EDUCATOR GUIDE

Roberson et al. 2007. Reducing Endogenous Tau Ameliorates Amyloid β–Induced Deficits in an Alzheimer’s Disease Mouse Model.

Table of Contents

I. ARTICLE-SPECIFIC MATERIALS
   a. Connect to Learning Standards
   b. Summary of the Article for the Teacher
   c. Data Activity
   d. Related Multimedia Resources from HHMI|BioInteractive

II. GENERAL USE OF Science in the Classroom
   a. Student Learning Goals (general)
   b. Using this Resource
      i. Learning lens
      ii. Deconstructing figures
      iii. References
      iv. Thought questions
   c. Suggestions for Classroom Use
ARTICLE-SPECIFIC MATERIALS

Connections to the nature of science from the article

- Provide explanations to observations and data.
- Recognize challenges and limitations of an experimental model.

The importance of this scientific research

- Will inform wildlife conservation and management policies.

The actual science involved

- DNA fragment analysis (genotyping)
- Polymerase chain reaction
- DNA extraction
- Statistics

Connect to Learning Standards

The Next Generation Science Standards

- Practice 2: Developing and Using Models
- Practice 4: Analyzing and Interpreting Data
- Practice 6: Constructing explanations (for science) and designing solutions (for engineering)

The AP Biology Standards

- Essential knowledge 3.A.1: DNA, and in some cases RNA, is the primary source of heritable information.
- Essential knowledge 3.A.3: The chromosomal basis of inheritance provides an understanding of the pattern of passage (transmission) of genes from parent to offspring.
- Essential knowledge 3.C.1: Changes in genotype can result in changes in phenotype.
- Essential knowledge 3.E.2: Animals have nervous systems that detect external and internal signals, transmit and integrate information, and produce responses.
Key Ideas and Details: CCSS.ELA-LITERACY.RST.11-12.2. Determine the central ideas or conclusions of a text; summarize complex concepts, processes, or information presented in a text by paraphrasing them in simpler but still accurate terms.

Craft and Structure: CCSS.ELA-LITERACY.RST.11-12.6. Analyze the author’s purpose in providing an explanation, describing a procedure, or discussing an experiment in a text, identifying important issues that remain unresolved.

Integration of Knowledge and Ideas: CCSS.ELA-LITERACY.RST.11-12.8. Evaluate the hypotheses, data, analyses, and conclusions in a science or technical text, verifying the data when possible and corroborating or challenging conclusions with other sources of information.
Summary of the Article for the Teacher

It is recommended that this not be used by students in place of reading the article.

General overview
It is well known that plaques made of amyloid-β proteins and tangles made of abnormal tau proteins are found in the brains of Alzheimer's disease patients, but the exact role of each of those proteins is still not completely clear. In the 1990s, scientists rallied around an idea called the "amyloid hypothesis," which states that amyloid-β first starts building up into plaques, causing tau proteins to become abnormal and cease functioning. This then causes neurons to die and tangles of abnormal tau proteins to form. The amyloid hypothesis led the field to focus on amyloid-β as the primary culprit in Alzheimer's disease, but years of unsuccessful treatments targeting the amyloid plaques meant that it was time for the role of tau to be more fully investigated.

This paper attempts to answer the question of how amyloid and tau proteins interact to cause the symptoms seen in Alzheimer's disease. It shows that tau mediates amyloid-β's function in a model of Alzheimer's disease. If there is no tau present, amyloid-β does not seem to be able to cause the usual damage. There are fewer memory problems and other related issues, even though the amyloid-β and the plaques it forms are still there. This means that tau has a bigger role in Alzheimer's disease than previously thought.

Why this research is important
This paper is the first clear evidence that the amount of tau in the brain can have an effect on how much damage amyloid-β can cause in the brain. Prior to this point, neuroscientists tended to either believe that amyloid-β or tau were the main culprit, but the research published in this paper shows that both proteins are likely involved, working together or having other synergistic effects.

Methods used in the research
- Transgenetic mice
- Rodent behavior and spatial learning tasks (Morris water maze, Y maze)
- Induced seizure
- Histology and immunostaining of brain tissue

Areas of further study
Since this paper's publication, the field has evolved tremendously, and the idea that both proteins play a critical role in the progression of the disease is now commonly accepted. Current studies test drugs that target the abnormal tau levels as well as the amyloid-β, and clinical trials are underway.
Discussion Questions by Standards

**Vision and Change Core Competencies and Disciplinary Practice**
Competency 6 – Ability to understand the relationship between science and society

- Why is it important to study Alzheimer's disease?

**AP Biology Science Practices**
Practice 4 – The student can plan and implement data collection strategies appropriate to a particular scientific question.

- Since it's not possible or ethical to breed people without tau similar to breeding mice without tau, what are some other ways we could study the effect of tau in Alzheimer's patients and other human populations?

Practice 6 – The student can work with scientific explanations and theories.

- What are some of the limitations of using a mouse model? What are some of the benefits?

**NGSS Crosscutting Concepts**
Concept 3 – Scale, proportion, and quantity: Students understand the significance of a phenomenon is dependent upon the scale, proportion, and quantity at which it occurs

- Why did the authors make the effort to test mice with three different levels of tau (normal, half, and no tau)? What can an experiment that uses three levels of tau tell us that an experiment with just two levels might not?

**Common Core ELA Standards, Science & Technical Subjects, Grade 11-12**
11-12.6 – Analyze the author's purpose in providing an explanation, describing a procedure, or discussing an experiment in a text, identifying important issues that remain unresolved.

- What is the next experiment you might want to do in mice to further examine how tau and amyloid-β interact?
Data Activity

This annotated paper is accompanied by three data activities on the paper's activity page.

The downloadable water maze activity is based on behavioral recordings made by one of the co-authors that are similar to the recordings described in the published study. The activity asks students to make predictions and determine whether the recorded animal is memory-impaired by making observations from video recordings and an image of a swimming path trace. An educator version with answers to the questions listed in the activity is also available.

The other two activities are links to resources from HHMI BioInteractive that complement the annotated paper and the water maze activity. The online interactive activity in particular will help students understand the anatomical and histological manifestations of Alzheimer’s disease and its genetic basis. In the other activity, students interpret and discuss a graph from the study. Educator guides accompanying both resources are available on the BioInteractive website.
Multimedia Resources from HHMI BioInteractive (www.BioInteractive.org)

**Online Interactives**

**Alzheimer’s Disease: Piecing Together the Evidence**

**Lectures**

**Memories are Made of This**

**Making Your Mind: Molecules, Motion, and Memory**
(http://www.hhmi.org/biointeractive/making-your-mind-molecules-motion-and-memory). Eric R. Kandel, MD and Thomas M. Jessell, PhD of Columbia University will help us understand how the brain is organized and identify the seat of human memory.

**Videos and Animations**

**Video: Think Like a Scientist – Inside Alzheimer's Disease**
(https://www.youtube.com/watch?v=mqeVxeBkcCA). In this HHMI and Nautilus Magazine collaboration, journalist Greg O'Brien reveals his struggle living with Alzheimer's Disease. Harvard scientist, Rudy Tanzi, explains the mechanism by which this disease insidiously robs the identities of those affected and explains what it means to think like a scientist when searching for a treatment.

**Video: Mice Navigate a Barnes Maze to Test Spatial Learning**
(http://www.hhmi.org/biointeractive/mice-navigate-barnes-maze-test-spatial-learning). Mice can be trained to use spatial cues to navigate a maze that tests their ability to remember specific locations.

**Video: Visualizing Learning**
(http://www.hhmi.org/biointeractive/visualizing-learning). Dr. Harshad Vishwasrao guides you through a collection of images showing neuronal growth and synaptic formation representative of anatomical changes that occur during learning.

**Animation: Molecular Activity in Aplysia Long-Term Memory**

**Animation: Molecular Activity in Aplysia Short-Term Memory**

**Animation: Molecular Basis of Early LTP (Short-Term Memory)**
Animation: Molecular Basis of Late LTP (Long-Term Memory) (http://www.hhmi.org/biointeractive/molecular-activity-aphysia-long-term-memory). Late LTP (long-term memory) involves dopamine activation of CREB to support new synaptic growth.

Feature Film (HHMI Tangled Bank Studios)
Can Alzheimer’s Be Stopped? (http://www.tangledbankstudios.org/films/can-alzheimers-be-stopped). Alzheimer’s disease ravages the minds of over 40 million victims worldwide, and it is one of the greatest medical mysteries of our time. Join investigators as they attempt to reconstruct the molecular chain of events that ultimately leads to dementia, and meet individuals from all walks of life who will reveal what it’s like to struggle with Alzheimer’s.

Data Point

Image of the Week

Collection
Neuroscience (http://www.hhmi.org/biointeractive/neuroscience-collection). A rich variety of videos, interactive modules, and animations to teach about the nervous system.
GENERAL USE OF SCIENCE IN THE CLASSROOM

Student Learning Goals

“One fundamental goal for K-12 science education is a scientifically literate person who can understand the nature of scientific knowledge.”

The U.S. National Academy of Sciences defines science as: “Any new finding requires independent testing before it is accepted as scientific knowledge; a scientist is therefore required to honestly and openly report results so that they can readily be repeated, challenged, and built upon by other scientists. Proceeding in this way over centuries, the community effort that we call science has developed an increasingly accurate understanding of how the world works. To do so, it has had to reject all dogmatic claims based on authority, insisting instead that there be reproducible evidence for any scientific claim.”

An important student learning goal, central to any understanding of “the nature of scientific knowledge,” is to give each student an appreciation of how science is done.

This includes knowing why:

- Scientists must be independent thinkers, who are free to dissent from what the majority believes.
- Science can deal only with issues for which testable evidence can be obtained.
- All scientific understandings are built on previous work
- It is to be expected that one scientist’s conclusions will sometimes contradict the conclusions of other scientists.
- Science is a never-ending venture, as the results from one study always lead to more questions to investigate.

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1 A Framework for K-12 Science Education, National Research Council, 2012
Using This Resource

Learning lens
The Learning Lens tool can be found on the right sidebar of each resource and is the source of annotations. Click on the headings to highlight portions of the text of the corresponding research article. A subsequent click on the highlighted text will produce a text box containing more information about that particular piece of text. Below is an example of the Glossary function of the Learning Lens.

An example of the resource with the Glossary, Previous Work, Author’s Experiments, News and Policy Links, and References and Notes tools turned on. The Glossary tool is in use.
Deconstructing figures
Annotation tabs within the text accompany each figure and are designed to help students deconstruct the methods and data analysis contained within each figure.

Fig. 1. Spatial distribution of head scales. (A) Head scales in most snakes (here, a corn snake) are polygons (two upper panels) with stereotyped spatial distribution (two lower panels): left (yellow) and right (red) scale edges overlap when reflected across the sagittal plane (blue). (B) Polygonal head scales in crocodiles have a largely random spatial distribution without symmetrical correspondence between left and right. (C) Head scales from different individuals have different distributions of scales’ sizes and localizations (blue and red edges from top and bottom crocodiles, respectively).

The authors took 120 color pictures of each animal to create detailed, three-dimensional models of reptile heads. Watch this video in which the authors further explain their modeling methods:

http://www.sciencemag.org/content/suppl/2012/11/29/science.1226265.DC1/1...
References
Selected references are annotated in the reference section of each resource. The annotations contain a short statement about how or why a reference relates to the current research study.

19. Lewejohann et al., Environmental bias: Effects of housing conditions, laboratory environment and experimenter on behavioral tests. Genes Brain Behav. 5, 64 (2006).
**Thought questions**

Thought questions are located above the learning lens in the right sidebar of each resource. These questions were written to be universal and applicable to any primary research paper. Thought questions do not have a single answer, or a correct answer, and can be used to stimulate discussion among students.
Suggestions for classroom use
In addition to the thought questions discussed above, other resources are provided for use in the classroom. These can be found at the beginning of the teacher guide.

General suggestions on how to use the *Science* in the Classroom articles:

1. Assign to student groups to read and discuss during class.
2. Assign small sections of the article to student groups to read and discuss during class, with the expectation that they will present or use jigsaw to teach the entire class what is in their part of the article.
3. Assign to individual students to complete during class or as homework.

Some ideas for interactive student engagement after reading the article:

1. Students write answers to discussion questions (for example, those linked to the standards or those linked to the diagrams).
2. Go over the abstract, as well as information about the purpose and structure of an abstract, and have students write their own abstracts for the articles in language that could be understood by their peers.
3. Have students edit the article, or parts of the article, to a simpler reading level.
4. Have students, alone or in small groups, use the annotated list of references to explain how the scientists who wrote this article built on the published work of at least one independent group of scientists in making their discoveries. In the process, did they produce data that supports the findings of the earlier publication that they have cited in the text? In what way does this article support the statement that scientific knowledge is built up as a “community effort?”
5. Use the article and discussion questions linked to the standards and the diagrams for a teacher-led classroom discussion. The discussion can focus on the nature of science and scientific research, as well as on the science in the article itself.
6. Have students give a classroom presentation about the article, parts of the article, or their answers to discussion questions.