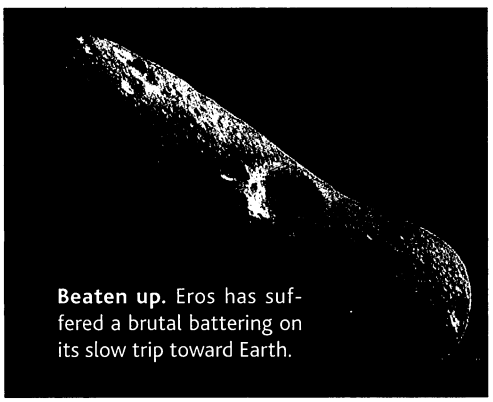
craft and is running the mission for NASA.

A group of planetary dynamicists is suggesting that Eros suffered such a battering because it was slow getting out of the main asteroid belt following the impact that tore it from its parent body. Most asteroids that escape toward Earth are blasted by a collision into one of two narrow zones, as William Bottke of Cornell University and Alessandro Morbidelli of the Observatory of the Côte d'Azur in Nice, France, point out. They usually remain in these regions for less than about a million years before Jupiter's powerful gravity slings them inward, so near-Earth asteroids like Eros should look relatively young. Instead, they argue, a gentle push from sunlight may have nudged Eros gradually into one of numerous, weaker "escape hatches" created by Jupiter and Saturn or even by little Mars (*Science*, 13 August 1999, p. 1002). Such a route would have taken Eros hundreds of millions of years longer to approach Earth.



Beaten up. Eros has suffered a brutal battering on its slow trip toward Earth.

Despite the prolonged pounding, Eros still seems to be in one solid piece. Impacts have pummeled the asteroid Mathilde, which NEAR flew by in 1997, into a flying bunch of boulders. Such collections can appear solid when covered with fine debris. But by combining NEAR estimates of the volume and mass of Eros, the radio science team led by Donald Yeomans of the Jet Propulsion Laboratory in Pasadena, California, calculates that the asteroid has a density of 2.4 grams per cubic centimeter, about the same as Earth's crust. That doesn't leave much room for the nooks and crannies of a rubble pile, Yeomans says: "It now looks like we have a fairly solid object" in Eros.

NEAR is getting hints about Eros's parent body as well. For decades, planetary scientists have been debating whether asteroids like Eros, whose spectral color makes them the most common type in the main belt, could be the source for the ordinary chondrites, the most common type of meteorite to fall to Earth. That's one reason NEAR was sent to Eros. If so, Eros, like its parent body, would have the same primitive composition throughout. But ground-based observations by Scott Murchie of APL and Carlé Pieters of Brown University had caught a hint of different colors on opposite sides of Eros. The colors, imperceptible to the human eye, suggest different mineral compositions. That implies that Eros's parent became hot enough inside to melt and form different minerals in separate places, a process the parents of ordinary chondrite meteorites never went through.

NEAR team member James Bell of Cornell now tells *Science* that "we do see [color] differences from place to place" on Eros, confirming the ground-based observations. That still doesn't necessarily mean Eros is mineralogically differentiated and an unsuitable source for ordinary chondrites, cautions Bell. Surface colors may have been altered by poorly understood "space weathering" over Eros's ages and ages of exposure (*Science*, 9 February 1996, p. 757). Best to wait, he says, for more NEAR data to get to the heart of Eros.

–RICHARD A. KERR

CREDITS: (LEFT TO RIGHT) NEAR/NASA; DURING *ET AL*

NEUROSCIENCE

New Stroke Treatment Strategy Explored

Strokes are among the most prolific killers in the developed world, claiming about 160,000 lives each year in the United States alone. Those who survive are often left physically and mentally impaired. Although new treatments can limit stroke damage, they have to be administered quickly to work. Now, researchers working with rats have come up with a new strategy that may guard against brain damage by taking advantage of the brain's response to injury.

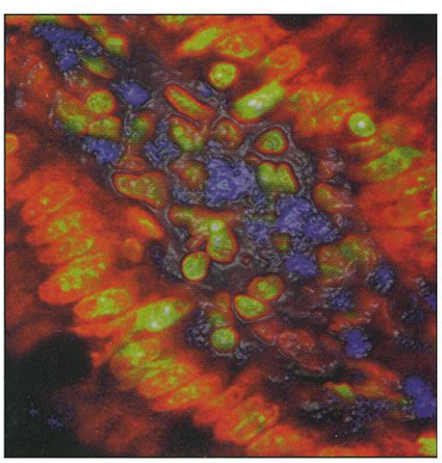
In this work, described on page 1453, neuroscientists in effect immunized rats against the brain nerve cell death caused by stroke and severe seizures. The team, led by Matthew During of the University of Auckland in New Zealand and Thomas Jefferson University in Philadelphia and his colleagues, vaccinated animals with a virus that had been genetically engineered to contain part of the NMDA receptor. Excessive stimulation of this receptor, which occurs when massive amounts of the neurotransmitter glutamate are released in the wake of a stroke, contributes to neuronal death. During's team theorized that the modified virus would stimulate the production of antibodies that could slip into the stroke-damaged brain, seek out NMDA receptors, and prevent them from being excited to death.

In the vaccinated rats, this strategy proved surprisingly effective. The protection against stroke damage "was as good as could possibly be expected," says neuroscientist Brian Meldrum of King's College Institute of Psychiatry in London. But the technique could pose dangers to humans. Neuroscientist James McNamara of Duke University in Durham, North Carolina, cautions that "immunizing people with neural antigens might have unwanted effects," including encephalitis or learning disruptions.

Other NMDA receptor–blocking drugs are already used clinically, but for optimal effectiveness, they have to be given within about an hour of a stroke, and many stroke patients do not reach help so quickly. To develop a treatment that could act almost immediately, During and his colleagues took advantage of the fact that the blood-brain barrier—the membrane that normally prevents large molecules such as proteins from entering the brain—breaks down after a stroke or other trauma. NMDA antibodies circulating in the bloodstream could then steal into the brain.

To test this, his team modified an adeno-associated virus so that it carried a piece of DNA that codes for a portion of the NMDA receptor. The researchers fed rats one dose of the virus and waited 1 to 3 months for antibodies to build up in the blood. Then, to simulate a stroke, they injected an artery leading to the brain with a compound that causes the artery walls to squeeze shut. The resulting lack of blood ordinarily devastates a large portion of the brain. But in the vaccinated rats, the lesion was 70% smaller than in controls.

During's team also induced a state of prolonged, intensifying seizures known as status epilepticus by injecting another set of rats with kainate, a compound that stimulates the release of large amounts of glutamate. In humans, long-lasting status epilepticus seizures can kill cells in the hippocampus. In the group of untreated rats, 68% progressed into full-blown status epilepticus and also suffered major cell death in the hippocampus. But just 22% of the vaccinated



Antibody triggers. Blue-stained immune cells in the gut respond to the NMDA receptor.

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

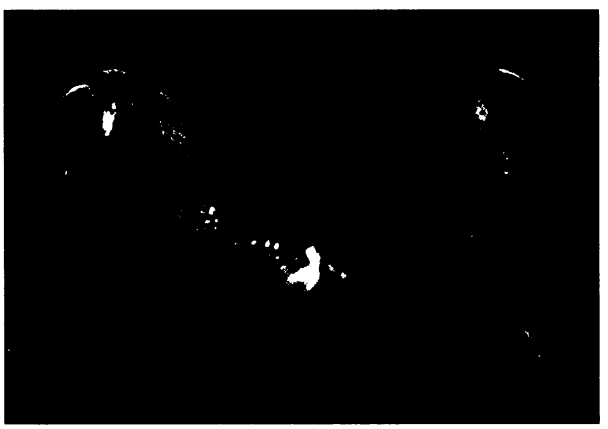
Death Triggers Regrowth Of Zebra Finch Neurons

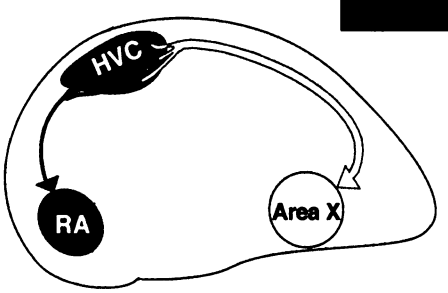
Until recently, scientists assumed that adult brains were doomed to constant, steady decline. Shortly after birth, it seemed, neurons lost their ability to grow, and cells that died could not be replaced—a gloomy outlook indeed. But in the past few years, scientists have found that certain kinds of neurons 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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