animals seized and their hippocampal damage was barely detectable.

As impressive as the results were, says McNamara of Duke, it's still not clear from this early study exactly how the antibodies subdue the NMDA receptor. But the approach is promising, he adds: "If the results are indeed mediated by antibodies, then [having antibodies available during] the fleeting and localized disruption of the blood-brain barrier would be advantageous."

Also unclear is how directly the strategy could be translated into a human treatment. The NMDA blockers already in use to treat stroke can cause hallucinations and other symptoms of psychosis in humans. While that may be an acceptable risk for someone who would otherwise lose more brain tissue to a stroke, it poses a problem for a pretreatment scheme that would allow NMDA inhibitors to circulate before an injury. The antibodies could also impair learning by blocking or damaging NMDA receptors, although During says that preliminary results suggest that this doesn't happen.

And During is not wed to the vaccination technique. Directly injecting NMDA antibodies could also do the trick, he says. During hopes to eventually test that in humans by treating people at extremely high risk for stroke with NMDA antibodies. After a hemorrhage on the surface of the brain, for example, people have a 50% chance of suffering a stroke within the next week. During's hope is to protect the brain before disaster strikes.

–LAURA HELMUTH

NEUROSCIENCE

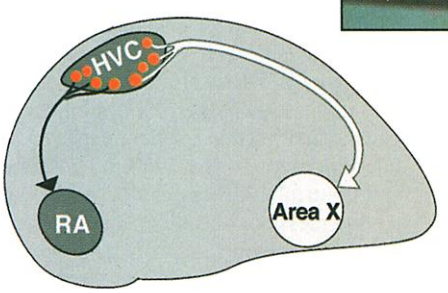
Death Triggers Regrowth Of Zebra Finch Neurons

Until recently, scientists assumed that adult brains were doomed to constant, steady decline. Shortly after birth, it seemed, neurons lost their ability to grow, and cells that died could not be replaced—a gloomy outlook indeed. But in the past few years, scientists have found that certain kinds of neurons can grow in adult brains, including those of humans. Not only has this turned scientific dogma on its head, but it has also provided the first glimmer of hope for those suffering from degenerative brain diseases or paralyzing spinal cord injuries. Exactly what allows some brain neurons to grow while others can't remains mysterious, however. Now, new work in songbirds may provide a clue.

In the 24 February issue of *Neuron*, neuroscientists Constance Scharff and Fernando Nottebohm of The Rockefeller University in New York City, Jeffrey Macklis of Harvard Medical School in Boston, and their colleagues report that the brains of adult male songbirds can recruit certain kinds of neurons to grow and replace cells that have died. What's more, the experiments suggest that the new neurons are fully functional. But the recruitment is selective; only certain cells have this phoenixlike quality.

The work suggests that "the brain can make new neurons, but it can't make all of them," explains neuroscientist Allison Doupe of the University of California, San Francisco. Researchers now hope to discover what causes that selective recruitment so that they can eventually trigger the growth of all types of neurons.

The new findings emerged from the Nottebohm team's investigations into a long-studied phenomenon in canaries. Male canaries use complex songs to court their mates. Each fall, however, the birds curiously lose their ability to carry a tune, and the songs become muddled. Then in the spring, just in time for courting season, the canaries regain the ability to sing their intricate songs.



Selective rebirth. Death of zebra finch neurons that project from the brain's HVC region to the RA region can trigger new neuron growth. But neurons that project to area X cannot regrow.

Decades of research by Nottebohm and others have provided a partial explanation for these changes. They have uncovered the key brain areas that govern this song behavior. One is the high vocal center, or HVC. Some neurons in this region send axons into the so-called RA region, which helps to control the muscles involved in singing. It turns out that in canaries, many of these HVC → RA neurons die each fall, around the same time the birds forget their complex songs. A short time later, a spurt of neuron growth occurs. Researchers have long wondered what triggers the neuron growth, as well as whether the cell death and regrowth affect singing ability.

Macklis, Nottebohm, and Scharff suspected that the stimulus for the neuronal regrowth might simply be the death of old neurons. To test that idea, they turned to the study of zebra finches. Unlike canaries, zebra finches do not forget their mating songs, nor do the neuron populations of their HVC region fluctuate seasonally. Rather, a few new neurons constantly grow into the region. To see whether neuronal death indeed triggers regrowth, the team used a method devised by Macklis that could kill selected types of neurons in living animals.

Working in zebra finches, the team selectively killed the kind of neurons that normally regrow—the HVC cells that send axons to the RA region. Some of these birds, like the canaries in fall, lost their ability to sing complex songs—an indication that loss of the HVC neurons indeed causes the canaries' decline in singing. The brain-damaged zebra finches "sound like they're muttering," compared to the birds' usually clear and precise notes, Scharff says.

Then the researchers injected the zebra finches with a radioactive compound that would enable them to see whether any neurons regrew to replace those that died. They found that neuronal death did seem to trigger cell growth. Birds in which HVC → RA neurons had been killed had three times as many new neurons as did control birds. And as the neurons grew back, the zebra finches' singing improved. After a few weeks, one bird had recovered its old song almost perfectly, and the three others had made partial improvements.

This ability to regrow seems to be specific to HVC → RA neurons, however. When the team used the same technique to kill neurons that project from the HVC to the so-called "area X," which are not normally produced in adult birds, no replacement neurons grew. Discovering why the HVC → X neurons failed to regrow could help scientists find ways to grow particular types of neurons in mammals, says developmental neuroscientist Ron McKay of the National Institute of Neurological Disorders and Stroke in Bethesda. Nottebohm agrees. "We have to figure out ways to loosen those restrictions" on regrowth, he says—an achievement that would surely be something to sing about.

–GRETCHEN VOGEL

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