Technology
PUBLISHED BY MIT Review

Wednesday, February 04, 2009

A Comeback for Lamarckian Evolution?

Two new studies show that the effects of a mother's early environment can be passed on to the next generation.

By Emily Singer

The effects of an animal's environment during adolescence can be passed down to future offspring, according to two new studies. If applicable to humans, the research, done on rodents, suggests that the impact of both childhood education and early abuse could span generations. The findings provide support for a 200-year-old theory of evolution that has been largely dismissed: Lamarckian evolution, which states that acquired characteristics can be passed on to offspring.

"The results are extremely surprising and unexpected," says Li-Huei Tsai, a neuroscientist at MIT who was not involved in the research. Indeed, one of the studies found that a boost in the brain's ability to rewire itself and a corresponding improvement in memory could be passed on. "This study is probably the first study to show there are transgenerational effects not only on behavior but on brain plasticity."

In recent years, scientists have discovered that epigenetic changes--heritable changes that do not alter the sequence of DNA itself--play a major role in development, allowing genetically identical cells to develop different characteristics; epigenetic changes also play a role in cancer and other diseases. (The definition of epigenetics is somewhat variable, with some scientists limiting the term to refer to specific molecular mechanisms that alter gene expression.) Most epigenetic studies have been limited to a cellular context or have looked at the epigenetic effects of drugs or diet in utero. These two new studies are unique in that the environmental change that triggers the effect--enrichment or early abuse--occurs before pregnancy. "Give mothers chemicals, and it can affect offspring and the next generation," says Larry Feig (http://www.tufts.edu/med/biochemistry/faculty/feig/feig.html) , a neuroscientist at Tufts University School of Medicine, in Boston, who oversaw part of the research. "In this case, [the environmental change] happened way before the mice were even fertile."

In Feig's study, mice genetically engineered to have memory problems were raised in an enriched environment--given toys, exercise, and social interaction--for two weeks during adolescence. The animals' memory improved--an unsurprising finding, given that enrichment has been previously shown to boost brain function. The mice were then returned to normal conditions, where they grew up and had offspring. This next generation of mice also had better memory, despite having the genetic defect and never having been exposed to the enriched environment.

The researchers also looked at a molecular correlate of memory called long-term potentiation, or LTP, a mechanism that strengthens connections between neurons. Environmental enrichment fixed faulty LTP in mice with the genetic defect; the fixed LTP was then passed on to their offspring. The findings held true even when pups were raised by memory-deficient mice that had never had the benefits of toys and social interaction. "When you look at offspring, they still have the defect in the protein, but they also have normal LTP," says Feig. The findings were published today in the *Journal of Neuroscience* (http://www.jneurosci.org/) .

"If the findings can be conveyed to human, it means that girls' education is important not just to their generation but to the next one," says Moshe Szyf (http://www.medicine.mcgill.ca/pharma/mszyflab/Main.htm) of McGill University, in Montreal, who was not involved in the research.

In a second study, researchers found that rats raised by stressed mothers that neglected and physically abused their offspring showed specific epigenetic modifications to their DNA. The abused mice grew up to be poor mothers, and appeared to pass down these changes to their offspring.

Previous research has shown that bad rat mothering can be passed down through this kind of DNA modification--but those changes are thought to be triggered specifically by maternal behavior. In the new study, researchers also had healthy mothers raise the offspring of stressed mothers, and found that the problems were only partially fixed. That suggests that the changes "were not due to their neonatal experience," says David Sweatt (http://neurobiology-uab.infomedia.com/bios.asp?action=form&recordID=146774) , a

neuroscientist at the University of Alabama at Birmingham, who oversaw the study. "It was something that was already there when they were born." The research was published online last month in *Biological Psychiatry* (http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6T4S-4VCNF2J-1&_user=10&_coverDate=01%2F15%2F2009&_rdoc=10&_fmt=high&_orig=browse&_srch=doc-info(%23toc%234982%239999%23999999999%2399999%23FLA%23display%23Articles)&_cdi=4982&_sort=d&_docanchor=&_c) .

The results of both studies are likely to be controversial, perhaps resurrecting a centuries-old debate. "It's very provocative," says Lisa Monteggia (http://www.utsouthwestern.edu/findfac/professional/0,,46977,00.html) , a neuroscientist at the University of Texas Southwestern Medical Center, in Dallas. "It goes back to two schools of thought: Lamarck versus Darwin."

In contrast to natural selection, in which organisms that are born well adapted to their environment survive and reproduce, passing down those successful traits, Lamarckian evolution suggests that animals can develop adaptive traits, such as better memory, during their lifetimes, and pass on those traits to their offspring. The latter theory was largely abandoned as Darwin's, and later Mendel's, theories took hold. But the concept of Lamarckian inheritance has made a comeback in recent years, as scientists learn more about epigenetics.

"I didn't set out to come up with findings that support neo-Lamarckian inheritance," says Sweatt. "But the research now makes it more plausible that these things may be real and may be based in molecular mechanisms."

Feig, on the other hand, argues that while the findings are "a Lamarckian kind of phenomenon it's still Darwinian, because the changes don't last forever." In Feig's study, the offspring of enriched mice lost their memory benefits after a few months.

Sweatt and others say that this type of inheritance may in fact be much more common than expected. Improving technologies are now providing a broader look at the epigenetic changes linked to environment and behavior. Scientists are starting to use DNA microarrays, which over the past few years have become widely employed in genetic studies of disease, to look at one specific type of change, known as DNA methylation. "The changes we see are not limited to a small number of genes," says Szyf, who is using the technology to study epigenetics and cancer. "Whole circuitries are changed."

DNA sequencing, which is rapidly dropping in price, can also be used to study DNA methylation. But epigenetics studies require high-volume sequencing, which has been prohibitively expensive. "In contrast to the genome, every epigenome is different in different types of cells," says Sweatt. "A human epigenome project would be the equivalent of 250 human genomes, because there are at least 250 cell types in the body." Cheap sequencing may soon make that type of study possible, he says.

The actual mechanism underlying these patterns of inheritance is somewhat mystifying to scientists. Feig theorizes that environmental enrichment triggers a long-lasting hormonal change: when the animal becomes pregnant, the hormone would somehow modify the DNA of the fetus, ultimately causing it to have improved memory and LTP as an adolescent. However, he cautions, there is no direct evidence of this, and no specific evidence that the behaviors are transmitted through epigenetic mechanisms.

Upcoming Events

BetterWorld at MIT Conference (http://www.betterworldatmit.org)
MIT Media Lab, Cambridge, MA
Friday, April 30, 2010
http://www.betterworldatmit.org (http://www.betterworldatmit.org)

FEI 2010 – The Annual Front End of Innovation Conference A New Front End: The Era of Collaboration (http://www.iirusa.com/feiusa/fei-home.xml?registration=FEI2010TECHREV)
Boston, MA
Monday, May 03, 2010 - Wednesday, May 05, 2010
http://www.iirusa.com/feiusa/fei-home.xml?registration=FEI2010TECHREV (http://www.iirusa.com/feiusa/fei-home.xml?registration=FEI2010TECHREV)

BIO International Convention (http://convention.bio.org)
Chicago, IL
Monday, May 03, 2010 - Sunday, May 10, 2009
http://convention.bio.org (http://convention.bio.org)

MIT Sloan CIO Symposium (http://www.mitcio.com)
MIT Campus, Cambridge, MA
Wednesday, May 19, 2010
http://www.mitcio.com (http://www.mitcio.com)

Tech Connect World (http://www.techconnectworld.com)
Anaheim, CA
Monday, June 21, 2010 - Friday, June 25, 2010
http://www.techconnectworld.com (http://www.techconnectworld.com)

2010 IEEE Conference on Innovative Technologies for an Efficient and Reliable Electricity Supply (http://www.ieee-energy.org/)
Waltham, Massachusetts
Sunday, September 27, 2009 - Tuesday, September 28, 2010
http://www.ieee-energy.org/ (http://www.ieee-energy.org/)