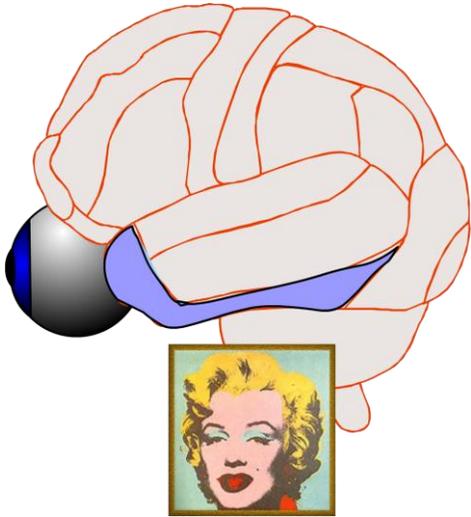


Association Areas and Memory



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The 5 main functional subdivisions of the cerebral cortex

1) The primary sensory areas (visual, somatosensory, and auditory) are the entry points for sensory information into the cerebral cortex.

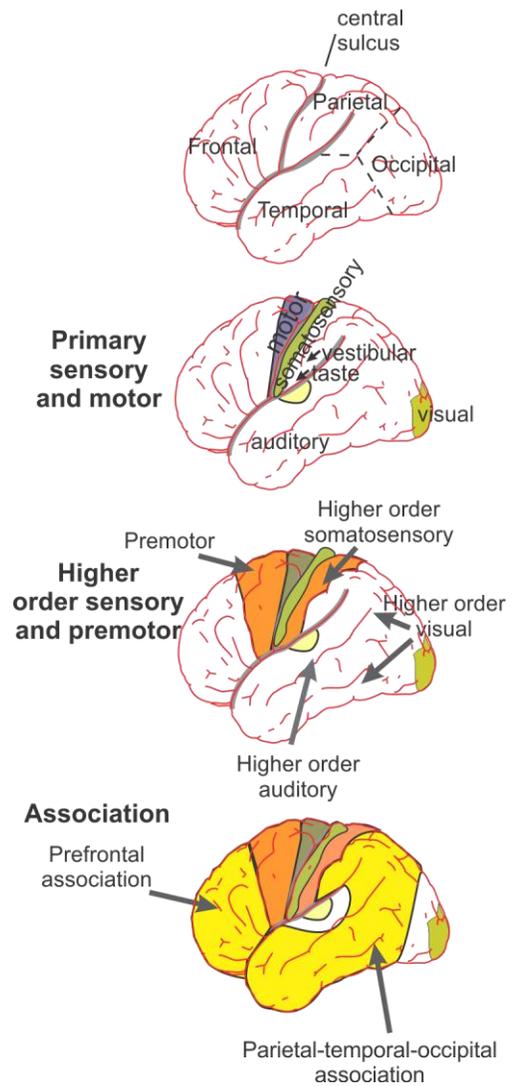
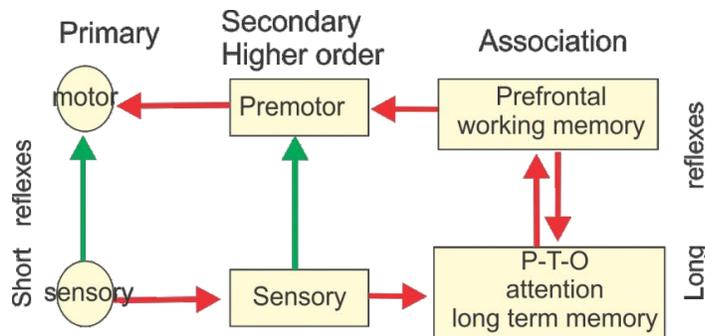
2) Higher order areas (secondary) lie near the respective primary area. This is where sensory information is further processed.

3) Association areas (prefrontal and parietal-temporal-occipital) are where different modalities combine, attention is shifted, planning occurs, and memories are stored. In humans, these occupy about 80% of the cortex.

4) Premotor areas are higher order motor areas that send commands to the primary motor areas.

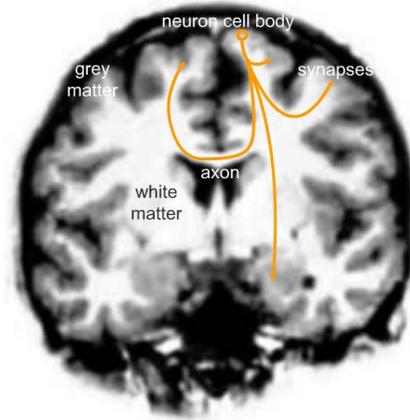
5) Primary motor areas send commands to the muscles. In the rat, primary sensory and motor areas occupy nearly all the cortex.

The connections between primary, secondary and association areas



Gray and white matter

The neurons in all areas of the cortex are confined to a thin sheet called the gray matter located in the brain's surface. The sheet is extensively folded to maximize its surface area within a given volume. Each mature human brain has about 100 billion neurons. Because each neuron connects to 1000 others, a signal from one neuron can, on average, reach any other neuron in the brain in less than 4 connections. These interconnections are, as we will see later, where our memory is.



All adjacent areas of the cortex are extensively interconnected as are selected distant **areas**. The neuron axon's form fiber tracts, several million miles in length, the **white matter** of the cortex.

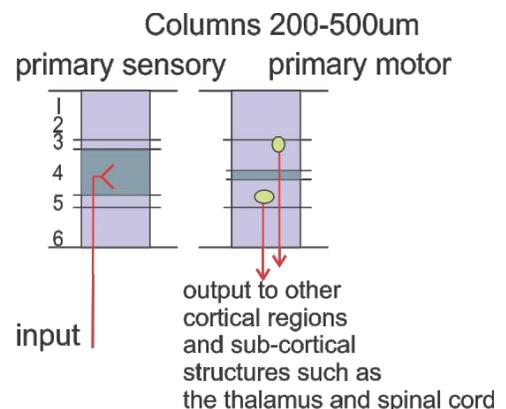
To send action potentials across such a network is metabolically costly. This cost is minimized by activating only a few percent of the neurons at the same time. If more than 5% fired *at once*, your brain would run out of oxygen and you would faint. In spite of this the brain, which is only 1 to 3% of the body mass, uses about 20% of the body's energy.

The grey matter requires more oxygen than white matter. To minimize the total oxygen supplied, blood is directed preferentially to areas of the grey matter that are in use. This is the basis of functional magnetic resonance imaging, **fMRI**, which reveals which areas of the cortex are most active in a particular task. fMRI adds the brain's functioning to the structure imaged by MRI. Diffusion tensor imaging (**DTI**) is another neat new MRI technique that reveals the axons in the patient's brain. This is being used to construct the [Human Connectome](#); all the neural connections in the human brain. Both techniques have exploded in popularity for research and in all likelihood will become a very popular clinically.

The extensive interconnections predispose the cortex to epilepsy. A locus of abnormal activity in one area quickly spreads to other regions, leading to a seizure. During a seizure, the brain can run out oxygen resulting in loss of consciousness.

The input and output layers

Information arrives in layer 4, spreads to more superficial and deeper layers, and is finally integrated by output cells whose bodies are located in layers 3 and 5. Layer 4 receives input from the thalamus and other cortical and sub-cortical regions. It is thickest in primary sensory regions. The striate cortex (primary visual) is so called because of its thick layer 4. Layers 3 and 5 send output to other cortical and sub-cortical regions. These layers are thickest in the primary motor cortex. These and



other anatomical differences allowed K. Brodmann to divide the cortex into 43 areas, more than 100 years ago. Only now are we confirming that each has a unique function and often contains more subdivisions. All have columns.

Functions of the association areas

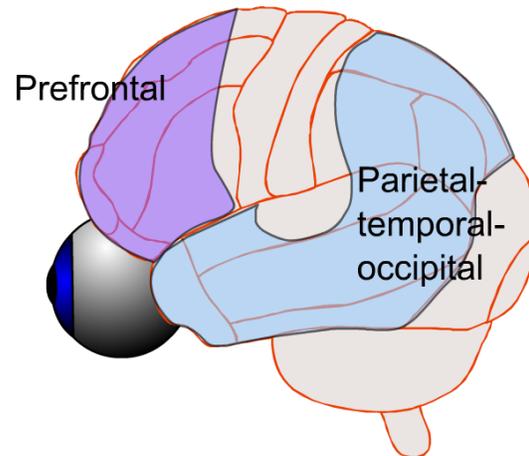
Prefrontal

Planning and working memory

The prefrontal cortex has become larger, as a percentage of total brain size, over the course of evolution. Close your eyes, wait, and then point to a particular object that you remember being in the room. Your ability to remember the location of an object is an example of spatial working memory, a form of short-term memory. Lesions in the prefrontal association cortex produce deficits in motor tasks that are spatial and delayed. Children prior to the age of 1 yr. have not developed this working memory. If a toy is hidden behind one of two covers, the child cannot find it. Out of sight is out of mind.

Decision-making

After lesions of the prefrontal cortex no anger is displayed when the patient makes mistakes. Because this has a calming effect, frontal lobotomies used to be a popular cure for aggression. Unfortunately, it also destroyed the ability to make decisions and to have initiative. Surprisingly neurologist António Egas Moniz won the Nobel Prize for medicine in 1949 for inventing this technique. Later Dr. Walter Freeman perfected lobotomies by using an ice pick hammered through the back of the eye socket into the brain. He performed thousands of lobotomies, each in minutes, from his office. His patients included Rosemary Kennedy, the sister of John F. Kennedy. Most students will correctly find this shocking and will, in 30 years from now, be equally shocked by some treatments they were taught.



Parietal-Temporal-Occipital (PTO)

Functions:

1) **Poli-modal convergence of senses**

Primary sensory areas are activated by a single sensory modality. In the PTO, we find areas activated by more than one modality.

The right PTO specializes in the spatial location of objects by touch, sight, or sound.

The left PTO specializes in language: the sound of words, written words (sight), or Braille (touch).

2) **Attention.** The PTO allows us to focus in on **specific objects** and neglect others. A simple analogy is that of a flashlight that selectively casts light on particular objects. One's capacity to attend to more than one object is limited to 3 to 5 objects.

3) **Memory.** The inferior temporal lobe is involved in long term memory. The right side is more involved with pictorial memory (e.g. faces) and the left side, in verbal memory (e.g. names of people). We will look at memory in detail later in this session.

Neglect

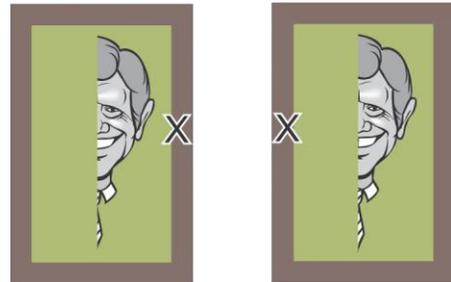
The opposite of attention is neglect.

Talking on your cell phone can cause inattention blindness. Researchers at Western Washington University questioned students who walked past a unicycling clown while they were talking into their cell phones. They were twice as likely of not noticing the clown than those not using cell phones. Inattention causes neglect. This is true whether you are walking, driving a car, or listening to this lecture.

A lesion of the **right parietal cortex** causes neglect of the **left half of objects**. The patient is unaware that one half is gone.

In a right V1 lesion, one is blind to everything to the left of where one's eyes look.

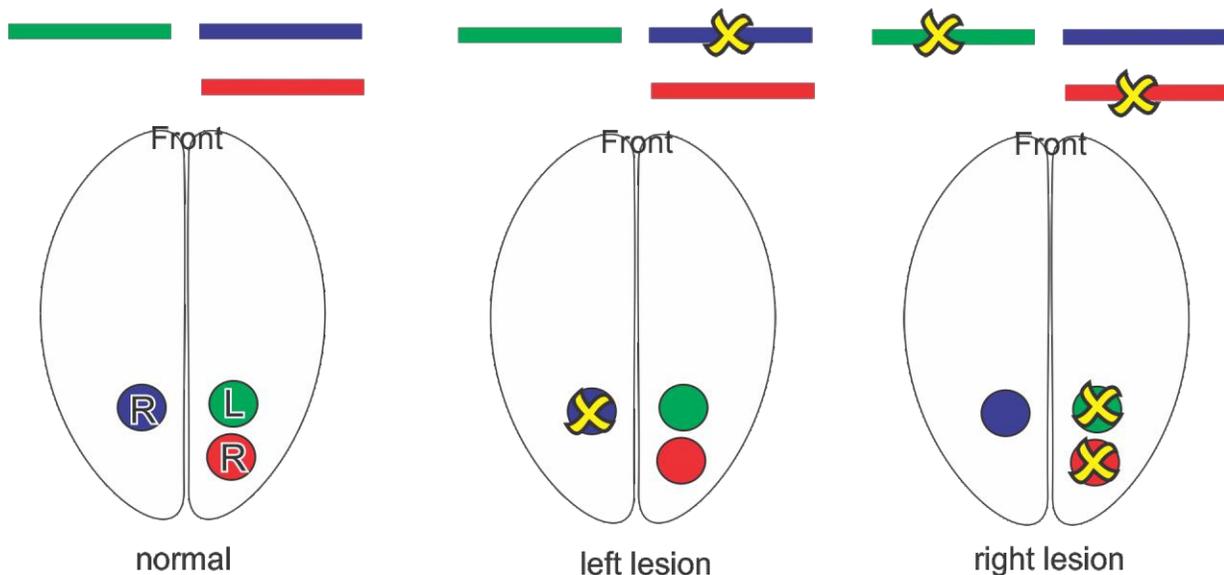
In many right parietal lesions, the left side of the face is neglected independent of whether you look (X) to the right or left of the face.



This is different from the deficit seen after a right V1 lesion. Here the patient is blind to everything to the left of where the eyes look.

You might suppose that a lesion of the left parietal cortex would result in neglect of things on the right. Strangely it does not. Functional imaging shows this is because the right parietal cortex contains a bilateral representation (of things on the left and right) while the left contains only a representation of things on the right.

Thus after a lesion on the left, the right side still attends to things on the right (as well as left). After a lesion on the right, the representation of things on the left is lost.



How and why do the two sides of the cortex differ in function?

a) In what tasks does each hemisphere excel?

Dominant (usually left) - sequential or serial tasks
e.g.: language (reading, writing, speaking, signing), analytic tasks (math $A=B$, $B=C$, therefore $A=C$)

Non-dominant (usually right) - tasks requiring parallel processing
e.g.: spatial tasks, intuitive (C resembles O as I resembles L), geometry, music

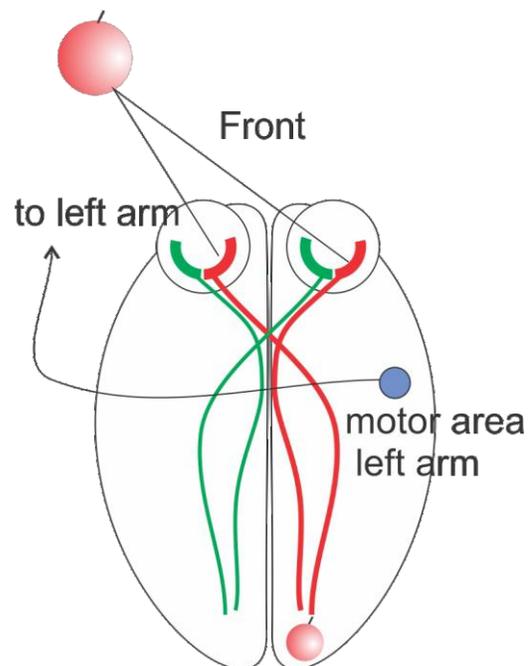
b) Patients with lesion of the corpus callosum

The corpus callosum is the large fiber tract that interconnects the two hemispheres. One extreme treatment for patients with severe epilepsy was to cut the corpus callosum.

When a patient with a sectioned corpus callosum is shown an apple on the left, the patient cannot name the apple because it is not seen by the language center on the left.

The patient can visually recognize an apple and pick it out from a group of other objects with his left arm (the one controlled by the right side of the brain).

Two independent brains can function in one person (e.g. patient would hug his wife with one arm and push her away with the other).



Learning and memory

First some definitions

Memory: information that is stored (e.g. the memory of grandmother) or the structure that stores this information (e.g. the strength of synapses in a particular part of the brain)

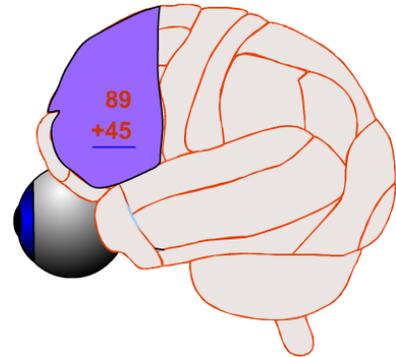
Learning: the storage process, the creation of memories (e.g. what mediates a change in synaptic strength)

Remembering: the retrieval of stored information

Types of memory

Short term / working memory

- A sort of scratch pad which allows for temporary storage of information.
- Example 1: storing numbers when adding
- Example 2: storing words that one reads to form a meaningful sentence
- Example 3: spatial location of objects when you close your eyes and point to remembered objects. It involves the frontal lobe and has a very limited capacity.



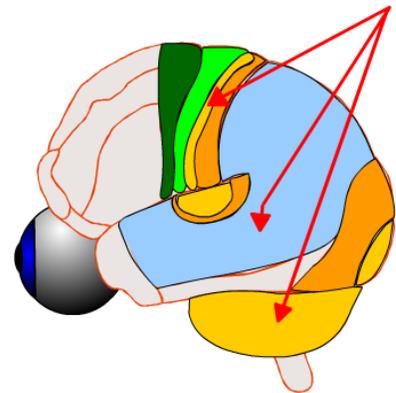
Long term

Two types of long term memory are procedural and declarative.

Procedural (knowing how)

Characteristics:

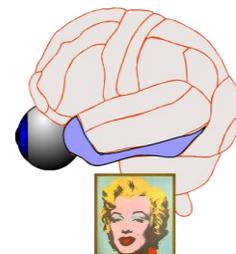
- includes skills such as skiing
- established slowly by practice
- one is not conscious of remembering the skill
- starts to develop at birth
- is not affected in amnesia
- is coded and stored in much of the CNS, for example, the tuning of binocular V1 cells during the critical period for stereopsis and in the cerebellum and motor cortex for motor skills.



Declarative (knowing that)

Characteristics:

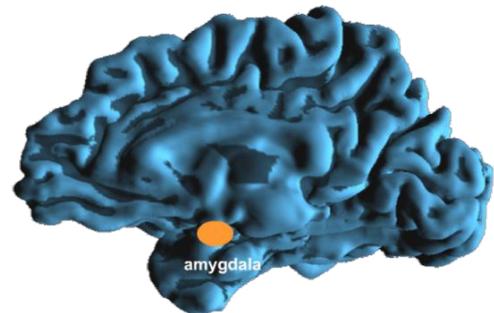
- representations of objects and events e.g. face of a friend
- involves associations e.g. name with face
- often established in one trial
- one is conscious of remembering
- starts only after the age of 2 yrs.
- affected by amnesia
- learning requires the hippocampus in medial part of the inferior temporal lobe.



- memories are stored in all the association areas but in particular in the inferior temporal lobe.
- visual aspects of places are recognized and stored in the parahippocampal place area (PPA) in medial inferior temporal lobe.
- visual aspects of faces, in the fusiform face area (FFA) in more lateral inferior temporal lobe.

The amygdala is also involved face recognition.

When we encounter someone we know two things happen: 1) the conscious **identification** of who that person is and 2) an automatic concurrent ‘glow’ of **familiarity**.



This ‘glow’ can occur without the conscious recognition of the person and is accompanied by autonomic responses such as sweating, (often unconscious). These autonomic responses are the basis of lie detector tests which measure changes in skin conductance caused by sweating.

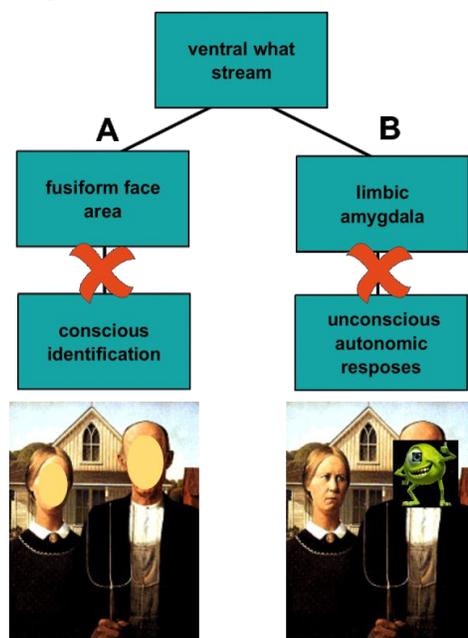
These two aspects of recognition are mediated by two parallel pathways:

- A. the inferior temporal cortex (fusiform face area).
- B. a more rapid activation of the amygdala.

A lesion of A but not B produces the sense of familiarity without being able to identify who that person is (prosopagnosia).

A lesion of B but not A produces the converse. The patient can identify who the person is but has no sense of familiarity. One young man, after a car accident, which affected the path through the amygdala:

1. could recognize his parents
2. but felt that they had been replaced by aliens (i.e. no sense of familiarity)

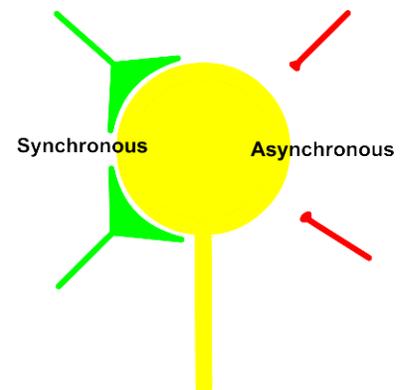


Molecular basis of long term memory

The key in long term learning is the NMDA receptor which opens only when the cell is strongly depolarized.

If two synapses fire at the same time (synchronously) they produce a larger depolarization than if they fire at different times (asynchronously).

Cells that fire together wire together. This is the basis for plasticity or learning throughout the CNS.



Mechanisms of learning procedural memories

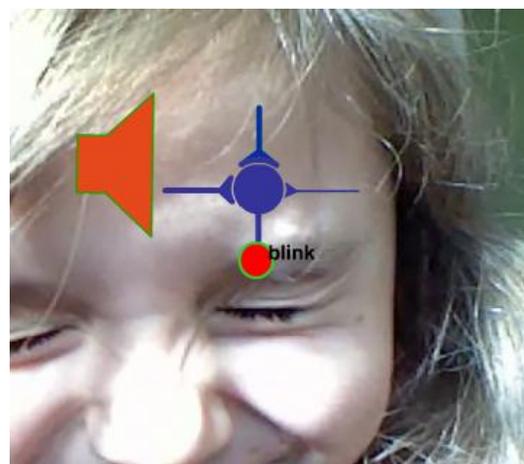
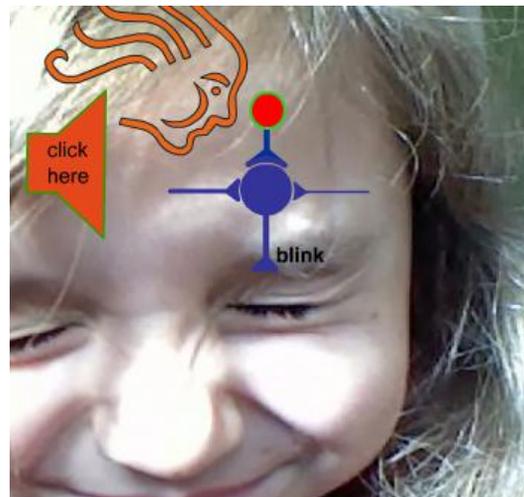
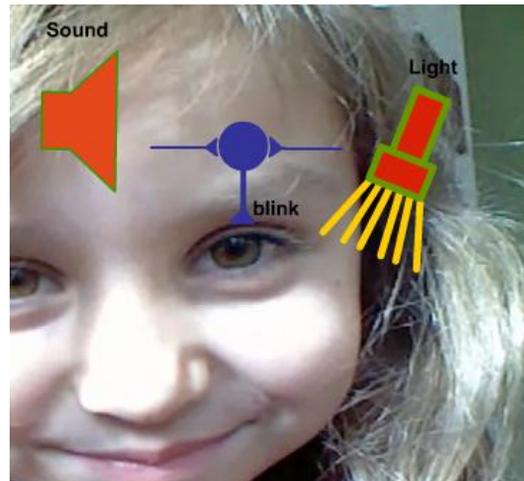
You can be trained to produce blinks in response to a sound by classical conditioning. To be conditioned you must be a naive subject; one that does not blink in response to a flash of light or a sound.

The next thing needed is a good teacher; a stimulus that will always produce a blink. A puff of air is a good teacher. A puff of air, through strong synapses, almost always produces a blink. This is called **classical conditioning**. The puff depolarizes the blink cell and this strengthens the synapse from the paired sound's synapse (on the left). Thus the puff of air teaches sound to produce a blink. A similar strengthening and pruning of synapses is the basis of all forms of long term memories. Trillions of such connections are changed in a similar way throughout one's life.

After conditioning, the synapse from the sound is strong and can produce a blink on its own. That is, the blink becomes associated to sound but not to some other stimulus such as a light.

Conditioning also involves pruning of connections. While connections from sounds are strengthened, those from light are weakened. A similar strengthening and pruning of synapses is the basis of all forms of long-term memories. Trillions of such connections are changed in a similar way throughout one's life in other parts of the brain.

This particular type of procedural memory involves the cerebellum. A lesion of the cerebellum eliminates the learnt blink to a sound. Such a lesion would also disrupt many other procedural memories such as those of skiing and bike riding.



Encoding long term declarative memories

The ventral stream

- 1) extracts the visual features which form an object,
- 2) encodes the form of these objects, and
- 3) stores it temporarily in working memory in the frontal lobe.

lobe.

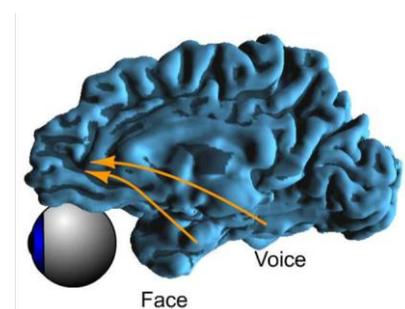
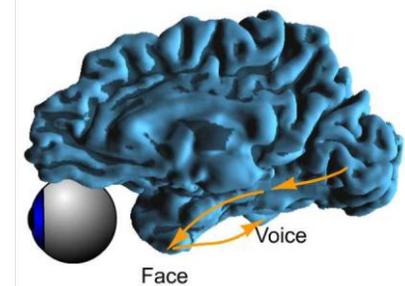
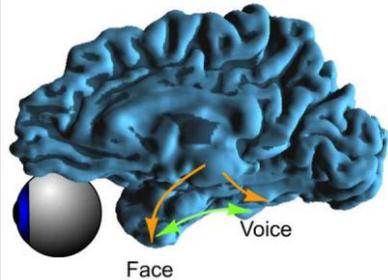
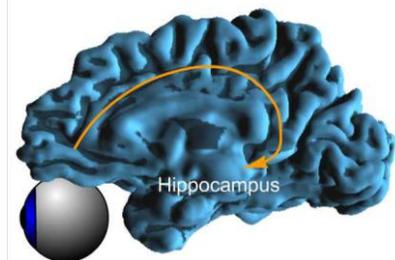
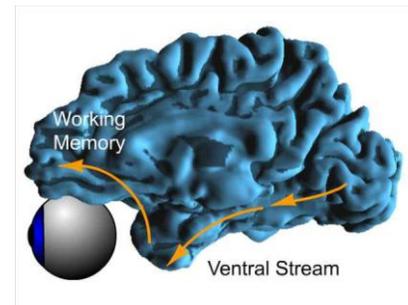
Consolidation of short term working memory into long-term declarative memory involves the hippocampus. Unlike procedural long-term memory which requires repetitive practice, declarative memory often requires only a single exposure. This is because the hippocampus is an excellent teacher. The hippocampus is located in the medial part of the inferior temporal lobe. It is a unique part of the cortex. Unlike other cortical areas, it continuously generates new neurons.

The hippocampus is well connected: an important attribute of a good teacher. It receives input from all the association areas and sends signals back to them as well as others thus creating new associations. The hippocampus associates the current features of the perceived object with other older memories related to the same object. The activation somehow binds together/associates various feature combinations into a rich multi modal memory. The memory of your grandmother's face is associated with the sound of her voice and a multitude of related memories.

This long-term memory requires changes in the structure of synapses. These structural changes involve the expression of genes and the synthesis of proteins.

Once this long term memory is formed, seeing the same object, e.g. grandmother's face, will activate the same associations directly, without the need of activating the hippocampus.

Remembering involves transferring these long term memories in temporal lobe association areas back to working memory in the frontal lobe by a process that is still poorly understood.



Brenda Milner's famous patient H.M.

H.M. had epilepsy resulting from a bicycle accident as a youth. To relieve this epilepsy, H. M.'s medial temporal lobe and hippocampus were removed bilaterally.

This had an unexpected effect on one type of memory.

What was not affected

Working: e.g. remembers names for as long as not distracted.

Old Procedural: e.g. language normal.

New Procedural: e.g. can learn new sports.

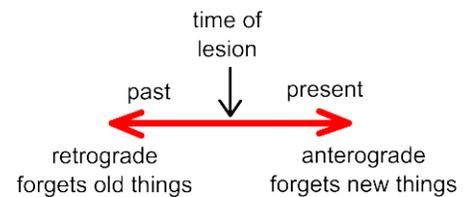
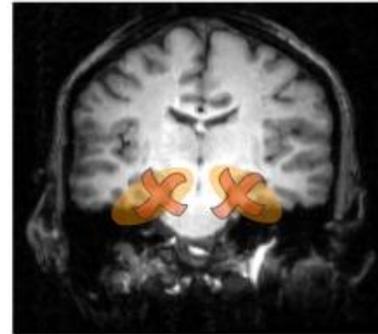
Old Declarative: e.g. recognises his mother.

What was affected

New Declarative: e.g. cannot remember new acquaintances.

The lesion of the hippocampus produced anterograde amnesia.

H.M. died in 2008 at the age of 82. Remarkably, late in life, he had trouble recognising himself in a mirror. His memory of himself was as he was at the time of surgery when he was 27. He was also unable to remember the contribution he made to our understanding of memory.



Practice problems

1. Deficits in delayed-spatial-response tasks (e.g. remembering for a brief time under which of 3 cups the egg is) are most likely to be associated with lesions in the
 - a) prefrontal association cortex.
 - b) posterior parietal cortex.
 - c) parietal-temporal-occipital association cortex.
 - d) occipital cortex.
 - e) temporal lobe.

2. A patient with a bilateral lesion of the medial temporal lobe and hippocampus cannot
 - a) calculate the sum of three numbers.
 - b) read books.
 - c) recognise a new acquaintance.
 - d) remember how to ride a bike.
 - e) write letters.

Answers

1. a)
2. c)

See also <http://www.tutis.ca/NeuroMD/L3AssMem/AssMemProb.swf>