Lesson 4: How does glucose affect memory in aging populations?

I. Overview
In this lesson, students learn about the role of adrenalin and glucose in age-related rapid forgetting. Using the models from previous lessons, students design and conduct their own experiments to discover possible reasons for age-related memory loss in elderly people. Students perform experiments using “Rat Recall”, a program simulating behavior of young and old rats in a task designed to test memory retention. Rat Recall allows students to test the effects of glucose and epinephrine on memory. This simulation builds on behavioral data collected in experiments conducted by neuroscientist Dr. Paul Gold at Syracuse University. After performing their group experiments, students work as a class to determine the roles that adrenalin and glucose may have in age-related memory loss.

Connections to driving question
Throughout this lesson students learn about the importance of glucose in fueling processes of memory formation. Students learn that in aging rats, the inability of adrenalin to increase blood glucose underlies age-related rapid forgetting.

Connections to previous lessons
Lessons 1-3 are designed to provide the knowledge base for students to conduct this experiment. In lesson 1, students learned that highly active organs, the brain in particular, need glucose in order to function. In the second lesson students learned how insulin and glucagon regulate blood glucose levels and subsequently built a blood glucose homeostasis model. In lesson 3, students generated a model of adrenalin’s actions on the body and blood glucose and applied this model to the fight or flight response. In this lesson, students will use their adrenalin model to investigate the physiological mechanism behind age-related rapid forgetting.

II. Standards
National Science Education Standards
- 12AS1.4 Formulate and revise scientific explanations and models using logic and evidence. Student inquiries should culminate in formulating an explanation or model. Models should be physical, conceptual, and mathematical. In the process of answering the questions, the students should engage in discussions and arguments that result in the revision of their explanations. These discussions should be based on scientific knowledge, the use of logic, and evidence from their investigation.
12ASI1.2 Design and conduct scientific investigations. Designing and conducting a scientific investigation requires introduction to the major concepts in the area being investigated, proper equipment, safety precautions, assistance with methodological problems, recommendations for use of technologies, clarification of ideas that guide the inquiry, and scientific knowledge obtained from sources other than the actual investigation. The investigation may also require student clarification of the question, method, controls, and variables; student organization and display of data; student revision of methods and explanations; and a public presentation of the results with a critical response from peers. Regardless of the scientific investigation performed, students must use evidence, apply logic, and construct an argument for their proposed explanations.

**Benchmarks for Science Literacy**

**Nature of Science: Scientific Inquiry**

- To be useful, a hypothesis should suggest what evidence would support it and what evidence would refute it. A hypothesis that cannot, in principle, be put to the test of evidence may be interesting, but it may not be scientifically useful. 1B/H9** (SFAA)

**III. Learning Objectives**

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| Describe why rats are used as a model organism and how this research relates to humans. | During discussion, possible answers include:  
- Rats have a similar physiology to humans.  
- Like humans, aging rats show deficits in cognition with advancing age.  
- We can study the effects of aging on the neuroendocrine system and cognition using paradigms that would be unethical to test in aging humans.  
We can use the results of these studies to help the aging population overcome cognitive deficits. | Activity 1 |
Develop a hypothesis about age-related differences in memory and design an experiment. | Students develop a well-formed hypothesis that predicts the effect that one of the following variables has on memory formation in rats:

- rat age (young vs. old)
- effect of glucose or epinephrine injection
- effect of different injection dosages

Based on their hypothesis, students should:

- Design an experiment that tests their variable
- Identify the independent and dependent variables
- Create a graph of expected results

Associated materials:
U7_L4_StudentSheet_RatRecall | Activity 2

Identify and explain laboratory methods in behavioral neuroscience. | During conversation and presentation of results students can explain the procedure of the experiment and how it tests for memory.

Associated materials:
U7_L4_StudentSheet_RatRecall | Throughout Lesson

Graph data and develop a scientific explanation that either supports or refutes their initial hypothesis based on their and others’ results. | During classroom discussion students are able to clearly discuss their experiment and the meaning of their results. This explanation should include a description of how the selected variable is affecting memory.

Ex: The injection of epinephrine increases memory in young rats as it triggers the release of glucose from the liver. Glucose then travels to the brain where it helps memory formation. In old rats, epinephrine does not produce an increase in memory. This may be because the number of epinephrine receptors are reduced or are not as sensitive in older rats.

Based on their experimental results and whole-class discussion, students complete a written explanation.

Associated Materials: U7_L4_StudentSheet_RatRecall | Activity 3
IV. Adaptations/Accommodations
If computer labs or computers are unavailable, contact project NEURON for the data sets that can be generated from Rat Recall. The program also comes equipped with video explanations of the task itself, which can be accessed through the project NEURON website.

V. Timeframe for lesson

Opening of Lesson
- Discussion and recap of lesson 3 and adrenalin model: 5-10 minutes

Main Part of Lesson
- Activity 1 – Introduction to Rat Recall: 10-15 minutes
- Activity 2 – Hypothesis Development and Planned Investigation: 15 minutes
- Activity 3 – Rat Recall Experiments: 20 minutes per experiment
- Activity 4 – Rat Recall Data Discussion: 15 minutes

Conclusion of Lesson
- Class discussion: 15 minutes

VI. Advance prep and materials

Activity 1: Introduction to Rat Recall

Materials:
- Rat Recall program downloaded from Project NEURON website.

Preparation:
- Have computer access. One computer for every 4-5 students.

Activities 2, 3, & 4: Hypothesis Development, Rat Recall Experiments, and Data Discussion

Materials:
- Stop watches (optional – students can use timers on video player)
- U7_L4_StudentSheet_RatRecall
- U7_L3_Image_AdrenalinDiagram (from Lesson 3)
- U7_L4_TeacherResource_RatRecallData_ANSWERS

Preparation:
- Hand out 1 stop watch per group of students
- Print enough copies of U7_L4_StudentSheet_RatRecall – 1 per student.
• Project the **U7_L3_Imagge_AdrenalinDiagram** for students to reference during the lesson if needed.

• ONLY the teacher should see **U7_L4_TeacherResource_RatRecallData_ANSWERS**. This should be used as a reference to help the teacher understand the data that students are collecting.

**Conclusion**

**Materials:**

• **U7_L4_Assessment_ConcludingQuestions**

**Preparation:**

• Have **U7_L4_Assessment_ConcludingQuestions** ready to be projected via the projector. Note that these questions can be introduced at the end of the lesson or at the start of the next lesson.

**VII. Resources and references**

**Teacher resources**


**References**


VIII. Lesson Implementation

Opening of Lesson:
**Adrenalin and epinephrine are used interchangeably throughout the lesson.**

Pose the question to the class, “From experience are there differences among old and young people with memory retention?” “Why do you think there is a difference?” “Is there a biological cause?” The goal of this lesson is to answer the main question:

How do age, dosage, and glucose/adrenalin play a role in memory?

Have this question written on the board for students to reference throughout the lesson. To answer this question students will be performing an investigation using rats. Ask students:

- Why would we use rats to study the effects of aging and adrenalin on memory?
  - Rats have a similar physiology to humans. Like humans, rats have the same organs, glands, hormones and physiological responses that are involved in stress response. Rats also exhibit the same age-related changes in memory.

To prepare students for the experiment, briefly review what they learned during Lesson 3. During this Q&A period, have the U7_L3_Image_AdrenalinDiagram (from Lesson 3) projected and if possible, the models that students made in Lesson 3.

Teacher Content Knowledge: Age-related changes in memory
Aging humans and rats experience age-related changes in memory. As they age, many animals tend to exhibit a form of memory disturbance, known as rapid forgetting. For example, they will remember things that they learned a long time ago with no problem, but they will often forget newly learned information in a matter of hours or days.

Not all aging humans have memory deficits. Current studies designed to test memory are biased against older subjects. For example, older subjects perform poorly on computer based memory tests because they are not familiar with the technology. Also, as we age, reaction time is much slower so many older adults perform accurately on the memory test but will respond more slowly, which will make them appear to have memory deficits. Also the types of memories that are stored by older humans are different than younger humans. For example, older humans are actually very good at (in fact better than younger people) at extracting the “big picture” of an event and summarizing information. Whereas younger humans are better at extracting minute details of an event. Many memory tests test for the details of an event versus the “big picture”, making aging humans appear to have worse memory.
Main Part of Lesson

Have students open up “Rat Recall” on the computers.

Activity 1: Introduction to Rat Recall

Split the class into the groups they were in for Lesson 3. Allow students to move about the room and get settled before moving on. It is important to first explain the Rat Recall Program to students and how the Inhibitory Avoidance Task works. Remind students that they learned about the inhibitory avoidance memory task in Checkpoint B of Lesson 3. Demonstrate a sample experiment by entering the variables young, epinephrine, and medium dosage to demonstrate how this experiment tests for memory. The inhibitory Avoidance Task is described below.

Teacher Content Knowledge: Explanation of the Inhibitory Avoidance Task

The inhibitory avoidance task takes advantage of the rat’s natural tendency to prefer dark places to brightly lit places.

The rat is placed in the chamber. Due to its natural tendency to avoid light, it will automatically move to the dark chamber. In this chamber the rat will receive a small electrical shock. This shock is tiny, less than a static electric shock. Do you think a rat would have a strong memory of this tiny shock? (No.) Instead immediately after the rat is shocked we inject it with epinephrine to induce a memory. What natural reaction are we trying to mimic by giving the rat epinephrine? (fight-or-flight response, adrenalin rush).

We wait two days and then put the rat back in the chamber. Remember, the rat instinctively wants to move the dark chamber. So, if he stays in the light chamber, we can deduce that the rat has formed a memory from two days prior. The strength of the memory is measured by the amount of time the rat stays in the light chamber. A rat that never leaves the light chamber would have a strong memory for the event (when it was shocked), while a rat that hesitates entering the dark chamber, but still enters would have a weaker memory for the event. A rat that enters the dark chamber without hesitation would have no memory of the event.

The amount of time it takes for a rat to move into the dark chamber (if at all) is called latency. During the Rat Recall experiments, the stopwatches are used to objectively measure latency. If a rat has a complete memory of the event, he will not cross to the dark chamber and we stop the stopwatch when he is picked up.
Scientific Practices: Asking Questions
Students formulate and refine questions that can be answered empirically in a science classroom and use them to design an experiment. By asking the right questions, students form a solid foundation for what they are testing and how it can be tested. Also, after students discover that the liver fails to respond to epinephrine in old individuals, they should be asking “why?” This question asking highlights an important part of the nature of science. Science is driven by questions and many times answering a question will generate even more questions.

Activity 2: Hypothesis Development and Planning Investigation
In their small groups, students will have the autonomy to develop their own hypotheses and plan their own investigations. Explain to students that they can test anything they want within the parameters of the program. There is no right or wrong hypothesis to test. For example the students can develop hypotheses based on:

- age differences
- treatment differences within an age group or across age groups
- dosage differences within a treatment or across treatments or within an age group or across an age group.

What is causing the difference in age-related memory? Is there a problem with a certain chemical? Why is dosage a factor? (Think of the dosage of caffeine or alcohol)

Hand out U7_L4_StudentSheet_RatRecall. Give student groups time to form their hypotheses and plan their investigation on the first page. If whiteboards are available, students can use them to write their answers to the student sheet and present them to the class. Make sure to emphasize to students that they will not be able to find an explanation from just one experiment. Instead each group will perform their own experiment and will present their results to the class. With an array of results from different experiments students will be able to form conclusions to the main question as a class. When groups have finished developing their hypotheses have the groups present their hypothesis and experimental design. In doing so, the class will see what each group is investigating and what variable they will be testing.

**Although it is good scientific practice to have multiple trials, there is no need to repeat trials in the Rat Recall Program. For the specific variables that are chosen, the same video will be played every time so there will be no variability in results. However, the concept and importance of multiple trials in experiments can be discussed with the students.
Scientific Practices: Planning and Carrying Out Investigations

Within the bounds of Rat Recall, Lesson 4 gives students the freedom to plan and carry out scientific investigations that closely mirror how the professional scientific community practices science. Different scientists or different groups of scientists perform different experiments to add to the collaborative effort of building knowledge. Having a community of experts allows scientists to contribute insight, critically review each other’s work, and generate discussion for the advancement of scientific knowledge.

Activity 3: Rat Recall Experiments

Once the students have designed their experiments they can progress to the data collection on Rat Recall.

**Important:** Students will be taking measurements only during the “memory testing” portion of the video. This is the scenario where rats are placed back in the chamber after 2 days. Remind students that they are to start timing once the rat has been placed in the lit compartment and they are to stop the timers once the rat has crossed all 4 paws into the dark compartment. It is best to model an example on the projector for the entire class. It is helpful to ask the class why it is important for everyone to have similar methods of measurement.

Tell students to record the data they are collecting in a data table in the space provided on **U7_L4_StudentSheet_RatRecall**. Following their data collection, have the students graph their data on the whiteboards to be presented. After the students have graphed their data, they should describe their data and discuss as a group what they can conclude. Do any new questions arise? Remind students that they will be presenting their results to the class and should prepare to do so.

Use the document **U7_L4_TeacherResource_RatRecallData_ANSWERS** as a helpful guide for the teacher to see what student results may look like.

Activity 4: Class Discussion

Have each group come up and briefly present their results to the class. After every group has presented their results have the class discuss all the results and conclusions as a whole to construct an explanation on why older rats may have a worse memory than younger rats on the inhibitory avoidance task. Students should be referencing the adrenalin model in their explanations. Allow students to drive this discussion themselves, but make sure you keep the discussion on track and guide them towards the right direction.

It is possible the groups may need to design new experiments if not enough information is present to answer the main question after the whole class discussion. There are two options that you can take here as the teacher. (1) Students can design entirely new experiments again. (2) Or, the whole class can
participate in forming a new experiment and the experiment can be carried out as a class via the projector. The second option allows for efficiency, and works off the momentum of class discussion to make students feel that they are “almost there,” instead of making students feel that they have to “go back” to square one.

When the class is able to pull together all the groups’ data, ask students to write an explanation to answer the main question. This can assigned individually for homework as well.

### Student Misconceptions

From Lesson 3 and from the experiment, students may form the idea that stress is good because it enhances memory. However, stress is good for memory only for the periods in which you are stressed. But chronic stress, which many people have, is actually detrimental for the brain. This has been heavily studied. Chronic stress can suppress neuron growth and development, impair learning, cause cell death in the brain, and change gene expression in the brain so that the brain is more or less responsive to particular neurotransmitter systems. So chronic stress is terrible for the brain and memory processing. It is really only the intermittent stress that is good for memory, and specifically memory of the event that caused the stress.

### Student Misconceptions

By working on glucose so intently in this unit, students should not assume that glucose is the only factor involved in memory. The conclusion of the lesson below works to highlight this point for the students. Along with the conclusion of the lesson, the following information can help you address any misconception or questions that students may have or ask about.

The brain is highly metabolic, so taking in glucose helps enhance the functioning of the brain. However, glucose cannot totally replenish brain function, especially in an aging or diseased brain. Many cellular processes and mechanisms begin to deteriorate. For instance, both calcium and neurotransmitters have been shown to be very important modulators of learning and memory and disturbances to either or both have been shown to disrupt learning and memory processes. Beyond biological explanations, attending to new information and surrounding oneself with cognitive stimuli is very important in order to learn new information.

There are many molecular changes occurring in the aging brain that can affect memory, learning, attention, and sleep. Glucose can only help with boosting energy availability, but as mentioned above, energy availability is not the only thing changing in an aging brain that contributes to memory loss.
Conclusion of Lesson

Have groups turn in U7_L4_StudentSheet_RatRecall stapled to their written explanation in answer to the main question. Although not necessary for the unit, but as a possible extension, students can write a lab report for this experiment.

Finally, to provide a more human connection to the experiment, introduce three critical thinking questions by projecting U7_L4_Assessment_ConcludingQuestions. You may decide to assign these questions for homework if time is limited. Or, these questions can be presented at the beginning of the next lesson. The following are the concluding questions and answers:

(1) Diabetes is caused by an increase in blood glucose. We see that people with diabetes II also have a very high risk for developing Alzheimer’s disease. If increased blood glucose enhances memory, then why would we see high amounts of blood glucose inhibiting memory in Alzheimer’s disease?
   • In the Rat Recall memory experiment we saw a dose response curve. That means increased glucose for the brain is beneficial to an extent. However, after a certain point, more glucose begins to harm memory formation.

(2) If you were a physician and looked at the data and conclusions from this experiment, what would you give/suggest to your elderly patients suffering from deficits in memory formation?
   • Making sure these patients eat breakfast in the morning and eat regularly spaced meals can help these patients tremendously. (However, as we will see in question 3 this is not a cure. Many other treatments including, antioxidants, medicine, and cognitive stimulation are also necessary.)

(3) (This question contains a graph for students to analyze to see if their predictions in Question 2 hold up). Is there memory improvement in the patients given glucose? Yes. What percent improvement was there? 100% improvement. Is this a complete cure for memory loss?
   • No, although there is 100% improvement in memory retention. Retention is still very low compared to a healthy youthful individual.

Assessments

Informal assessment plays a large role in this lesson. While students are working, constantly move between groups to observe student work and discussion, and scaffold understanding when needed.

U7_L4_StudentSheet_RatRecall
   • Along with this completed worksheet, students also present their question, hypothesis, experimental design, and later in the lesson, results and analysis.

Written Explanation to Concluding Question
   • Collect student explanations as a way to either summatively or formatively assess student understanding.
Teacher Content Knowledge: Explanation of the mechanism underlying age-related memory loss in the inhibitory avoidance task

If students look at the data collected comparing the latency to cross of young and old rats after treatment with glucose and epinephrine, they will notice that epinephrine enhances memory only in the young rats and not in the old rats. However, glucose is able to enhance memory in both young and old rats. Given the background that students have on the effects of epinephrine on the body, they should realize that epinephrine leads to an increase in blood glucose. So if epinephrine is unable to affect memory in old rats, but glucose on its own does, then this means that epinephrine is not acting to increase blood glucose in old rats, which suggests that epinephrine doesn’t function to breakdown glycogen in the liver in old rats.

The answer to the main question brings forth an array of even more questions. Epinephrine is not acting to increase blood glucose in rats, but why? What is the mechanism? Is epinephrine not released? Is there a problem with the receptor? Do liver cells not respond to the signal? Is there a problem with epinephrine at other target sites such as the eyes, heart, and muscles? Is there enough glycogen in the liver? Students will want know the answers to these questions. Explain to students that this is the very nature of science. When scientists have a question, they perform tests to figure out an answer. This is what the students did with this experiment. However, almost always, an answer to one question will lead to even more questions. After stating this, if students are curious about the exact mechanisms, the information below provides the explanation for what is going wrong with adrenalin in the elderly.

For a Deeper Molecular Explanation:

In aging animals, there is evidence that both the receptors on the liver are not functioning properly and that the cascades that are initiated by adrenergic signaling are also less efficient. In fact, there are less adrenergic receptors expressed on the cell surface of liver cells in aging animals. There is evidence that in aging animals there is active transport of the adrenergic receptors from the cell surface to be degraded. There is an increase in the protein arrestin, which binds to adrenergic receptors and causes their internalization from the membrane and subsequent degradation. Thus, the receptors for epinephrine are less abundant on the liver cells for signaling. Also, there is ample evidence demonstrating that the signaling cascades associated with adrenergic signaling are less robust in aging liver cells. Under normal (younger) conditions when epinephrine binds to the adrenergic receptor, the enzyme adenylate
cyclohexyl gets activated which will lead to the activation of a protein kinase that activates glycogen phosphorlyase (the enzyme responsible for the breakdown of glycogen). However, in an aging animal the proteins involved in this cascade are less efficient and produce less of a change (less amplification of the signal) so that the protein kinase that is responsible for breaking down glycogen is unable to activate as many glycogen phosphorylase enzymes. In addition, in the aging animal, glycogen storage is also inept. So even when there is ample signal to break down glycogen in the cell, there is less glycogen to break down in the cell so there is less release of blood glucose due to less glycogen available to break down.

Thus, it is likely a combination of (1) lack of receptors, (2) inefficient signal amplification of the receptors and (3) a lack of glycogen to break down in aging animals that lead to the lack of increase in blood glucose following epinephrine administration in old rats.

References