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Learning and Physiology: An Intricate Interaction

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Presented by:

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2006 Lindback Award Winner

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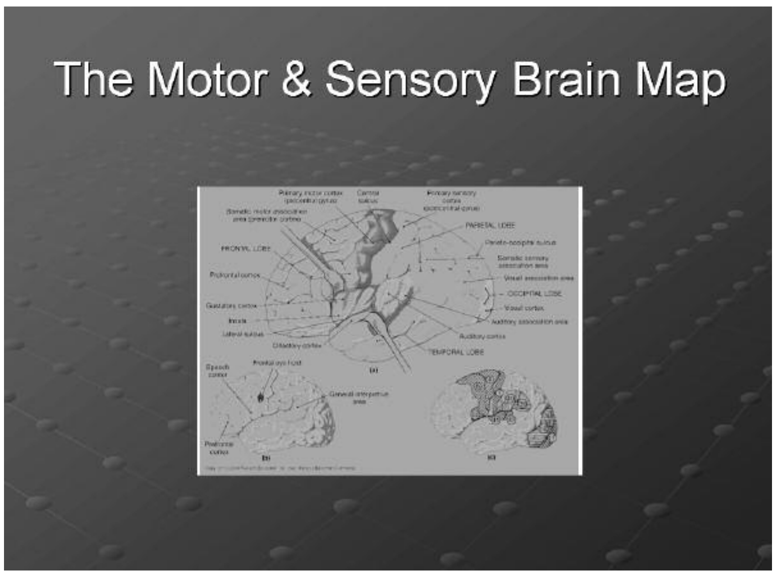
In 2003, Community College of Philadelphia inaugurated the annual Lindback lecture, which is given by the recipient of the previous year's Lindback award. The Lindback lecture provides an opportunity for the entire academic community to draw on the teaching mastery and scholarship of the Lindback awardee. This publication serves to memorialize this lecture.

As I contemplated what to present at this lecture, suggestions flowed in from my colleagues in multiple departments. Marcia Epstein, with a steady voice and guiding hand, nudged me along to my title. Mary Anne Celenza and I had some fairly esoteric discussions on the current research in memory and learning. After some soul searching, I decided to explore the currently accepted content on how the brain structurally and functionally creates memory. The information base on the physiology or function of the brain has expanded rapidly within the last 10 years. The research has moved from theory based in animal models and human disease analysis to normal subjects. I will then discuss how my teaching practices have been framed by this work.

Knowledge of specific areas of function in the cerebral cortex has been known since the 1900s. A cytoarchitectonic map was published in 1909 by a German neurologist Dr. Korbinian Brodmann.

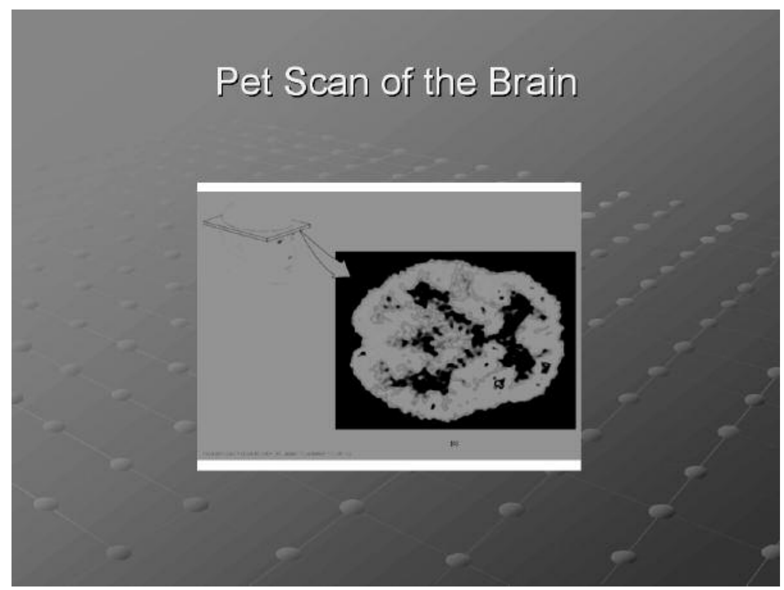


He established a specific numerical system related to patterns of cells in the cerebral cortex. Over time, some of Dr. Brodmann's areas were found to correspond to specific functional cell groups that process and store defined sensory and motor activity.

It is now well known that the components of memory are housed in various areas of the cerebral cortex. For example, the visual information of watching a teacher write on the board is processed at the primary visual cortex in the occiput. Visual interpretation of the words seen by the student is stored in the visual association areas.

The teacher's voice speaking the words is processed at the primary auditory cortex in the temporal lobe. Most specifically, the interpretation of the sound as a word, sensory speech, is processed in Wernicke's area. If processing how to speak the words yourself, motor speech, this occurs in an area called Broca's area. Broca's area is in the inferior frontal lobe near the tip of the temporal lobe. To move the muscles in your face and tongue to form the words, the primary motor cortex at the back of the frontal lobe activates the individual muscles.

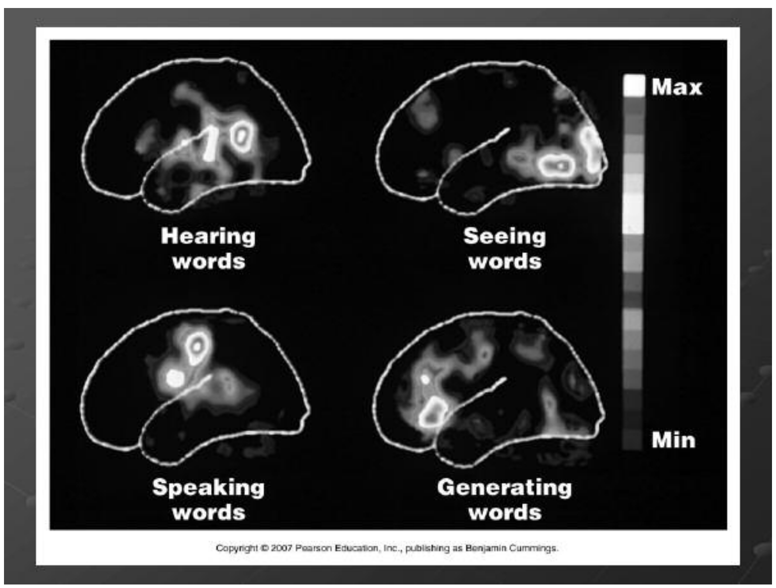
Your brain functions as a parallel processor. The activities of hearing and vision, as described, can be done in these various areas simultaneously in most people. You have no perceptible delay while performing multiple tasks.



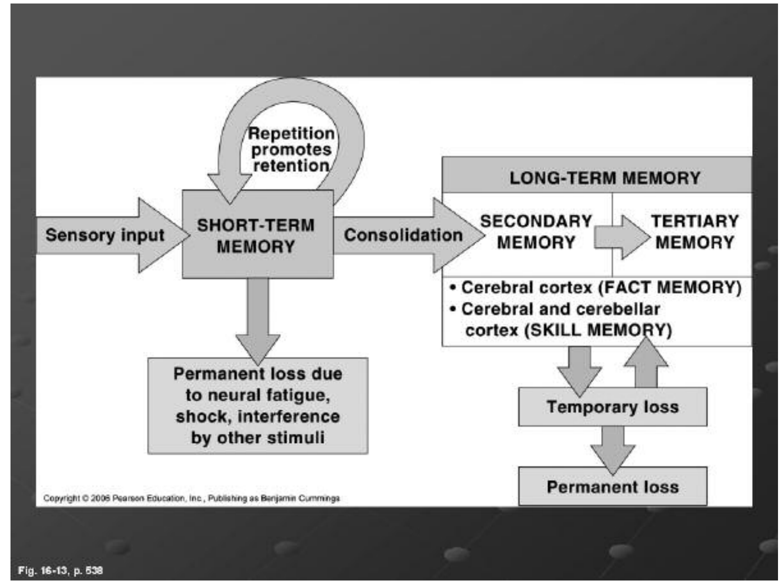
The research exploration of this knowledge involves some of the most notorious and controversial studies found in the history of science. The legality of research on humans forced decades of work to shift to animal models or work based in patients with disease or dysfunction. Only in recent times has radiological studies advanced to allow a look at brain activity or function without harming the study subject.

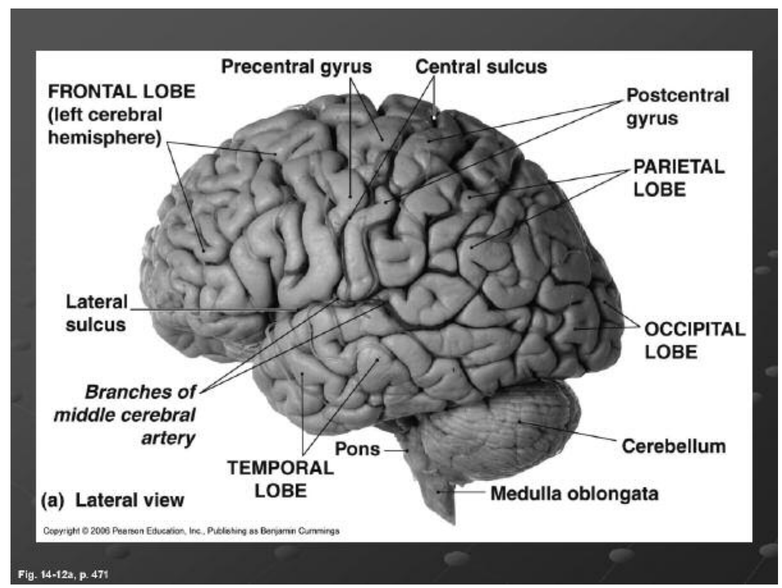
Positron Emission tomography or PET scans have confirmed the accuracy of some of Dr. Brodmann's areas down to the micrometer. The PowerPoint image is showing a PET scan of an alert, awake person. The areas with higher cellular activity are reflecting red. The less active areas reflect green to blue.

Slide 3 (below) shows how the nerve cell activity generated from each of these brain functions causes an increased release of positrons. Positrons, as defined by Webster's Dictionary, are subatomic particles with the same mass and spin as electrons, but have a positive charge. The positron emission is picked up by a monitor, and an image is created that reflects the chemical activity of the nerve cell groups.



Now that we can see where particular types of thought are processed, we still have to explore the basic issues of memory.



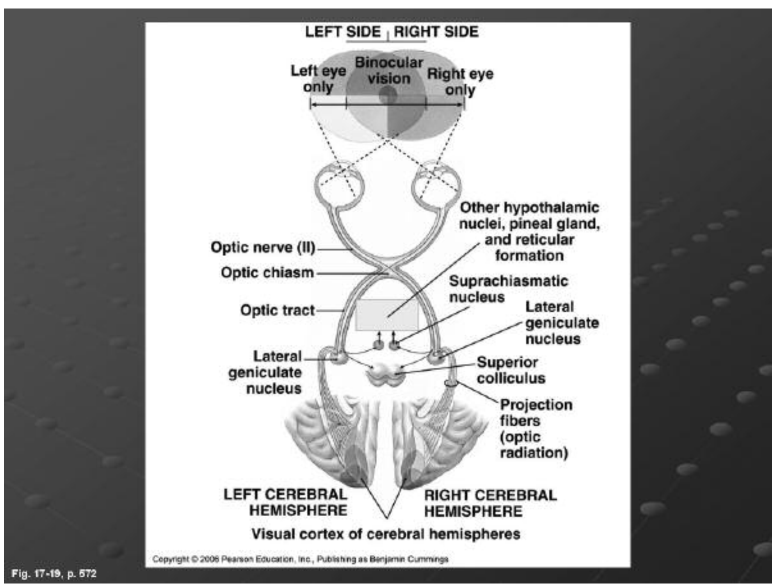


Memory is subdivided into three general categories from a physiological perspective: sensory memory; short-term, sometimes called primary memory; and long-term memory.

Sensory memory is what you are doing when you are scanning or just observing things for the most part. It lasts for fractions of a second and causes very little change in the nerve cell membrane.

If sensory information, information that is seen, heard or felt, is evaluated as important, it will shift into a short-term memory. Short-term memories are converted into an electrical signal by a specific type of receptor. This electrical signal is passed by nerves along a brain pathway to be processed by the appropriate cortical region—vision to the occiput, touched objects to parietal lobe, etc. This memory is only for a limited time—a few seconds to a few minutes maximally and has a limited number of bits of information. Short-term memory can be lost quite easily. Any distraction, like cell phones ringing or the teacher digressing to a new topic, can disrupt the processing of short-term memory, and the information will be lost.

Long-term memory can be categorized several ways. It is usually divided into explicit and implicit memory. Explicit memory

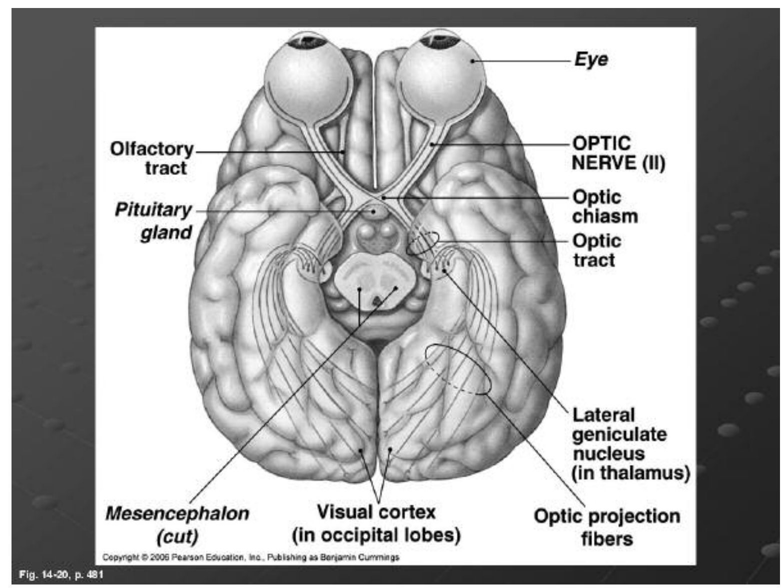


concerns the retention of facts like names, dates and details. Features of the explicit memory are stored in the separate regions of the brain but will require the use of the hippocampus, a memory integration structure, and the amydala, an emotional center of the brain, for future recall.

Procedural or implicit memory involves learned repetitive skills, like dancing, playing the piano or writing letters. This type of memory is stored in the cerebellum, a structure below the cerebral cortex.

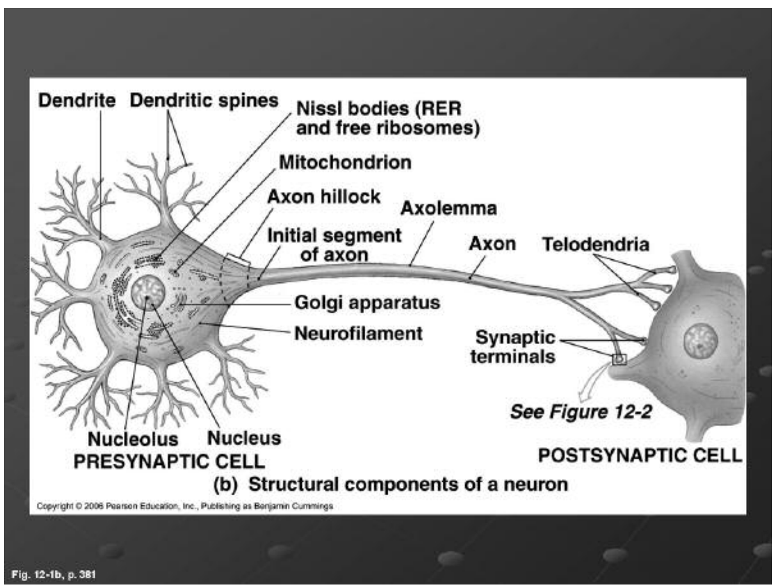
Memory can also be subdivided as secondary memory, a type of memory that fades, or time or tertiary memory, those lifelong memories easily recalled and retained over time. Let us look at the particular pathways used in the classroom.

Visual information travels into the eyes and at the retinas is converted into an electrical signal that is transferred down the optic nerve. Lateral field vision, those things seen at the margins of your vision, is transmitted back on the same side of the brain, but medial field vision crosses to the opposite side of the brain. The information from both eyes is carried into the optic tracts passing

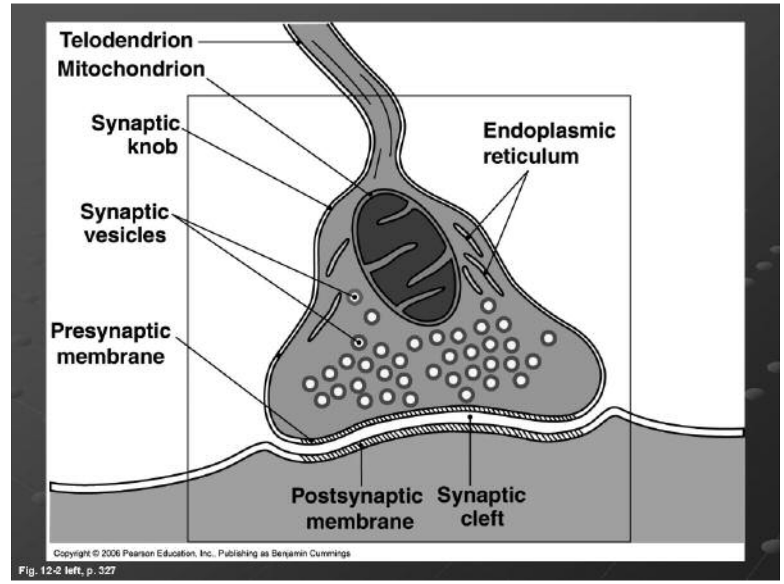


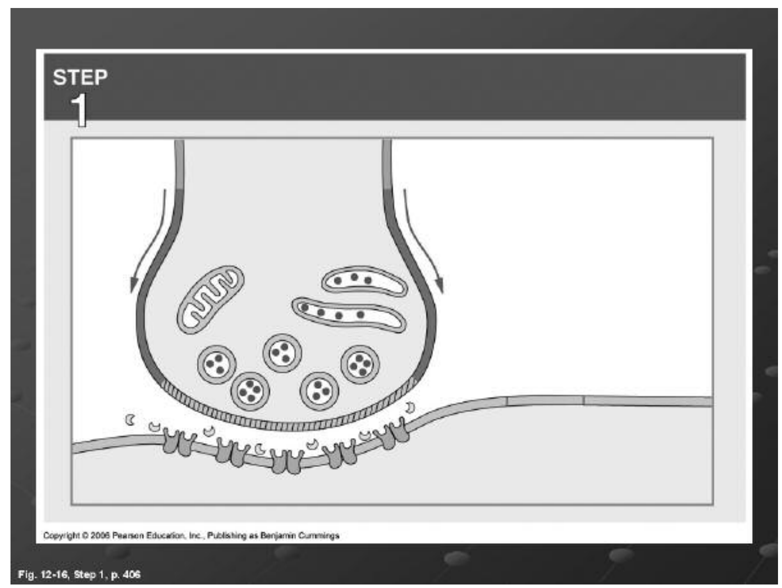
into two relay points. The lateral geniculate is part of the thalamus, a structure responsible for variety of duties that include carrying neurons responsible movement, as well as emotional regulation. The lateral geniculate is a key synapse point for neurons in the visual system. A second neuron set will start here and extend via the optic radiations to the primary visual cortex at the back of the head. Visual information is evaluated and stored here, as well as the nearby visual association areas. The other relay point, the superior colliculus, allows eye movements to adjust to movements in the head.

Long-term memory formation involves structural changes in neurons. This change is called long-term potentiation as defined by Bliss and Lomo in 1973. The chemical messenger glutamate is released from one neuron and travels across the nerve synapse, a space between the cells, to bind on the postsynaptic membrane receptors. This allows for calcium to flow from the synaptic space into the postsynaptic structure, usually another neuron.



Calcium binds to a structural protein called calmodulin inside the cell. This binding reaction turns on an intracellular pathway of chemical reactions, which results in new protein structures being





formed in the neuron. This structural change related to the cell's cytoskeleton has been correlated to memory formation.

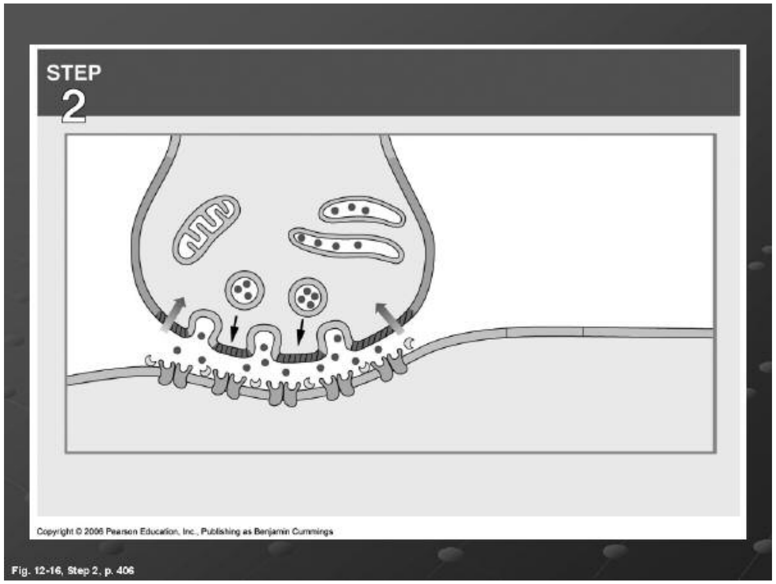


Fig. 12-16, Step 2, p. 406

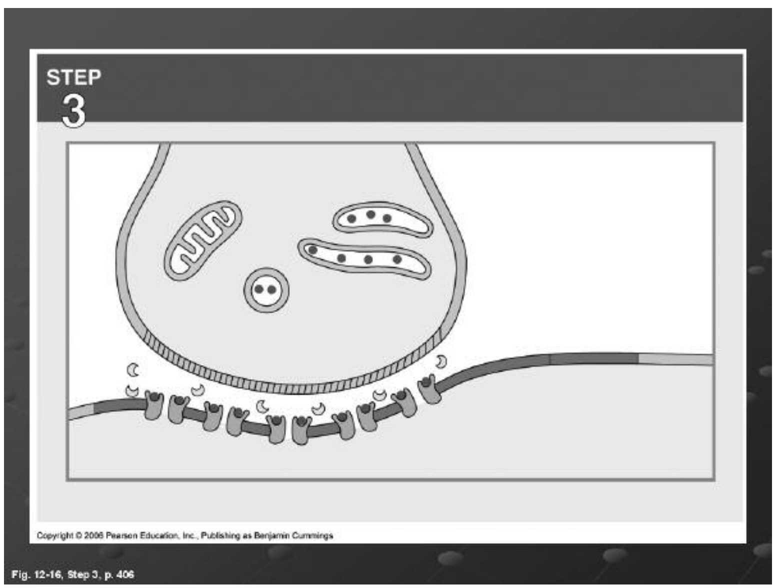


Fig. 12-16, Step 3, p. 406

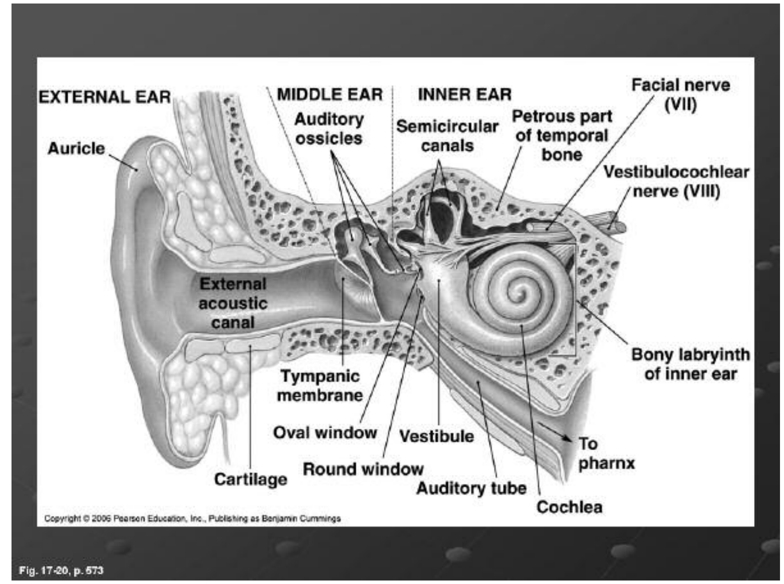


Fig. 17-20, p. 573

The receptor on the postsynaptic membrane has been specifically identified as the NMDA receptor. NMDA, N-methyl D-aspartate, has been found to have an essential role in synaptic plasticity. Synaptic plasticity, or the structural development of new intercellular connections, implies that memory function will increase the number of connections or synapses between nerve cells. This facilitates the transmission of electrical signals.

To shift this to less technical terms, the memory becomes more defined and easier to recall, and the pathways used to create the memory work more efficiently because they have better connections.

The NMDA receptors have some structural subtypes. They involve two amino acid-based neurotransmitters, glycine and glutamate, that can turn on the receptor's function. The different subtypes or variants of NMDA are present at different percentages depending on your age. This discovery was published by Drs. Liu and Murray in 2004. It is currently not clear if these NMDA receptor's variants are linked to why it's easier to learn some types of things when younger in age, but this receptor's discovery builds the case.

In research on hearing, Norman Weinberger has worked on issues of learning and memory for much of his career at the University of California, Irvine. Dr. Weinberger has found that there is a receptive field for acoustic frequency.

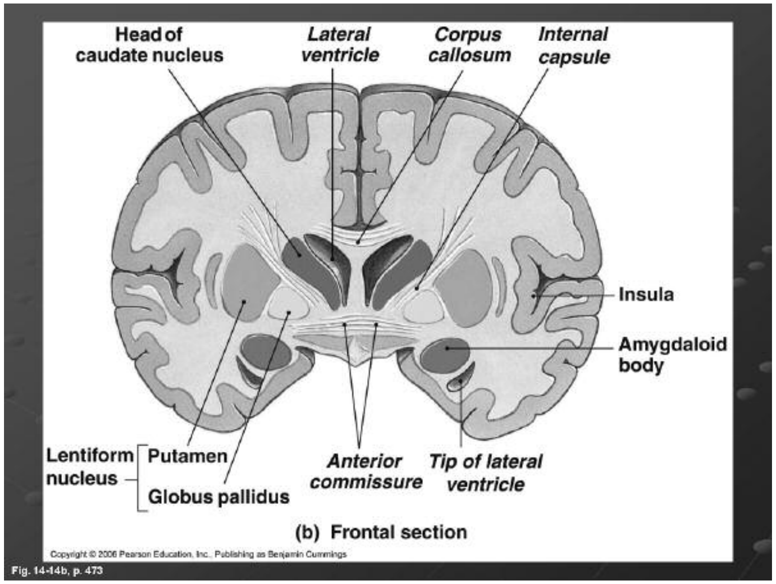


Fig. 14-14b, p. 473

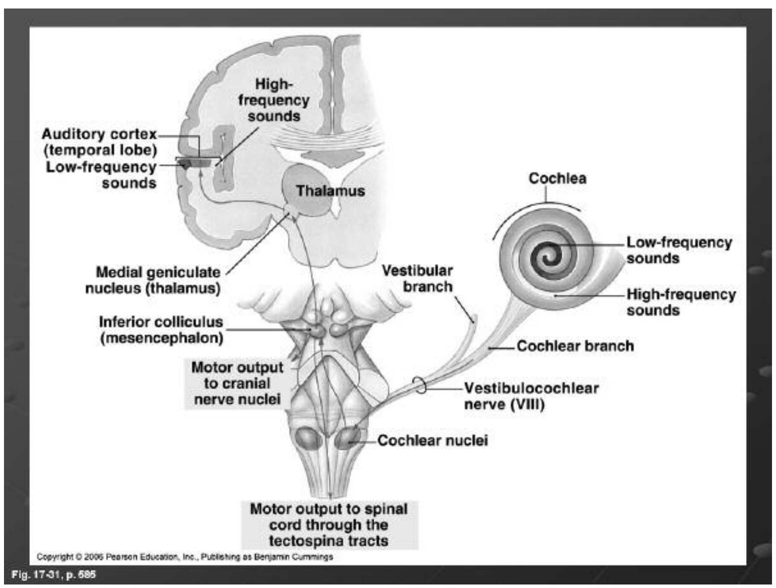


Fig. 17-31, p. 585

The appropriate frequencies can generate permanent changes in the cells found in the primary auditory cortex. This receptive field plasticity seems to be dependant on a different neurotransmitter than glutamate. It's called acetylcholine. Acetylcholine's actions in an area of the brain called nucleus basalis seem to cause a "store now" signal. Discrimination of something important, a "selective attention," is possible. The nucleus basalis has been traditionally cited as a motor control area involving muscular activities. How it

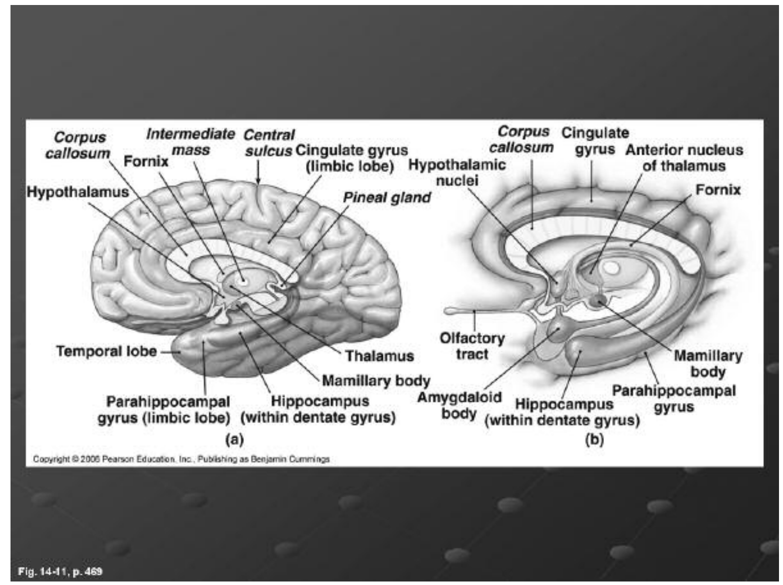
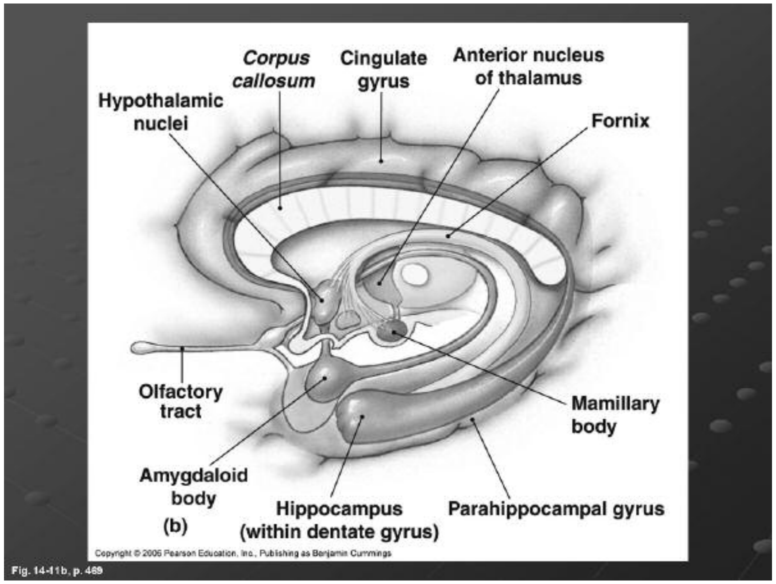


Fig. 14-11, p. 469

is involved with the sensory activity of hearing is still unclear. I have included the pathway used for hearing so you can see how auditory information travels to its primary brain processing area in the temporal lobe.

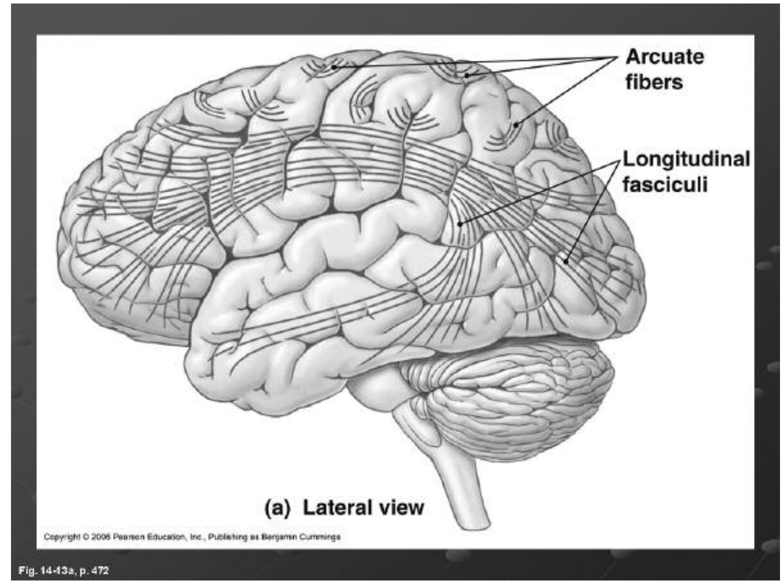
Dr. Weinberger and Dr. Joe Tsien have advanced the knowledge base on memory coding. Memory codes, as defined by Dr. Weinberger, are "a relationship that describes the transformation of an experience into an enduring neural form." According to research by Dr. Tsien, neurons active during an event contain a subgrouping, a "neural clique" active in the hippocampus.



A memory, visual or auditory, is now going to be placed in a defined subset by location, estimated importance and emotional evaluation. An event can be "remembered" based on a particular subset clique. You can then review the event from a varied perspective. This research has not advanced to normal human models, so it's still theory at best. It presents strong evidence that aligns with research on memory traces, sometimes called memory engrams. Memory traces involve series or blocks of neurons and their pattern of activity. This type of neuron group would be laid down by usage of words whose patterns are familiar by frequent use.

Memory networks were first postulated by Dr. Donald Hebb in 1949. Dr. Hebb recognized that a memory cannot reverberate forever, and that some alteration in the nerve network must occur to make a memory permanent. Three key aspects to support his postulate have come to light.

First, research on the hippocampus has shown that this structure and its nearby parahippocampal formation aids in reintegrating the various components of an experience back into an event.



Second, the limbic system structures help create the emotional overlay of memory. The amydala has connections via its basolateral cell groups to the thalamus, the prefrontal cortex, higher order decision and judgment centers, as well as connections processing a wide range of body surface and internal organ information. The amydala's corticomedial cell group receives input from lower brain centers controlling heart rate and blood pressure, as well as special senses like olfaction, or smelling. Unfortunately, the hippocampus and the amydala seem to have an abundance of aversion centers. Those centers perceive negative emotions. This makes sense from an evolutionary perspective so that negative experiences retained in memory allow avoidance of repeating the remembered event. Centers for positive experiences tend to be associated with gratification, like feeding.

Third, research done in 2001 by neurobiologist Ben Barres of Stanford University noted that astrocytes, a cell in the brain typically responsible for aiding neuron function but not processing thought, may have an action that helps neurons create synapses. Recall from earlier in this presentation that synapses are the connections between nerve cells. His later research in 2003 found that astrocytes secrete proteins called thrombospondins that aid this synaptic creation. Under what conditions astrocytes make this protein and how to turn on its production are still under investigation. His lab identifying this action has huge implications. Now that the protein that makes connections in your brain has been isolated, could it be created as a drug? If a delivery system to the brain can be found, should we increase our processing ability? Note that I'm not saying this protein will make you smarter. This creates some ethical questions that must be addressed as the research advances.

Now that we looked at how memory is formed, stored and recalled, you may ask, what is the link to my classroom? How do I incorporate this information in my teaching? I try and verbally repeat the most important issues of a topic in more than one lecture. I give the students lecture outlines and leave space for them to write key words that relate to the main issues of that content. This allows for better cycling in short-term memory for both auditory and visual cortices. The repetition helps consolidation into long-term memory. Asking the students to verbally repeat difficult words activates the auditory associations, as well as Broca's area in the brain.

Teaching and learning are emotion-filled activities to the brain. I'm not a person who tells jokes, which can disrupt short-term memory, but I let the students know that I like what I teach. Students sometimes tell me they start liking the content because I enjoy teaching it.

In Anatomy and Physiology courses, many chapters that present major concepts of the book will spend multiple pages or sections teaching small independent facts or factors that contribute to how a specific function works. I limit the instruction of those specifics and take my class right to the summary charts. All those small factors are shown contributing to a larger function, like the heart's pressure/volume curves. I want the students to develop a long-term memory trace on the big picture, not the components. The visual memory of interrelated actions is what students will be tested on repeatedly in clinical courses. Students need to have a working knowledge of how things work together. I reintroduce concepts from the feeder courses to Anatomy and Physiology and have them

place the information in context to the current topic being discussed. This integrates across the boundaries of a two-part course.

Like many teachers, storytelling has a place in science instruction. When facts or concepts can't be visualized, placing the content into a scene or story allows learning without direct experience. For those of us who teach concept-based courses, stories are often our best chance to make course content relevant and real.

In closing, I hope this presentation has helped you in your understanding of physiology, memory and learning. In the many months since I received the Lindback award, my exploration into this topic area allowed me to review what kinds of research are occurring. I dismissed information from many animal studies because the questionable human application to their work raised more questions than answers. Much of the research presented today involves human subjects or generally accepted models. I want to acknowledge that most of the images I've used today are from the image bank provided by Pearson Publishing and are related to our current textbook, *Martini's Fundamentals of Anatomy and Physiology*. I thank you for your patience and kind attention.

Question and Answer Session

What is the function of storytelling in science?

The use of storytelling helps take concepts that are difficult to visualize or describe and places them in a context that is easily understood by students. In Anatomy and Physiology (A/P), we talk about concepts like diffusion, and the text conversation is somewhat dry. If you then describe how a person getting off the Broad Street subway during peak periods is a perfect example of the random molecular movement driven by concentration from the platform to the street, they understand immediately. The other primary application of storytelling in A/P is talking about clinical situations. When you present someone's story in the context of the course material, it places the content into a framework that has meaning and value for the student's career aspirations.

Do you see in the future that there will be less use of animals for research? Do you think the research will one day be transferred more to human beings?

While exploring the data for this presentation, I found all kinds of research in fairly esoteric areas like analogies to mouse brain function from the movement of mouse whiskers. Research into normal human function has advanced because of instrumentation like PET (positron emission tomography) and functional MRI (magnetic resonance imaging), which allows us to view cell function without cutting or damaging tissue. As technology expands, the use of animal models will change or disappear from study for some applications.

In some cases of brain injury, different parts of speech seem to be more difficult to express than other parts of speech, such as nouns for example. Are you familiar with the research, and why that might be the case?

There are two brain areas that came up in the research of Dr. Sakai. On the left hemisphere, the left premotor cortex in the frontal lobe has been found to be associated with syntax and sentence comprehension. On the left temporal lobe and near its attachment with the parietal lobe, phonology and lexicosemantics are processed. These areas align with difficulty in pronunciation and annunciation. These areas of the brain are seemingly damaged with some stroke patients because the area's blood supply was affected.

Do you find greater brain density in a child raised multilingual as compared to learning one language at a time?

The research I found had different terminology depending on its source. Neurophysiologists and neuropsychologists each have their own terminology when it comes to learning.

There is some research that I was alluding to about language. It looked at factors related to children who learned one primary language and moved to another country to acquire another secondary primary language versus children who were being trained to be multilingual. The research is not yet clear, but it is being studied.

There is a question of learned environmental patterns of speech from the parents contributing to difficulty when the child transitions into the academic setting. The brain adjusts or "rewires" to the new patterns of different sound sets.

Does this have to do with brain stimulation when the brain is still plastic?

That's a pointed question. As most neurophysiologists will now pretty much agree, if you're going to put your money someplace, it better be Head Start. The issue of plasticity and the development of the interconnections in a child's brain that received excellent stimulation versus a child with limited stimulation is a highly controversial topic. The research is now clear on this. Children who are from backgrounds with limited mental stimuli in the preschool period will never have the density of interconnections they would have had if they were more mentally stimulated in their preschool years. It is also very difficult to tell individuals who are from underserved educational areas that they will never have the potentiality, brain physiology wise, of a child from another area who is socioeconomically advantaged. The research is showing there is a huge difference primarily because we lose most of our neurons as we age. You have millions of neurons in the early phase of your life with normal high volume loss through puberty. A child has normal losses of the brain neurons down into the 300,000s, so if you did not develop deep interconnections early on, you have primary cell loss in addition to having less interconnectiveness. Your ability to learn and the pathways for learning are fewer. The research is clear, but it's controversial, so science types don't say too much about it.

Is there any evidence that supports the idea that these types of enriched environments for children, such as listening to Mozart, creates better settings? Do you really need to have that kind of environment to create more stimulation? Does it have to be Mozart, or can it be hip-hop? Can it be any kind of stimulation?

To flip the question to a certain extent, is all this high level of stimulation in multiple areas of intelligence creating a child with more interconnections? Is that your question?

The research is not showing specificity on the type of stimuli. I postulate that the reason why early research tended to emphasize classical music was because, for those of us who are somewhat music purists, classical music has a lot more mathematical modeling than some other areas of music. There isn't anything I found that currently shows to be of benefit. There is nothing clear at this point. What seems to be clear is that there will be some target ages by which certain types of learning would be optimal. The research is not clean yet about the stimuli favored for particular types of skill acquisition, like language. The research tends to be going more toward target age acquisition than in the direction of superloading children all at once with all possibilities of stimuli.

What about high levels of visual stimulation?

If people are exposed to very high levels of visual stimulation, especially from TV or videos, the brain can adapt—in a sense, speed up the attention center. As a result, they can have trouble focusing and concentrating on tasks with lower levels of stimulation.

I did not find anything specifically related to that, but what I did find, due to the fact that the brain has more negative response centers in the limbic system, was that the high density of negative imagery exposed to children is having an effect on them. The research is showing that the major impact on children is that the imagery makes them more "hair triggered" to negative imagery. We are "prebuilt" for heightened sensitivity to negative emotion more than positive emotion. The ongoing research is showing that the high level of negative and perverse imagery that children are seeing makes their brains more triggered to motor-specific responses. They are more restless and aggressive. We are not hardwired for joy and happiness. From what I found, we are hardwired to hopefully avoid negative imagery. Since memory and emotion are linked, are we "hair triggering" kids to be negative? That's an interesting question, isn't it?

I am with you on negative imagery on a macro level, but can you talk more about the micro level? I am getting lost.

The amydala is a center for rage, aggression and fear. If there is one specific place, that's it. We have high levels of processing with

stimuli seen as negative. The brain seems to be more evolutionary, built to recognize and thus avoid repeating things seen as negative. There are direct links between the primary memory centers and the limbic system as related to negative emotion. As you well know, you retain negative memories really well. Everyone remembers unpleasant things much better sometimes than positive because the brain is wired to retain the negative imagery for avoidance. We were never built from a physiological perspective for the levels of negative imagery that we are exposed to. This high level of activation increases the memory density. This has a negative implication in the classroom. I've tried to stay strict to the research, but it has an implication. If you have an angry classroom, students are going to develop negative responses to the content. If you're a person who yells at your class, the students are linking the content to the negative experience. Since emotion and memory are tightly linked, the question we have to ask ourselves is, are we teaching the students what we want them to learn?

The research is showing that people respond to the emotions presented. Since this is an educational environment, if you have a hostile class, the students are picking up the negative emotion and the angriness linked to the class content. It's a hand-in-hand relationship. I don't know if that's what we want to do as professionals. Students retain the experience, not the facts.

In memorization, do we connect events to things we already know? Is that a strategy for improving memory?

You have to link new knowledge onto prior or known knowledge. Every time we learn something new, it's layered onto related known information. That is what the memory clique discussion was about. Memory cliques are the physical structures that hold known information in specific brain areas about defined categories of information. The memory of an event is permanently altered by the layering on of new information. This is why it's possible to create false memories of an event.

It's is well known that there are a lot of drugs that block the memory of an event and block its transfer to long-term memory. This phenomenon was discussed in relation to why Princess Diana's guard who survived the car crash cannot remember the events of the crash. He was loaded with drugs in the ER to save his life, but that blocked his ability to retain the memories of the event.

Is there stem cell research that looks at the ability of people to learn better with neurological learning issues?

We have heard for a long time that the brain cannot heal or repair itself. Well, that is not completely true. It has been found that you can have new neuron development in the hippocampus and parahippocampus. They were the areas responsible for memory integration.

Also, now that we know about thrombospondins and that they can improve synaptic connections in existing cells, should we create a drug version of it? If you could afford to buy it, should you be able to improve your brain's interconnections? If the drug cost $20,000 a shot, should we let people who can afford it get it? Notice that I'm not saying you will be smarter. The ethical questions surrounding this discovery are huge. These questions are beyond me to answer.

Lindback Lecture

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