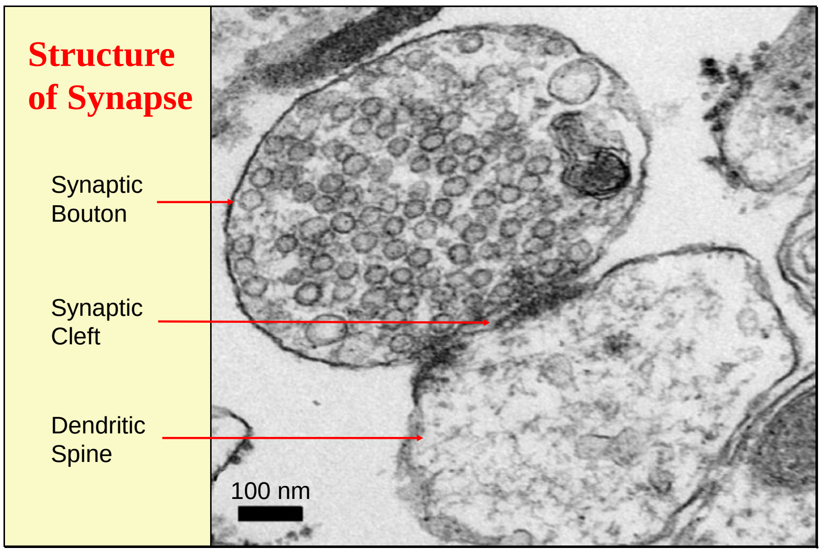
Charles Scott Sherrington in Michael Foster's *Textbook of Physiology* (1897)

Graham Johnson, 2005

The essence of the human brain is in its synapses. The synapse is the place where one neuron makes contact with another.
The word "synapse" was first used by Charles Sherrington. The etymology combines "haptein, come in contact, touch" with "syn, together." A poetic neurophysiologist might translate it as "kiss."

A Greek scholar at Cambridge, A. W. Verall, a translator of Euripides, suggested the Greek word for "contact." This fits with the neuron theory which requires that neurons be separate from each other though in contact.

Although proposed in 1897, the synapse was not clearly understood until the early 1950s when neurophysiology showed that the synapses functioned chemically and electron microscopy showed the anatomical structure of the synapse.
There are over 10 trillion synapses in the adult human brain – the brain of an infant has even more.
The pattern of their activity encodes the soul.

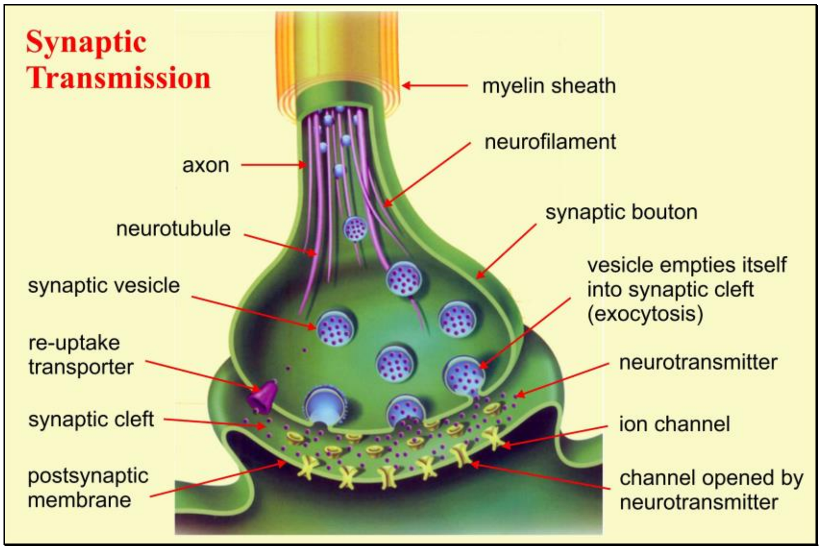


The synapse was not fully visualized until the electron microscope. Using light microscopy anatomists could see structures that suggested the locations where contact occurred – dendritic spines and synaptic boutons, for example. However, Golgi stains seldom showed both of the two neurons involved in a synapse and, when they did, it was difficult to see the synapse clearly.

This electron-microscope slide shows an axonal terminal (synaptic bouton) synapsing on a dendritic spine. Within the bouton are multiple synaptic vesicles containing neurotransmitter and some mitochondria to provide the energy for synaptic function.

Between the axonal terminal and the spine there is a small space – the synaptic cleft.

The postsynaptic membrane is fuzzy – it contains special receptors and enzymes to respond to the neurotransmitter released at the presynaptic membrane.



This diagram shows what occurs when a synapse is activated. The action potential is conducted down the myelinated axon and arrives at the synaptic bouton

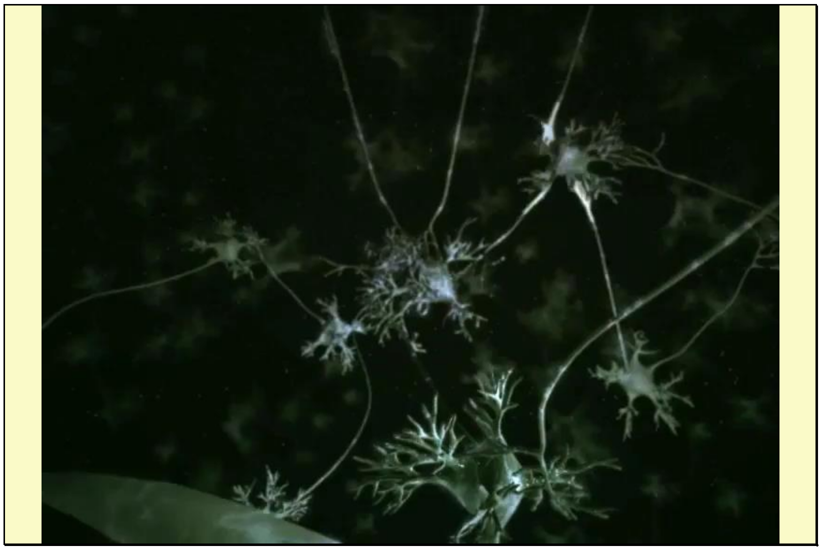
The action potential causes release of neurotransmitter from the synaptic vesicle into the synaptic cleft

The neurotransmitter binds with specific receptors on the postsynaptic membrane.

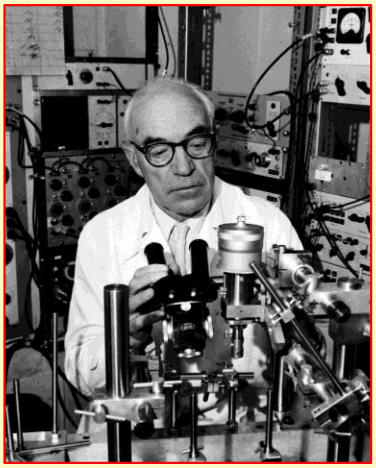
This opens ion channels. Depending upon which channel is opened the postsynaptic membrane potential may increase or decrease.

The effect of the transmitter is brief – usually lasting between several milliseconds and several tens of milliseconds.

The neurotransmitter is then either broken down or taken back up into synaptic bouton by re-uptake transporters.



This movie is from Carter *The Human Brain Book* shows the action potential coming to the synapse and releasing neurotransmitters.



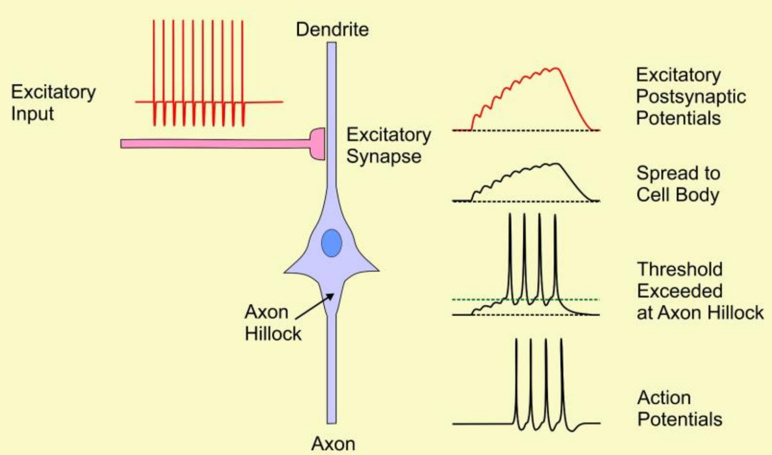
John Eccles (1903-1997)

John Eccles was born in Australia. Though trained in clinical medicine he became more interested in basic neurophysiology. He was awarded a Rhodes scholarship to study with C. S. Sherrington at Oxford. Though he initially thought that the synapse was electrical, his experiments showed that is was chemical. He was the first to record excitatory and inhibitory post-synaptic potentials. He shared the Nobel Prize with Hodgkin and Huxley in 1963. In his later life he wrote extensively about the relations between brain and mind.

John Eccles was the scientist who first clearly demonstrated the neurophysiology of synapses. He initially thought that synapses caused direct electrical transmission from one cell to another. However, his experiments showed otherwise.

He was active in the Pontifical Academy of Sciences, and organized for them a famous symposium on the *Brain and Conscious Experience* (1966). A later influential book was *The Self and Its Brain* (1977) with Karl Popper. Philosophy comes easily to those who study the brain.

Synaptic Transmission



This shows what happens electrically at a simple excitatory synapse on the dendrite of a pyramidal neuron in the cerebral cortex.

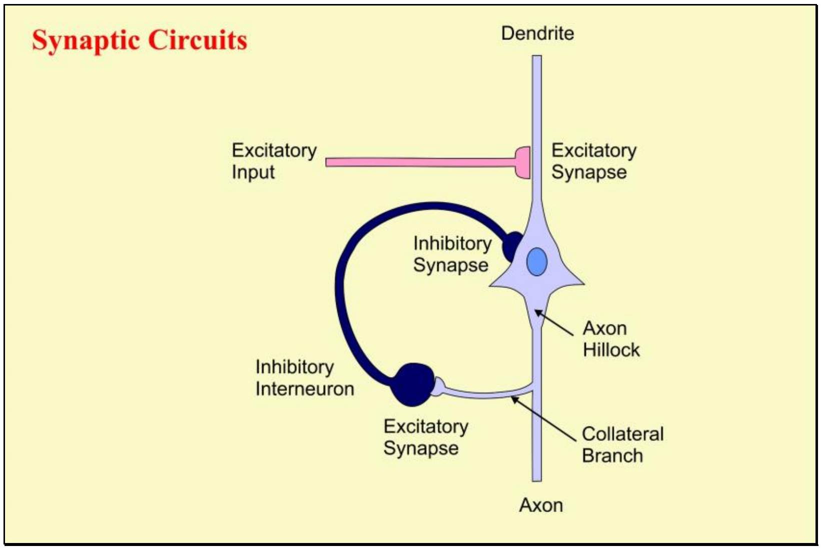
Each arriving action potential releases transmitter from the synaptic bouton.

The multiple transmitter-releases cause a summating excitatory postsynaptic potential.

This spreads to the cell body and then to the axon hillock. There is some decrease in the potentials with the spread.

The axon hillock contains voltage-dependent sodium channels and if the membrane potential there reaches threshold it generates action potentials.

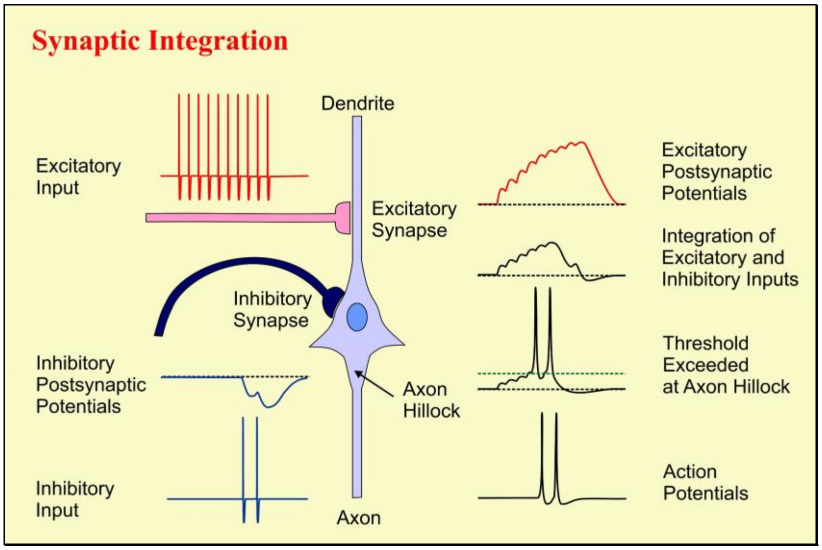
These action potentials are conducted down the axon.
Thus there is a simple transmission of excitation from input to output.



The cortex contains multiple synapses. Some are excitatory; some are inhibitory.

An inhibitory transmitter causes the postsynaptic membrane to become more negative. It does this by opening different ion channels from those opened by the excitatory synapse. For example it may open potassium or chloride channels rather than the sodium channels opened by excitatory transmitters. A more negative potential makes it harder for the neuron to be brought to threshold for excitation.

In this illustration, a collateral branch of the axon leading away from the pyramidal cell excites an inhibitory interneuron that feeds back onto the pyramidal neuron.



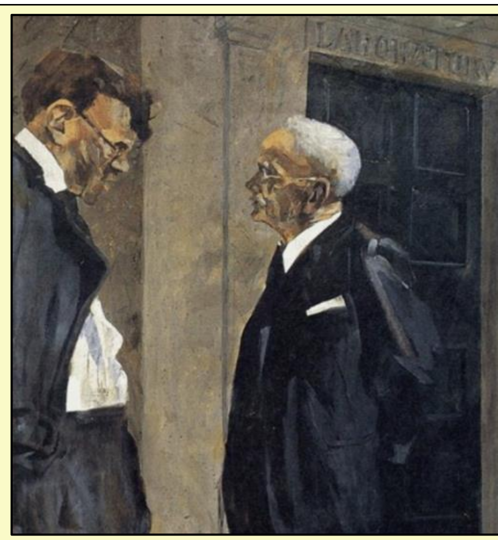
This illustration shows what can be recorded in such a synaptic circuit.
Excitation of the dendrite causes action potentials at the axon hillock.
Axon collaterals then activate inter-neurons that connect back to the pyramidal neuron.
The interneuron causes inhibition at the cell body. This is delayed by the time taken to activate the interneuron and for it to release its inhibitory transmitter.
The result is a cortical cell that responds to the onset of a stimulus but not to its continuation.
The neuron thus integrates all of its inputs – both excitatory and inhibitory in order to “decide” whether to respond of not.

Teacher and Students

Charles Scott Sherrington (Nobel, 1932)

John Carew Eccles (Nobel, 1963)

Other students of Sherrington were Ragnar Granit (Nobel, 1967), Harvey Cushing, and Wilder Penfield



The genealogy of neurosciences has many “family trees.” Eccles who demonstrated the function of synapses studied with Sherrington who first proposed the idea of the synapse.

If I were to trace my family tree, it goes back to Edgar Adrian – the man who gave us the "all or none" law. He trained Hallowell Davis who taught Robert Galambos who supervised my doctoral thesis.

Sensations

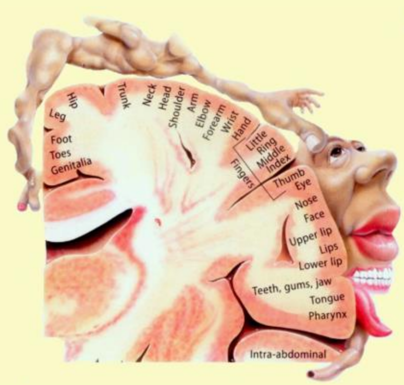
Sherrington classified sensations as
- "exteroceptive" (concerned with the outside world)
- "proprioceptive" (concerned with the position of the body in space)
- "interoceptive" (concerned with internal organs)

Though we are very accurate in the first two types of sensation, we are not generally conscious of our internal organs. They become perceptible when the neuronal activity is intense. The sensations are not well localized and are often painful.

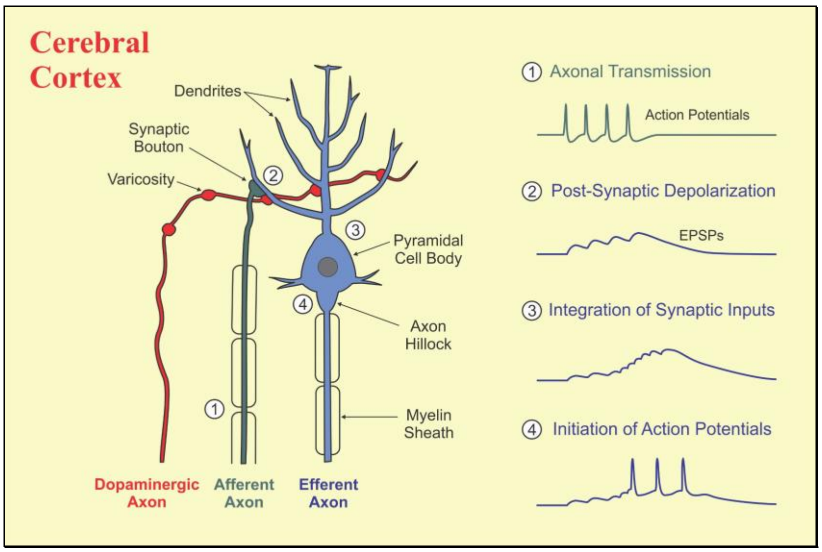
Body sensations are mediated by two different pathways:
- spinothalamic (light touch, pain, temperature, internal organs)
- dorsal columns (fine spatial and temporal discriminations, position)

Exteroceptive sensations are visual, auditory and olfactory.
Somatosensory sensation is proprioceptive (joint-position sense), exteroceptive (actively touching or feeling objects) and interoceptive (e.g., gut sensations – these are not very precise and are often interpreted as painful).
Information about body sensations is carried to the spinal cord along the sensory nerves of the peripheral nervous system. Impulses then travel to the brain along two ascending pathways in the spinal cord

Organization of Somatosensory Cortex



The impulses triggered by somatosensory stimuli travel to the spinal cord and are then conducted to the brain via two different pathways, the spinothalamic tract for pain and temperature and the dorsal columns for fine discriminatory sensations. These fibers come to the brainstem and then project through the thalamus to the somatosensory cortex on the postcentral gyrus. The sensations are arranged topographically with the legs on the medial surface and the face laterally. The area of the cortex devoted to a particular part of the body varies with the sensitivity of the region. Hands and lips occupy far more space on the postcentral gyrus than arms and legs. The distribution of the sensations is often shown in a homunculus (little man) with big hand and big lips.

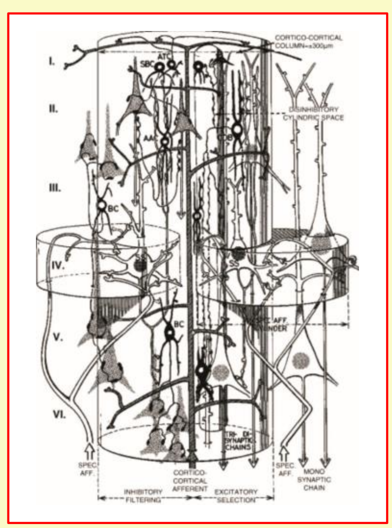


Sensory information arrives at the cortex from the thalamus and synapses on the pyramidal cells. These then respond and send the information on to other parts of the brain. Special neuromodulator systems can alter the response depending on the context. We shall consider these systems in a later session.

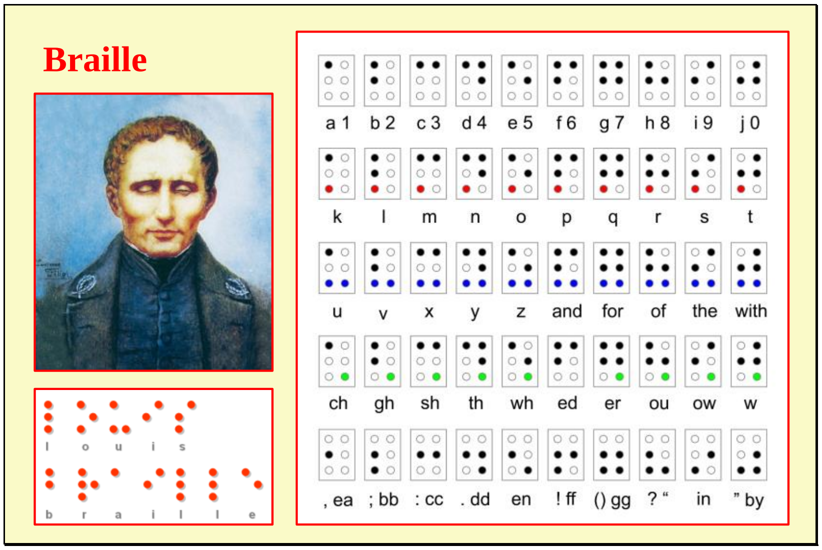
Cortical Columns

The cerebral cortex is organized into multiple overlapping columns. In the somatosensory cortex, each column receives input from a specific region of the body.

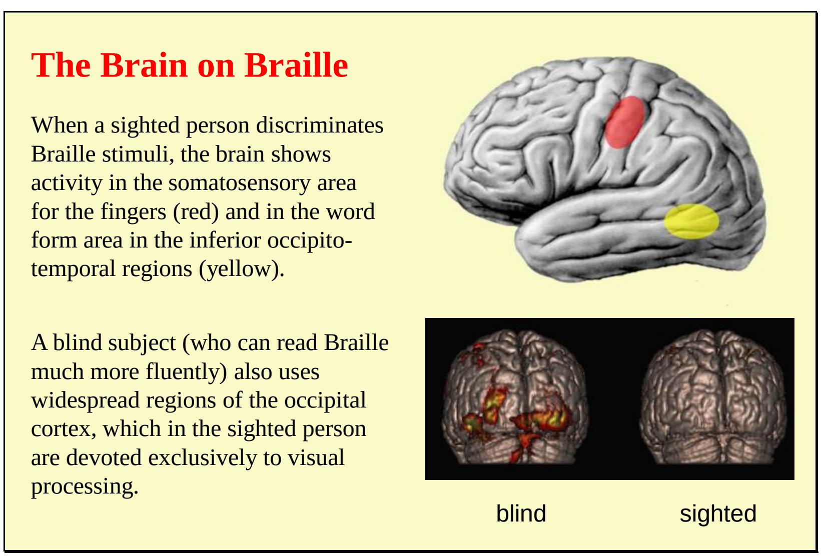
János Szentágothai (1912-1994)



The somatosensory cortex is organized as a set of columns, each dealing with a specific part of the body.
Each column receives input from the thalamus. There are multiple excitatory and inhibitory connections within the column
The diagram is from Szentagothai, a famous Hungarian anatomist.



Blind people can read using a system of tiny palpable bumps arranged in a rectangle.
This was invented by Louis Braille (1809-52) who lost his eyesight at age 3 due to an accident while playing with an awl in his father's workshop.
At the age of 15 he invented his reading system.
The upper two lines are set up in a sequence of ten, and this is enlarged to 40 by the pattern of the lower two bumps.



Normal people process braille in the somatosensory cortex specific to the fingers.
A blind subject also uses areas in the visual cortex to process the somatosensory information.
This is striking evidence of neuroplasticity – cortical regions that normally process visual information become connected to the somatosensory system.

Synapses and Neural Networks

The great topmost sheet of the mass, that where hardly a light had twinkled or moved, becomes now a sparkling field of rhythmic flashing points with trains of traveling sparks hurrying hither and thither. The brain is waking and with it the mind is returning. It is as if the Milky Way entered upon some cosmic dance. Swiftly the head mass becomes an enchanted loom where millions of flashing shuttles weave a dissolving pattern, always a meaningful pattern though never an abiding one; a shifting harmony of subpatterns.

Charles Scott Sherrington (1942)

The quote is from Sherrington’s book *Man on his Nature*. He is describing the activation of the cortex when an animal awakens.
His main metaphor is the “enchanted loom”
The loom weaves its pattern in the synapses of the cerebral cortex.
The video shows a computer model of a cortical column. As the neurons are activated they become brighter.
The movie comes from the Cajal Blue Brain Project, which uses super-computers to model cortical activity.
https://www.youtube.com/watch?v=HN1iX_3CXLY