

THE GENETICS OF LEARNING AND MEMORY

Another Great Debate

Is Butter Better?

Which one is better for you, butter or margarine? The merits of butter vs. margarine have been debated since 1869 (yes, for 133 years!). Just as everyone gets comfortable with the answer, a new study comes out that heats up the debate again. Other familiar medical and scientific debates include: Are low carbohydrate diets a safe, reliable way to lose weight? Should you take aspirin to reduce your risk of a stroke? Do cell phones increase the risk of brain tumors? The answer to each of these should be based on scientific evidence. Shouldn't they stand the test of time?

Sometimes new data do conflict with the existing evidence for a scientific explanation. When this happens, scientists need to examine both sets of data carefully to determine if the conflict can be resolved through further experimentation, or if a new explanation needs to be proposed. Here is an example of another scientific debate taking place over the growth of new neurons in learning and memory centers of the brain.

**A NEW SCIENTIFIC DEBATE:
SHOULD WE QUESTION THE EVIDENCE OR THE EXPLANATION?**

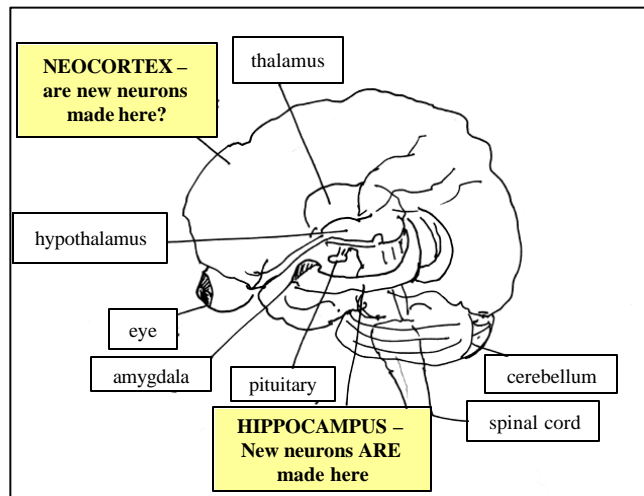
Of the 100 billion nerve cells in your brain, how many of them have been made since your birth?

Did you say “zero”? If you said that 10 years ago, your answer would have been correct. But if you gave that answer today, your answer may be wrong. How is it possible for a scientific explanation to change?

The Background

Until just a few years ago, scientists were confident that no new neurons were made after birth. They explained that all of our neurons were formed before we were born. In the past decade or so, scientists have begun to question this explanation by showing that new neurons are made in two regions of the brain – the hippocampus and the olfactory bulb. And these new neurons have been discovered in bird, mouse and human brains.


For years, scientists have searched for nerve cell growth in other areas of the brain. Despite these efforts, scientists have come up empty, leading to the conclusion that only some regions of our adult brains make new neurons.



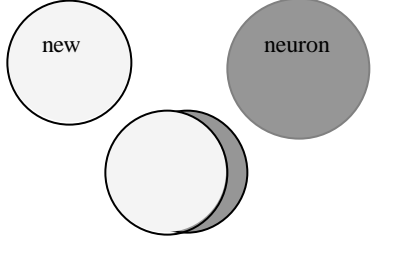
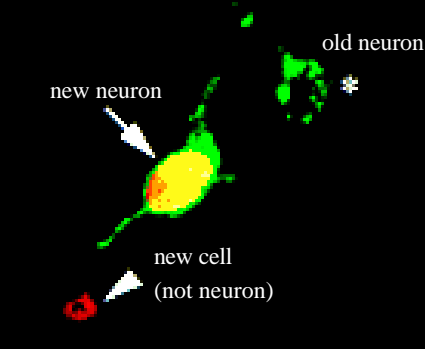
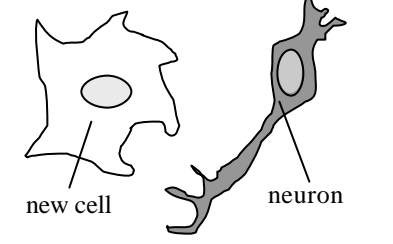
In 1999, an extraordinary report by Elizabeth Gould provided new evidence for neuron growth in the neocortex of monkeys. In humans, the neocortex, or “thinking cap” is important for reasoning and remembering. If this new report is valid, it may lead to advances in restoring human memory in patients with brain injuries and Alzheimer’s disease.

The New Evidence

In order to test whether new neurons were being made in the neocortex, researchers working with Dr. Gould used a technique to visually “tag” cells according to their cell-type and age.

	<p>Think of going to a dance club. Walking in, everyone pretty much looks the same. But under the lights on the dance floor, people wearing white t-shirts appear to “glow”. Under the lights of a microscope, “tagged” cells glow, allowing scientists to tell them apart from other cells.</p>
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DNA is made within new cells. Cells were tagged with a fluorescent molecule that detects DNA synthesis, which occurs only in new cells. If cells were found that were glowing, that would be evidence that new cells were being created. A second tag that only detects neurons was used to distinguish neuron cells from non-neuron cells.

 <p>Cells tagged as both “neuron” and “new” appear as a different color.</p>	
 <p>Some tags label the whole cell, other just label the nucleus.</p>	<p>Tags provide evidence for new cells in the neocortex.</p> <p>This photograph of nerve cells is part of the original article published in SCIENCE Volume 286, Number 5439 Issue of 15 October 1999, pp. 548-552 ©1997 by The American Association for the Advancement of Science.</p>

Using these cell tags, Gould’s research team found evidence of individual cells tagged as both “new” and “neuron” in the neocortex.

The New Explanation

The data that Gould and her colleagues collected showed that cells tagged as both “new” and “neuron” were present in the neocortex of adult monkeys. Based on this new evidence, Dr. Gould and her colleagues concluded: “Although most neocortical neurons are generated pre-natally, our findings indicate that neurons are added to primate neocortex in adulthood”. Dr. Gould’s findings directly conflict with evidence from previous studies that suggested that no new neurons were formed in the neocortex after birth. However, the conclusions from her work have created a lot of excitement in neuroscience and medicine.

So why is this significant for medical knowledge?

The amazing conclusion that new neurons can grow in the brain raises the possibility that nerve cells can be replaced. "It shows there are natural mechanisms in the brain that, someday, might be harnessed for therapeutic purposes to replenish damaged areas of the

brain," says Dr. Gould (<http://www.princeton.edu/pr/news/99/q4/1014-brain.htm>). For example, this could lead to new therapies to treat brain diseases such as Alzheimer's.

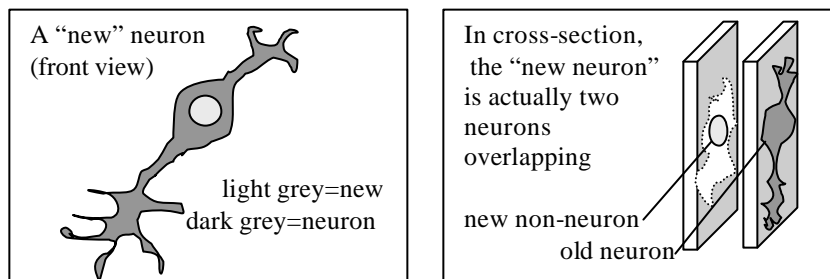
The areas of the brain where new neurons were discovered are important for learning and memory. Dr. Gould and her colleagues predict that: "The presence of new neurons in brain areas involved in learning and memory... may play a role in these functions... Perhaps these immature neurons are capable of undergoing structural changes rapidly and therefore may serve as a substrate for learning."

Overall, if these discoveries hold up, they could change how we think about the brain and human memory. But, there may be a twist...

Challenging the New Explanation by Re-Examining the New Evidence

Dr. Gould's research led not only to excitement about new neuron growth, it also led to some skepticism from other scientists.

Two researchers in particular, Pasko Rakic and David Kornack tested the evidence from Gould's study and found that they could not reproduce her results. By taking a more careful look at the cells Gould claims are "new neurons", they observed that the "new neurons" were really just a new non-neuron cell hiding behind an old neuron cell. For example, an old neuron (there since birth) could have been overlapping a new cell that is not a neuron (like a glial cell).



Both studies were carefully designed and although the data appear to be valid, the two studies reach different conclusions. So how does this debate get resolved?

The Debate

The debate over new neurons in the neocortex still continues. Research teams on both sides of the debate are working to reproduce the two studies side-by-side. The results from reproducing the studies may strengthen one argument and weaken the other.

In addition to these two groups, researchers around the globe are collecting evidence and providing explanations to add fuel to the debate. So where does this leave us? Are our brains capable of producing new neurons?

Even though we might want to know the “correct” explanation for the data, the debate and uncertainty over the growth of new neurons is not a sign of weakness. Many of the strongest scientific explanations have developed through debates like this one. All of the research and debate between scientists will eventually strengthen the prevailing scientific idea – whether it is that new neurons grow in the neocortex or not. For now, it is probably best not to count on brain cell regeneration and hold on to the brain cells that we’ve got.

Decide for Yourself: Read the Literature

Go to the Explore!Gallery to see the actual research articles, published in the Journal *Science*. In addition, researchers from the two opposing sides make their cases in a published debate. Read the debate and the original articles to decide whom you would side with.

Research Articles

Gould, E., Reeves, A., Graziano, M., and Gross, C. (1999). Neurogenesis in the Neocortex of Adult Primates. *Science* 286: 548-552.

Kornack, D., and Rakic, P. (2001). Cell Proliferation Without Neurogenesis in Adult Primate Neocortex. *Science* 294: 2127-2130.

Debate

Nowakowski, R., Hayes, N., Gould, E., and Gross, C. (2000). New Neurons: Extraordinary Evidence or Extraordinary Conclusion? *Science* 288: 771

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Questions for Discussion

Please answer the following questions:

1. What are the two rival explanations discussed in this article? What evidence do the two groups use to support their explanations?
2. Dr. Rakic and Dr. Kornack don't accept Dr. Gould's conclusion. Why not? Where do they think she made a mistake?
3. The research described here relates to what you have learned about neurons and the molecular basis of memory. Are structural changes in neurons required for both long and short-term memory, or are they a characteristic of only one type of memory? How would new neurons contribute to long-term memory?
4. Of the following, pick the most scientifically accurate statement and defend it:
 - a. The research reported here is an example of sloppy, poorly done science, as scientific knowledge should not change. If it does, something or someone is wrong.
 - b. The research reported here is an example of how science is typically done, and how scientific knowledge can change. These changes are due to new technology, new evidence, or new ways of thinking.
5. Which of the aspects of the nature of science listed below can be found in the article? List the characteristics of science and/or scientific knowledge found in the article and discuss them.
 - ?? Scientific knowledge changes over time to be consistent with evidence and/or new reasoning.
 - ?? Scientific knowledge is reliable because it is continually tested and evaluated.
 - ?? Scientific explanations are often debated, leading to the tentative yet durable nature of science.
 - ?? Evidence and explanations are not the same.
 - ?? Objectivity is an important part of the scientific process.
 - ?? Scientific data must be the result of carefully designed tests and observations and the data must be repeatable.
 - ?? Scientific investigations are based upon an understanding of existing ideas.
 - ?? Because scientists are influenced by what they already know, multiple explanations can be produced from the same set of data.