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New neurons take six months or more to mature in non-human primate brain

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New neurons take more than six months to mature in adult monkeys and that time is likely even longer in humans, according to researchers at the University of Pittsburgh School of Medicine, the University of Illinois, and Pennsylvania State University. Their findings, reported this week in the online version of the *Proceedings of the National Academy of Sciences*, challenge the notion that the time it takes for neurogenesis is the reason anti-depressant medications are not fully effective until three to five weeks after treatment begins.

The dentate gyrus of the brain's hippocampus is known to be where new neurons still form in adult mammals, and this region is thought to play a significant role in learning and memory, cognitive change with aging, depression and schizophrenia, and other brain processes, said Judy Cameron, Ph.D., professor, Department of Psychiatry, University of Pittsburgh School of Medicine, and senior scientist, Oregon National Primate Research Center, Oregon Health and Science University.

"Expanding our knowledge beyond rodent models to understand how neurons mature in non-human primates will give us more insight into what happens in the human brain," she said. "In rodents, neuronal maturation happens in four weeks, which is considerably different than what we have found in our monkey studies."

Dr. Cameron, co-senior scientist William T. Greenough, Ph.D., of the University of Illinois, and the team gave adult monkeys injections of an agent called BrdU, which gets incorporated into replicating DNA and

thus serves as an indicator of new neuron formation. At different time points after the injections, they examined the brain tissue to look for markers of stages of maturation in tiny neurons called granule cells.

Six weeks after an injection, 84 percent of the new cells still bore markers of immaturity and were immature in shape; in a rodent, all of the cells would have matured by this time. Only a third of the monkey granule cells had markers of maturity up to 28 weeks after BrdU injections.

That means the majority of new granule cells will not reach maturity until more than six months have passed, Dr. Greenough and colleagues said. Also, because the human brain is larger than the monkey brain and takes longer to develop, maturation of adult human neurons would likely be further lengthened.

The longer period of new granule cell maturation in primates argues against the hypothesis, based on rodent models, that the onset of effectiveness of antidepressant medications at three to five weeks is related to neurogenesis and maturation of these cells.

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