

### Plasticity: With Neurogenesis, Old Brains Can Be Young Again

Stretching and relaxing the mind causes neurogenesis. The benefits of “learning how to learn” or following the learning cycle are not limited to young persons but can be enjoyed by all. If you want to maintain a healthy brain into old age, it's important to do this. Good habits of learning established now can give you strong protection against mental decline. If you are elderly, practising the learning cycle can rejuvenate your brain.

Neurogenesis gives adult brains similar plasticity to that seen in infant brains, according to results from a new study published this week in *Neuron*. Researchers found that new neurons between four to six weeks of age in the adult mouse brain undergo a brief critical period of increased adaptability to stimuli before maturing, a similar process to what occurs in newborn animals.

Evidence shows that the same is true for humans. Neurogenesis happens when we learn, but only when we learn in the natural way and do things in the right order. You will find more information about how to do this in the tutorials.

“I think it's very interesting, and it suggests that these new neurons go through different developmental stages functionally and that at a specific period after their production, they may be especially sensitive to stimuli involved in learning,” Elizabeth Gould of Princeton University in Princeton, N.J., who was not involved with the study, told *The Scientist*.

Scientists have long debated the physiological behavior of new neurons in the adult brain. Behavioral studies suggest that new neurons in adult brains have to mature for one to three weeks before becoming integrated into existing circuitry, said senior author Hongjun Song of

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Written by NHA

Thursday, 30 April 2009 03:41 - Last Updated Wednesday, 31 July 2013 14:46

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Johns Hopkins University School of Medicine in Baltimore, Md. The new findings, however, showed that the maturation period is slightly longer -- new neurons in the adult age about four to six weeks before integration into the existing network of mature neurons.

To examine whether new neurons were physiologically similar to old neurons, Song and colleagues monitored electrophysiological properties of newly generated dentate gyrus cells in the adult mouse hippocampus. They infected the cells with a retrovirus expressing green fluorescent protein and examined brain slices in vitro in response to stimulation, to see whether they showed long term potentiation (LTP), an indication of learning and memory. At two weeks of age, the neurons showed levels of LTP similar to those seen in mature neurons. Between four to six weeks of age, however, the neurons showed increased sensitivity to stimuli and significantly higher levels of LTP, after which LTP fell to levels seen in mature neurons. This is the same pattern exhibited by neurons from newborn mice. It's unclear whether new neurons exhibiting high plasticity have any transient effects on existing mature neurons, the authors note.

“Not only are the new neurons connected up early, but they are showing a form of synaptic plasticity that we know is associated with learning very early on,” said Gould.

Song said he was surprised by the timing of the plasticity and the similarity of new neurons in adults to neurons in newborns. “It's a different environment but basically [adult cells] do exactly the same thing normally a young cell would do in fetal development,” he said.

“That is very interesting to show that after let's say two months, the newborn neurons could become identical to preexisting neurons. That was not known,” said Pierre-Marie Lledo of Pasteur Institute in Paris, France, who was not involved with the work.

When Song's group blocked the expression of a particular N-methyl-D-aspartate receptor known to be involved in early postnatal development, NR2B, new adult neurons no longer displayed a period of increased plasticity, suggesting that this receptor is important for plasticity in both the adult and newborn brain.

Results from the study suggest that new neurons, by showing a reduced threshold for response, are more involved than their mature neighbors in memory formation, said Paul Frankland of the

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Hospital for Sick Children Institute in Toronto, Canada, who was not involved with the work.

This is consistent with findings he published earlier this year, which showed adult mice recruit new neurons during spatial memory tasks. "What that suggests is that there's something special about the contributions these new neurons may make. And I guess the question that is unanswered, and that people are interested in, is what is the nature of that contribution? What's special about these new neurons?" Frankland said. "I think that's probably what people are going to ask in the next two to three years."

Song said he plans to investigate the molecular mechanisms that determine how young cells incorporate into old circuitry. The findings may ultimately help reveal how stem cell therapy can repair the brain. Ideally, a few new neurons will rejuvenate the system, he said. "I think the idea is emerging that adaptation of old circuitry or increasing plasticity of the old circuitry can help with recovery," he said.

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### Sources

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