Lesson Overview

Students will consider how they make memories. They will visit numerous atoms on G2C Online dealing with memory, and then decide which information best explains how we make new memories in our brains.

Description of Activity

In LTP—Make a Memory, students initially respond to a free-write question asking how we make memories. After some students share what they wrote, students will hear Dr. Josh Dubnau (Creating Memories, #1426) explain what we do and do not know about memory creation. Following that presentation, students will work in pairs to visit different atoms of the Learning & Memory section of G2C Online in order to explain Dubnau’s statement that “memories are stored in brains by the brain’s ability to dynamically and rapidly alter the number and strength of connections amongst the huge network of neurons that makes up the brain.”

Background

The process by which new memories are made, so that we remember what we have learned, has not been firmly established. The majority of neurobiologists agree that mechanisms that cause neurons to respond to stimulation more efficiently are the driving forces behind memory formation. The process of long-term potentiation (LTP) is critical to increasing synapse-efficiency and involves changes in dendrites.

Cognitive and neural scientists agree that memory formation has various stages and proceeds from short-term memory (STM – typically less that a minute), to long-term memory (LTM – relatively permanent) is how new memories are made. The hippocampus is the brain structure most closely related to long-term memory formation, but the precise mechanism behind the leap from STM to LTM has yet to be explained.

Goals and Objectives

Students will be able to:

• explore the Learning & Memory section of G2C Online.
• select appropriate atoms that deal with how the number and strength of connections among neurons change resulting in more efficient responses to stimulation.
• explain, in their own words, steps describing how “memories are stored in brains by the brain’s ability to dynamically and rapidly alter the number and strength of connections amongst the huge network of neurons that makes up the brain.”
Assumptions of Prior Knowledge

Students should have a basic knowledge of principles of genetics, understanding of the biological basis of behavior and comprehension of fundamentals of cognition and memory.

Common Misconceptions

Students often think:
- Adults cannot grow new neurons.
- When changes occur at the dendrites of a neuron, those changes occur at all of the dendrites of the neuron.
- New memories only occur with repeated exposure to stimuli.
- Scientists know all of the steps involved in memory formation and retrieval.
- Memories are consistent over time.

Implementing the Lesson

Time allotment
1 (or 2) x 50-minute class

Before Class

Become familiar with G2C Online, especially the Cognitive Processes > Learning & Memory section. Preview the Long-term Potentiation (#549) video animation.

If necessary, reserve computers for this lesson.

Two versions of the student worksheets have been prepared. The first set provides less guidance to students so that they can freely explore G2C Online in whatever pattern interests them. This helps students to control their own learning, and develop research and note-taking skills. On the other hand, if they do not navigate wisely, using this worksheet can leave students with inadequate information, or take considerably more time than is available for this lesson. The second worksheet set specifies atoms for students to visit in a particular order. The strengths and weaknesses of the two approaches complement each other. If you deem it appropriate, you can differentiate the assignment within your classroom, and then have pairs with different assignments share their work.

Photocopy the following student worksheets:
Make a Memory, pages 1-3 or
Make a Memory, pages 4-6
During Class

You may want to begin by asking students to respond to the focused free-write question, “How do we make new memories?” Inform students that they have 5 minutes to write their answers. They should write the whole time as much as they can about the topic. Monitor student progress as they write. After 5 minutes, have students pair up with a partner to read their responses to each other. Choose a volunteer who has a good response to share it with the class.

Tell students that for the remainder of the class, they will take a closer look at what neuroscientists have learned about what happens when we make new memories.

Present the video Memory – Creating Memories (#1426) on G2C Online. After viewing Dr. Dubnau’s interview, direct students to the Main Menu, and select Learning & Memory to find out more about Dr. Dubnau’s statement:

> On some level we understand (or at least we believe we understand) that information is stored in brains, information meaning memories of our past experiences – that those memories are stored in brains by the brain’s ability to dynamically and rapidly alter the number and strength of connections amongst the huge network of neurons that makes up the brain. And we understand a lot about how neurons, or relatively a lot, about how neurons do that.

Ask them to complete the student worksheet.

**Recommendations for Evaluation:**

The teacher can assess understanding by evaluating completed worksheets prepared by each pair of students.

A possible examination question to be answered by students is, “Explain how a new memory is made at the neuronal level.”

Students can prepare questions for a Jeopardy category dealing with the biological basis of behavior—memory.

**Suggestions for Extended Learning**

Students can explore other levels of Learning & Memory on G2C Online.

Groups of students can prepare a storyboard that would enable a class of high school introductory biology students to understand how information is stored in brains. In their storyboards, students can indicate the sequence of atoms they would use, and narration they might provide. A storyboard template can be found at: http://www.thinkport.org/Technology/template.tp Students can read Nobel Prize Laureate Eric Kandel’s book In Search of Memory: The Emergence of a New Science of Mind, and discuss what they learned with other members of the class.
Glossary

**Action Potential** - An action potential is a brief and large change in the electrical potential across the membrane of a cell. It is also called an impulse. Action potentials sweep rapidly along the length of the membrane and trigger the release of neurotransmitters.

**AMPA Receptor** - The alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptor receives glutamate at the postsynaptic cell. It is thought to be highly important to long-term potentiation.

**CREB1** - CREB1 is a cAMP response element-binding protein that works as a transcription factor. In neurons, these proteins are involved in the formation of long-term memories and long-term potentiation. It is a CREB activator which facilitates long-term memory formation.

**CREB2** - CREB2 is a cAMP response element-binding protein that works as a transcription factor. In neurons, these proteins are involved in the formation of long-term memories and long-term potentiation. It is a CREB repressor which inhibits long-term memory formation.

**Dendrite** - Dendrites are the parts of a neuron that receive information, conducting electrical signals toward the cell body. They extend from a neuron like branches on a tree.

**Dendritic spine** - A dendritic spine is a small protrusion that receives inputs from a synapse. Each neuron typically has many thousand dendritic spines.

**GABA** - Gamma-aminobutyric acid (GABA) is the primary inhibitory neurotransmitter in the central nervous system. In early stages of development, GABA can be excitatory.

**Glutamate** - Glutamate, an amino acid, is an excitatory neurotransmitter important for information processing in neuronal networks, especially in the hippocampus and cerebral cortex.

**Hippocampus** - The hippocampus is the structure in the brain most closely aligned to memory formation. It is important as an early storage place for long-term memory, and it is involved in the transition of long-term memory to even more enduring permanent memory. The hippocampus also plays an important role in spatial navigation.

**Kinases** - A kinase is an enzyme that is specialized for adding a phosphate group to a protein substrate.

**Long-term Depression** - Long-term depression is a long lasting reduction in the strength of synaptic transmissions.
Long-term Memory (LTM) - Long-term memory (LTM) is a relatively permanent form of memory. It involves new protein synthesis that gives rise to new synaptic connections.

Long-term Potentiation (LTP) - Long-term potentiation is an enduring increase in the amplitude of excitatory postsynaptic potentials as a result of high-frequency (tetanic) stimulation of afferent pathways. It is measured both as the amplitude of excitatory postsynaptic potentials and as the magnitude of the postsynaptic-cell population spike. LTP is most often studied in the hippocampus and is often considered to be the cellular basis of learning and memory in vertebrates.

Memory - Memory is an organism's ability to register, retain, and retrieve information over time.

Neural Code - The neural code involves different patterns of nerve cells firing on either side of the synapse. It is this pattern that encodes information necessary for cognition.

Neurogenesis - Neurogenesis is the production of new neurons.

Neurotransmitter - Neurotransmitters are chemical messengers released into the synapse by the pre-synaptic neuron. They can change the resting potential of the postsynaptic neuron by activating post-synaptic receptors. Common examples are glutamate, GABA, serotonin and dopamine.

Neurotransmitter Receptor - A neurotransmitter receptor is a special protein that binds with a neurotransmitter and excites or inhibits the post-synaptic neuron.

NMDA Receptor - NMDA (N-methyl-D-aspartic acid) is a type of glutamate receptor. It is located on the post-synaptic neuron and is thought to be involved in long-term potentiation.

Plasticity - Plasticity is the change in the strength of synaptic connections between neurons. Long-term potentiation is a form of synaptic plasticity.

Post-synaptic terminal - The post-synaptic terminal is the region of the dendrite of the neuron that is being stimulated.

Pre-synaptic terminal - The pre-synaptic terminal is the region of the terminal branch of an axon that releases neurotransmitters into the synaptic cleft.

Short-term Memory (STM) - Short-term memory is a relatively temporary form of memory. Short-term memory involves alterations in preexisting proteins and alterations in the strength of preexisting connections. Unlike long-term memory, it does not give rise to new synaptic connections.

Synapse (synaptic cleft) - A synapse is the space between two nerve cells, where a nerve impulse moves from one neuron to another.
**Transcription**- Transcription is the process by which messenger RNA (mRNA) is copied from DNA. RNA polymerase is the enzyme that facilitates this transcribing process.

**Translation**- Translation is the stage in protein synthesis where messenger RNA (mRNA) is decoded to produce proteins. This process is facilitated by subcellular structures called ribosomes which, along with transfer RNA (tRNA) molecules, translate the code carried by the mRNA into a sequence of amino acids.

**Resources**

*Related Readings:*


*Web Resources:*


New York State Biology Chemistry Professional Network (http://biochemnetwork.com/)

Thinkport (Partnership between Maryland Public Television (MPT) and Johns Hopkins University Center for Technology in Education (CTE))
http://www.thinkport.org/Technology/template.tp
American Psychological Association
National Psychology Standards for High School Psychology

I. RESEARCH DOMAIN

CONTENT STANDARD IA-3: Research strategies used by psychologists to explore behavior and mental processes.
   3.1 Describe the elements of an experiment.
   3.2 Explain the importance of sampling and random assignment in psychological research.

II. BIOPSYCHOLOGICAL DOMAIN

Standard Area IIA: Biological Bases of Behavior
CONTENT STANDARD IIA-1: Structure and function of the neuron
   1.1 Identify the neuron as the basis for neural communication.
   1.2 Describe how information is transmitted and integrated in the nervous system.
   1.3 Analyze how the process of neurotransmission can be modified by heredity and environment.

CONTENT STANDARD IIA-2: Organization of the nervous system

CONTENT STANDARD IIA-3: Hierarchical organization of the structure and function of the brain
   3.1 Identify the structure and function of the major regions of the brain.

Standard Area IVB: Memory
CONTENT STANDARD IVB-1: Encoding, or getting information into memory
   1.1 Characterize the difference between surface and deep (elaborate) processing.
   1.2 Identify other factors that influence encoding.

CONTENT STANDARD IVB-2: Sensory, working or short-term, and long-term memory systems
   2.1 Describe the operation of sensory memory
   2.2 Describe the operation of short-term memory and working memory.
   2.3 Describe the operation of long-term memory.

CONTENT STANDARD IVB-3: Retrieval, or getting information out of memory

CONTENT STANDARD IVB-4: Biological bases of memory
   4.1 Identify the brain structures most important to memory.
National Science Education Standards

Content Standard A: Science as Inquiry
- Identify questions and concepts that guide scientific investigations
- Formulate and revise scientific explanations and models using logic and evidence
- Recognize and analyze alternative explanations and models

Content Standard C: Life Science

The Cell
- Cells have particular structures that underlie their functions. Every cell is surrounded by a membrane that separates it from the outside world. Inside the cell is a concentrated mixture of thousands of different molecules which form a variety of specialized structures that carry out such cell functions as energy production, transport of molecules, waste disposal, synthesis of new molecules, and the storage of genetic material.
- Most cell functions involve chemical reactions.
- Cells store and use information to guide their functions. The genetic information stored in DNA is used to direct the synthesis of the thousands of proteins that each cell requires.
- Cell functions are regulated. Regulation occurs both through changes in the activity of the functions performed by proteins and through the selective expression of individual genes. This regulation allows cells to respond to their environment and to control and coordinate cell growth and division.

The Molecular Basis Of Heredity
- In all organisms, the instructions for specifying the characteristics of the organism are carried in DNA, a large polymer formed from subunits of four kinds (A, G, C, and T). The chemical and structural properties of DNA explain how the genetic information that underlies heredity is both encoded in genes (as a string of molecular "letters") and replicated (by a templating mechanism). Each DNA molecule in a cell forms a single chromosome.
- Changes in DNA (mutations) occur spontaneously at low rates. Some of these changes make no difference to the organism, whereas others can change cells and organisms. Only mutations in germ cells can create the variation that changes an organism’s offspring.

The Behavior Of Organisms
- Multicellular animals have nervous systems that generate behavior. Nervous systems are formed from specialized cells that conduct signals rapidly through the long cell extensions that make up nerves. The nerve cells communicate with each other by secreting specific excitatory and inhibitory molecules. In sense organs, specialized cells detect light, sound, and specific chemicals and enable animals to monitor what is going on in the world around them.
- Organisms have behavioral responses to internal changes and to external stimuli. Responses to external stimuli can result from interactions with the organism’s own...
species and others, as well as environmental changes; these responses either can be innate or learned.

- Like other aspects of an organism’s biology, behaviors have evolved through natural selection. Behaviors often have an adaptive logic when viewed in terms of evolutionary principles.
- Behavioral biology has implications for humans, as it provides links to psychology, sociology, and anthropology.

**Content Standard E: History and Nature of Science**

**Nature of Scientific Knowledge**

- Scientific explanations must meet certain criteria. First and foremost, they must be consistent with experimental and observational evidence about nature, and must make accurate predictions, when appropriate, about systems being studied.
- Because all scientific ideas depend on experimental and observational confirmation, all scientific knowledge is, in principle, subject to change as new evidence becomes available.

**Historical Perspectives**

- Usually, changes in science occur as small modifications in extant knowledge. The daily work of science and engineering results in incremental advances in our understanding of the world and our ability to meet human needs and aspirations. Much can be learned about the internal workings of science and the nature of science from study of individual scientists, their daily work, and their efforts to advance scientific knowledge in their area of study.
**Answer Key**

**Focused Free-write: How do we make memories?**

Answers will vary depending on what students have previously learned in science, health, and social studies classes, as well as what their life experiences have been.

Frequently responses deal with making a memory on the cognitive level. One student wrote:

_Bombarded by millions of stimuli, I pay attention to a very limited number of them. The ones in my sensory memory that I attend to move into short-term memory. If I rehearse what's in short-term memory, it may move into long-term memory. Or instead of just rehearsing the information, if I form associations between new information and what I already know, I may form a memory that will stay with me my whole life._

**For students using LTP—Make a Memory Student pages 1-3**

Because _G2C Online_ has such an extensive number of atoms with information about making memories that might interest your students, it is not possible to anticipate which of the possible atoms they will choose. Among those that may appeal to them are the following:

<table>
<thead>
<tr>
<th>Atom 1</th>
<th>Atom 2</th>
<th>Atom 3</th>
<th>Atom 4</th>
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<tr>
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**Summary: (for either student worksheet)**

Again, answers will vary. What follows is just one possible answer.

_What “memories are stored in brains by the brain’s ability to dynamically and rapidly alter the number and strength of connections amongst the huge network of neurons that makes up the brain” means is that:_

- **Neurons send signals called action potentials to other neurons**
- **At the junctions between the pre-synaptic neuron and the post-synaptic neuron the pre-synaptic neuron releases neurotransmitter molecules (chemical signals), such as glutamate, that can produce an action potential in the post-synaptic neuron.**
- **Patterns of action potentials can activate the biochemistry of learning when glutamate activates the NMDA receptor which results in phosphorylation of proteins eventually even resulting in formation of a new synapse.**
- **Short-term memory (STM) involves changes in pre-existing proteins, usually through protein phosphorylation and alteration in the strength of pre-existing connections.**
- **Long-term memory (LTM) involves gene expression, new protein synthesis and the growth of new synaptic connections.**
### Possible completed table:

<table>
<thead>
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<th>Atom #</th>
<th>What the information says</th>
<th>What I think the information means</th>
</tr>
</thead>
<tbody>
<tr>
<td>1444</td>
<td>The brain has evolved to adapt to the environment, to change constantly in response to changes in the world around us, to learn. This unique ability is driven by communication between many billions of neurons, which send signals by way of tiny electrical charges known as action potentials. Neurons are connected by a multitude of networks, which allow them to communicate in hugely complex ways. Communication is coordinated by chemical signals that travel across synapses – the junctions where neurons connect.</td>
<td>Learning and memory involve communication among neurons. This communication has an electrical component and a chemical component. The electrical component is the action potential that is generated along the axon of the neuron. The chemical component involves secretion of a neurotransmitter across the synapse.</td>
</tr>
<tr>
<td>550</td>
<td>When patterns of action potentials arrive at synapses in the central nervous system, they cause the release of glutamate, the neurotransmitter, from the pre-synaptic terminal onto receptors on the postsynaptic side. One of the most important receptors is the NMDA receptor, and when that one is activated during the process of learning, it activates the biochemistry of learning. When the NMDA receptor changes its shape, it opens up a channel, through which a calcium ion that is normally found outside the cell, races into the inside of the postsynaptic terminal. Once inside calcium ions may bind onto proteins called kinases. Kinases are enzymes that add a phosphate group onto other proteins. So, when a kinase becomes activated, it adds a phosphate onto other proteins, which are now altered and do many different jobs in the nerve cell. Some of those proteins cause receptors to be added onto the surface of the cell. Other sorts of proteins change the structure of the nerve cell and the synapse itself. Other proteins are responsible for making new synaptic proteins. As well as proteins at the synapse, the signals from the synapse go all the way to the nucleus and control the gene expression and the synthesis of RNA itself. All of these proteins on the postsynaptic side of the synapse control many different properties of the nerve cell, and it is these properties that are activated and very carefully regulated during the process of learning and memory.</td>
<td>The neural code involves transmission of information among neurons in networks. When an activated neuron secretes the neurotransmitter glutamate across the synapse, it may activate a whole series of changes starting with an NMDA receptor in the post-synaptic neuron. Changes at the receptor enable calcium ions to bind with kinases that catalyze reactions phosphorylating proteins. Phosphorylated proteins may cause lots of changes in the neuron that are associated with learning and memory.</td>
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<td>1277</td>
<td>Communication in brain cells is guided by interactions between genes and biochemicals at the synapse. These interactions can lead to the formation of new synapses, which can facilitate long-term learning. The formation of a memory in the neuron begins at the synapse. Memories begin to form when a series of action potentials arrive at the presynaptic terminal. The action potential causes a sudden shift in the electrical potential across the membrane. Calcium ions rushing across the membrane activate glutamate vesicles that spill out across the synaptic cleft. NMDA and AMPA receptors on the postsynaptic neuron react differently to the glutamate. AMPA receptors open sodium and potassium ion channels in the postsynaptic neuron. When sodium enters the postsynaptic terminal, it depolarizes the postsynaptic membrane. NMDA receptors change shape allowing calcium ions in. Calcium binds to calmodulin that then activates other proteins called kinases which are enzymes that add a phosphate group onto other proteins. Activated cAMP protein kinase moves to the nucleus of the postsynaptic cell, where it binds to another protein called CREB. CREB controls transcription of DNA. When activated, CREB transcribes DNA in the cell nucleus to produce RNA. RNA travels back to the synapse, where it synthesizes new proteins to change the structure of the synapse. Changes include growth of new synapses, which are thought to be the basis of long-term memory.</td>
<td>The basis for memory may be the molecules involved in reactions at the synapse. When the neurotransmitter glutamate is released into the synapse, a cascade of ionic movement and chemical reactions are initiated at postsynaptic receptors resulting in activation of CREB. This leads to synthesis of new proteins that result in the growth of new synapses. The growth of new synapses is thought to be the basis of LTM.</td>
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| 1284 Changes During LTM | An interesting question that has emerged in the study of long-term memory is, since long-term memory involves genes and therefore the nucleus (an organelle, which is, in principle, in contact with every synapse of a neuron), does that mean a neuron must change every one of its several thousand synaptic connections in a long-term process, or, can one in the long term, restrict certain connections, alter their strengths, and not others?

This is fundamental because if every long-term process is neuron-wide, the ability to store information in the brain is dramatically restricted. But if a neuron can store different kinds of information at different terminals, you obviously expand the information power of a nerve cell dramatically. All the recent studies of the last three or four years have shown that you can have long-term changes that are synapse-specific. So, you retain the informational power of the individual neuron. |
| 1279 STM and LTM Differences | Short-term memory involves alterations in pre-existing proteins. Long-term memory involves new protein synthesis.

The way that happens is short-term memory involves recruitment of signaling pathways in the brain that activate enzymes - calmodulin dependent protein kinase, or the cyclic AMP dependent protein kinase, and produce actions locally on the release machinery for transmitter control in the presynaptic terminal and on postsynaptic receptors.

Long-term memory involves the movement of those signaling pathways into the nucleus to turn on gene expression, and that turning-on of gene expression gives rise to the growth of new synaptic connections.

So, short-term memory involves alterations in pre-existing proteins, usually through protein phosphorylation and alteration in the strength of pre-existing connections. Long-term memory involves gene expression, new protein synthesis and the growth of new synaptic connections. |
| 549 LTP | Long term Potentiation (LTP) is very widely studied in the hippocampus. Using a small slice of brain from the hippocampus, an electrode can be placed on the axon for stimulating them, and another electrode can be placed on the dendrites for recording the synaptic response. Electrically activate an axon to produce an action potential, which then produces a synaptic response on the dendrites. If we give a high frequency stimulation for a second or so, and then return to giving a single action potential every minute, we will see that there has been a significant increase in the strength of synaptic transmission which over the course of the next hour or so, is maintained. This is long-lasting increase in synaptic strength called long term potentiation (LTP). At this point, a low frequency stimulation is given, and now we go back to recording a single action potential every minute, and there has been a reduction in synaptic strength that is long-lasting. This is long term depression. |
| 1284 Changes During LTM | Changes can occur in only some of the synaptic connections with neurons and not in others. |