

Famous Monkeys Provide Surprising Results

New data from macaques confiscated from a Silver Spring researcher a decade ago challenge neuroscience dogma

EXPERIMENTS THAT ARE AMONG THE MOST controversial ever performed on research animals have yielded results that challenge neuroscience dogma about how much “rewiring” goes on in the adult brain after nervous-system injury. But even before these findings hit the scientific literature (this week’s *Science*, p. 1857), animal rights activists are calling them nothing more than a politically driven effort to justify scientifically bankrupt research.

At issue once again are the Silver Spring monkeys. These 16 crab-eating macaque monkeys and one rhesus monkey gained fame 10 years ago when Alex Pacheco, then a lab technician and now head of People for the Ethical Treatment of Animals (PETA), accused his boss, Edward Taub of the Institute for Behavioral Research, of inflicting unnecessary pain on the monkeys and failing to provide them with adequate food and veterinary care. He convinced the local police to confiscate the animals, and since then, PETA and other animal rights groups have been locked in a legal struggle over who should have the ultimate say about the animals’ fate.

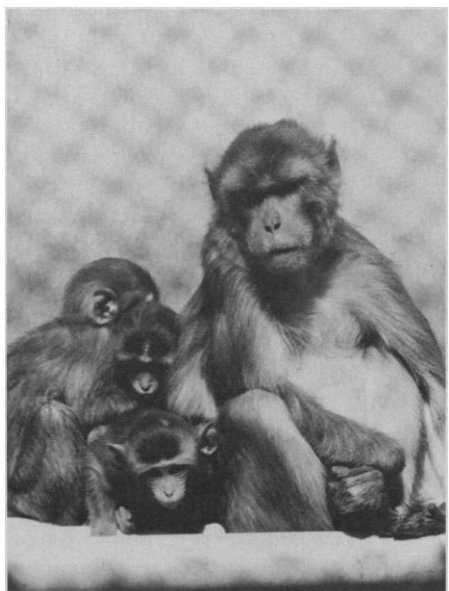
“There’s an incredible irony here,” says Robert H. Wurtz, a neuroscientist at the National Eye Institute and current president of the Society for Neuroscience. “The animal rights activists are keeping these monkeys alive. It’s the scientists who wanted to put them to sleep a decade ago. Since the animal rights activists have kept them alive, they’re now, as it’s turning out, incredibly valuable animals.”

The macaques’ value to science arises indirectly out of experiments conducted in the late 1970s by Taub. He wanted to determine whether the animals could be trained to use an arm even when the nerve leading from the arm to the brain had been severed. Taub also wanted to probe for new nerve connections in the spinal cord that might accompany the behavioral improvements.

When the monkeys were confiscated in 1981, that research was put on hold. Then, in 1987, a group of scientists led by Mortimer Mishkin, a neuroscientist at the National Institute of Mental Health (NIMH), suggested that the monkeys provided a unique opportunity to look at a

different question: what happens to portions of the brain deprived of sensory input over a long period of time. The researchers secured permission to go forward with this inquiry even as the custody battles raged, and their results, as explained in this week’s paper, proved surprising.

Although Taub had thought the reorganization might take place in the spinal cord, more recent work by Michael Merzenich of the University of California at San Francisco and Jon H. Kaas of Vanderbilt University suggested there might be changes in the brain as well. Sensory nerve impulses from various parts of the body go to a brain structure called the somatosensory cortex; a particular part of that structure responds to each portion of the body. If the brain suddenly loses sensory input from some part of the body—the thumb, for example—Merzenich showed that there is a tendency



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Controversial animal. One of the last two remaining Silver Spring monkeys (right) and friends.

for nerve impulses from a neighboring part of the body (a finger, say) to encroach on the area dedicated to the thumb.

Merzenich’s work showed only a small amount of encroachment: on the order of 1 or 2 millimeters. Mishkin and his colleagues asked how large the encroachment might be if the input from an entire limb was cut off.

When they probed the area of the somatosensory cortex formerly dedicated to the arm, the researchers found that now they could find responses to stimulation of nerves as far away as the face. And the reorganization extended over a brain area 10 to 14 millimeters long, an order of magnitude greater than what Merzenich had found.

These results challenge a long-held dogma in brain research. Nobel Prize-winning work by David Hubel and Torsten Wiesel in the early 1960s had shown that, for the visual system, there is a critical period shortly after an animal is born where changes in a sensory system—in this case, input from the eyes—can result in a “rewiring” of the brain connections. Once the animals pass that critical period, the connections are “hardwired,” that is, unable to change. According to Marigotka Sur, a neuroscientist at the Massachusetts Institute of Technology, the plasticity newly demonstrated by Mishkin and his colleagues may alter researchers’ opinions about when these changes can take place.

Tim P. Pons, Mishkin’s colleague at NIMH, says the question to ask now is whether the reorganization starts with the cortex, or whether, as is likely, it is preceded by changes in an intermediate structure between the cortex and the spinal cord. And, he adds, “If we know the mechanism and rules by which this stuff is operating, then there’s the possibility that we can harness this type of reorganizational capacity for therapeutic purposes.”

Animal rights activists remain skeptical, to say the least. “They have to publish something that wows the scientific community,” says physician Neal Barnard, president of the Physicians Committee for Responsible Medicine, a group that has sought to block experiments on the monkeys. Barnard adds: “Had this been done on anything other than celebrity animals, I doubt that *Science* would have published this.” But *Science* editor Daniel E. Koshland denies that the decision to publish the Pons paper was motivated by political considerations; the Mishkin paper, he says, went through the ordinary peer review process.

And what of the last two monkeys still available for research, now being kept at the Delta Regional Primate Center near New Orleans? The U.S. Supreme Court has cleared the way for a Louisiana state court to hear arguments about why PETA should be granted custodial rights to them. And Pons and Edward Jones, a neuroanatomist at the University of California at Irvine, have continued to work with the one remaining macaque. After becoming political celebrities, the monkeys may yet become famous for the research these new findings will generate.

■ JOSEPH PALCA