The Mind and the Brain: Neuroplasticity and the Power of Mental Force - Jeffrey M. Schwartz, Sharon Begley (2003)

Chapter 4. THE SILVER SPRING MONKEYS

We surgically abolish pain.

—Edward Taub

When night fell, Ingrid Newkirk would stand outside, walkie-talkie in hand, playing lookout as Alex Pacheco slipped through the darkened labs of the Institute for Behavioral Research (IBR) in Silver Spring, Maryland, taking photos and scribbling in his notebook. Over the course of several weeks in late August and early September 1981, Pacheco surreptitiously escorted a number of sympathetic veterinarians and primatologists who supported animal rights through the facility, showing them the rusty cages encrusted with monkey feces, cages whose bent and broken wires poked up from the floor like stakes that threatened to impale the monkeys. He showed them the signs of rodent infestation and of insects. But mostly he showed them the animals: sixteen crab-eating macaques, all adult males, and one adult female rhesus. Among the seventeen, thirty-nine fingers had been gnawed off, and arms were covered with oozing, unbandaged lesions. Was this standard for a primate lab, Pacheco asked each expert, or was something wrong—very wrong—here?

What Pacheco didn't know was that experiments conducted in this lab, grisly though they may have been, would overturn the dogma that the adult brain cannot be rewired.

In May 1981 Pacheco, then a twenty-two-year-old political science student at George Washington University, had applied for a job at the privately owned lab, four miles east of the nation's premier biomedical campus, the National Institutes of Health (NIH), in Bethesda. He was trying to decide whether he wanted to make a career of biomedical research, Pacheco had told Edward Taub, IBR's chief scientist. He was so fascinated by animal research, in fact, that he would gladly accept the unpaid, volunteer position that Taub offered him. As Taub told the *Washington Post* ten years later, he went home that night and raved to his wife, Mildred, an opera singer, about the "marvelous student" he had just met: "I told him there was no position, but he volunteered to work, out of pure interest," Taub marveled. But Pacheco's "pure interest" was not what Taub thought it was.

As a student at Ohio State University, Pacheco had burned with the passion of a true believer, and his true belief was that animals were needlessly subjected to cruelty, even torture. He had organized protests against the local farmers' practice of castrating their pigs and cattle without anesthetic; angry ag majors threatened to do the same to Pacheco one night. Pacheco had hoped to study for the priesthood, but instead he moved east and joined Newkirk, nine years his senior and already an experienced animal rights leader, to form People for the Ethical Treatment of Animals (PETA). Newkirk, who had worked undercover at a Maryland

animal shelter and exposed the appalling conditions there, suggested that Pacheco do the same in a lab. He therefore obtained a Department of Agriculture list of federally funded facilities where scientists used animals for biomedical research; of them, IBR was closest to his apartment in Takoma Park, Maryland. Exactly what IBR did, Pacheco had no idea. As it turned out, Taub would be conducting experiments on the very species of animal that Pacheco, who had divided his childhood between Mexico and the United States, once had as a pet. Pacheco's Chi-Chi, like most of Taub's animals, was a crab-eating macaque (that's the species' common name, not its dietary preference) or cynomolgus monkey, *Macaca fascicularis*.

What we do here, Taub explained to Pacheco, is deafferent the monkeys' limbs. Afferent, or sensory, input from the body enters the spinal cord over the dorsal (back) routes to the spinal nerves. If nerves innervating some part of the body—an arm, for instance—are cut where they enter the cord, then that part of the body loses all sensation. The animal no longer feels its arm, or leg, or whatever limb has been deafferented. Taub was particularly interested in depriving single limbs, usually one arm, of afferent input and observing how that affected the animal's use of the arm. Because only the sensory nerve from the arm, and not the motor nerve, would be severed, it seemed logical that the adult animal would be able to continue using the arm. But a leading theory in behavioral psychology held that sensory input was crucial to motor function. This is what Taub planned to test. To do so, he performed the surgery on nine of his sixteen crab-eating macaques: Billy, one of the monkeys, had the sensory nerves to both arms severed, and the eight others had the nerve to a single arm severed. Seven other macaques, and Sarah, the lone rhesus and the only female, served as the controls. Taub had just received an $180,000 grant from NIH to continue this investigation.

Taub found that the deafferented monkeys, consistent with a long-standing theory in neurophysiology, did not naturally use the deafferented limb; without feeling, the arm seemed to hang like a dead weight, and the monkeys in many cases appeared to forget it was even there. So Taub tested whether the monkeys' reluctance, or refusal, to use the impaired limb could be overcome. Using a straitjacket to restrain the good arm, which the monkeys favored for tasks from ambulating to eating, he left them no option (if they wanted to get around and to eat) but to use the damaged one. He strapped the monkeys into chairs and, if they failed to flex the "affected arm," as Taub delicately called the seemingly useless one, administered a strong electric shock to them. Subjected to these massively stressful "negative reinforcements," the animals did indeed move the senseless limb. Eventually, Taub would examine the monkeys' nerves to see whether they had undergone any change—to see whether, for instance, any had grown back as a result of the animals' being forced to use the deafferented arm. That would mean killing the monkeys. But if the experiments showed what Taub expected and hoped, the results just might lead to new treatments for victims of stroke and brain trauma.

Pacheco wasn't interested in looking that far ahead. All he saw was what lay before him, and what he saw sickened him. The animals were housed in rusty old cages whose filth was surprising, for a lab; Pacheco reeked every night, recalls Newkirk, with whom he was living. Inspectors from the U.S. Department of Agriculture, which enforces lab animal laws, visited Taub's lab during Pacheco's time there; they reported no serious deficiencies. Given that, Pacheco wasn't sure what, exactly, would qualify as a deficiency (apparently not the monkey corpse he had found floating in a vat of formaldehyde). The living ones might well have envied the dead: they would spin around constantly, bouncing off the cage walls, masturbating compulsively—as macaques caged alone are wont to do. But these animals had an additional habit that horrified Pacheco. They chewed their deafferented limbs raw and gnawed off their fingers. From the shoulder down, of course, the affected limbs had no feeling.

Pacheco began documenting what he saw, shooting photographs and taking notes. When he told Taub he wanted to work nights and weekends, a grateful (and unsuspecting) Taub gave him the keys to the lab. That's how Pacheco came to be inside on those late summer nights in 1981, with Newkirk acting as lookout, each equipped with a walkie-talkie they had bought at a toy store. From August 24 to September 4, Pacheco sneaked five veterinarians and primatologists into the lab. Animal rights sympathizers, they provided the PETA pair with affidavits testifying to the conditions of the animals and of the lab. The next month, Newkirk and Pacheco took the affidavits and photos to the local police department.

The Montgomery County, Maryland, police raided the Institute for Behavioral Research on September 11, seizing all seventeen monkeys: Adidas, Allen, Augustus, Big Boy, Billy, Brooks, Charlie, Chester, Domitian, Hard Times, Hayden, Montaigne, Nero, Paul, Sarah, Sisyphus, and Titus. (Some of the monkeys had been named by Taub's students and assistants; the classical names came from Taub himself, who had long felt that some of the Roman emperors had not received their due from historians.) Taub had not been working that Friday, but when he rushed to the lab after an assistant phoned to tell him about the raid, he couldn't believe what was happening. He told a reporter, "I'm surprised, distressed and shocked by this. There is no pain in these experiments. We surgically abolish pain." Although neither Taub's experimental methods, nor the conditions in his lab, were grossly out of line with then-common practice, on September 28 the prosecutor charged Taub with seventeen counts of animal cruelty. The saga of the Silver Spring monkeys—one that would drag through the courts for ten years, embroil powerful congressmen in the fate of seventeen monkeys, and do more than any other single incident to launch the animal rights movement in the United States—had begun.

Edward Taub has mellowed in his later years. Yet you can still detect, in the self-assurance, shadows of the arrogance that once so infuriated other researchers that their faces would turn crimson and their lips would be reduced to sputtering as, in one case that he delights in telling, they lost their adopted English and fell back on their native Finnish to denounce him at a scientific meeting. And you can still detect

the figurative thumbing-of-the-nose at scientific paradigms that provoked his bosses, even when they grudgingly granted him permission to carry out studies that threatened (or promised?) to topple those paradigms, to demand that he allow "observers" in, to keep an eye on him. And you can still detect the almost naïve view that scientific truth would vanquish ignorance and sentimentality. But although Taub had no trouble questioning the received wisdom in neuroscience and harbored no doubts that he, an outsider from the lowly field of behavioral psychology, had the right to question neuroscience "facts" dating back a century, it never dawned on him that using what were then (regrettably) not-uncommon laboratory procedures would earn him a singular distinction: the first scientist ever charged with animal cruelty.

Taub was born in New York City in 1931. After receiving his undergraduate degree in psychology from Brooklyn College in 1953, he began working toward his doctorate at Columbia University. As a grad student, he worked with monkeys at the Jewish Chronic Disease Hospital in Brooklyn. It was there that he was introduced to the experimental procedure that would first break him and then make him: limb deafferentation. "This was my advantage: that I was a psychologist who had never studied neuroscience except on my own," he says. He therefore had not been inculcated with the conventional wisdoms of the field, one of the most important of which dated back to classical experiments by the British neurophysiologist Sir Charles Sherrington.

In 1895 Sherrington, working with F.W. Mott, reported the results of a now-classic experiment in which he deafferented a single upper forelimb or lower limb of rhesus monkeys. Sherrington pioneered deafferentation experiments, painstakingly severing the sensory nerves but leaving motor nerves intact, much as Taub would some sixty years later. Sherrington and Mott sought to investigate whether the animals would continue to use the deafferented limb. They found, instead, that after they cut the sensory nerves, the monkeys stopped using the affected limb. The animals were completely unable voluntarily to grasp, to support their weight, or to ambulate with the deafferented limb. The "volitional power," as Sherrington and Mott called it, "for grasping with the hand etc. had been absolutely abolished." Even when Sherrington restrained a monkey's remaining good arm, deferred feeding time, and then put a morsel within reach, the monkey did not use its deafferented arm to reach for the food. The only movements it seemed willfully capable of were crude rapid jerks, which were induced in the monkeys by causing them to "struggle," as when they tried to free themselves while being held awkwardly. Sherrington attributed these motor actions to reflex effects triggered by movements in intact parts of the body. Since the motor nerves were still intact, why should somatosensory deafferentation abolish the ability of the monkey to move that arm? This was even more perplexing given that stimulating the motor area of the cerebral cortex elicited totally normal movement of the affected limb. Reflecting on the 1895 results in 1931, Sherrington said this served as "a caveat

against accepting the movement excited electrically at the motor cortex as any close homologue of a willed one."

What the disconnection of sensory nerves did, Sherrington argued, was abolish a critical "influence of sensation upon voluntary movement," thus interfering with a basic mechanism necessary for the expression of "volitional power." As we will see, this observation somewhat overstated the case. In any event, working with Derek Denny-Brown, Sherrington replicated the deafferentation study, publishing virtually identical results in 1931, a year before he won the Nobel Prize.

Researchers as late as the mid-1950s continued to report that sensory deafferentation led to loss of motor ability. These results and others led Sherrington to conclude that the modulation of reflex pathways is the basis for purposive feedback plus learning guide the next movement; this produces its own feedback, which, again in conjunction with learning, eventually produces, after countless iterations, purposive, sequential movement. This theory came to be called "Sherringtonian reflexology."*

"Reflexology was the dominant view in neuroscience, even more dominant than the idea that there is no plasticity in the adult brain," recalls Taub.

The idea was that if you were interested in voluntary behavior, which was thought to be just an elaboration of a simpler phenomenon, it made more sense to study the simpler phenomenon. At this point it is hard to grasp how influential Sherrington's views were in psychology and certainly in neuroscience. Since we were psychologists, God help us, we decided [in the mid-1950s] that we would use the relatively new techniques of conditioned response to reevaluate the Sherringtonian canon, not because we had any reason to think it was wrong but because we could apply these new techniques to his ideas, which were so dominant.

But something else was lurking in the back of Taub's mind. While doing the usual literature search for previous experiments in preparation for his own, Taub happened on a 1909 book by one H. Munk called *Ueber die Functionen von Him und Rückenmark* (On the functions of the brain and spinal cord). In it, the German scientist recounted how he, too, had performed unilateral deafferentation experiments on monkeys. Yet his results differed dramatically from Sherrington's of fourteen years earlier. Munk claimed that it was possible to induce a hungry monkey to lift food to its mouth with the unfeeling arm under two conditions: if the intact arm were restrained, and if the initial halting attempts by the deafferented arm were immediately rewarded. Until Taub stumbled on them, Munk's observations had been essentially ignored and, in effect, lost to science.

In 1957 Taub and two colleagues at the Brooklyn hospital began a series of experiments designed to test Sherrington's theory that sensation is necessary for intentional, goal-directed movement. They confirmed that monkeys whose arm had been deafferented failed to use it if given any say in the matter. But Taub

suspected that the deafferented animals retained what he called "a latent capacity for purposive movement." The experiments he designed were meant to "force the expression" of that capacity; in other words, the monkeys would be induced to use their "useless" limb. What was required, Taub suspected, were three things: motivating the monkeys, keeping the motor tasks simple, and repeating the motor trials.

Taub provided the motivation in the very first set of experiments, conducted two weeks after deafferentation surgery. The monkey sat, immobilized, in a "restraining chair." He heard a tone. If he flexed his deafferented right arm so that it broke a light beam five inches above a waist-high board within 3.5 seconds of hearing the tone, nothing else happened. But if he did not move his senseless arm, usually by flexing the elbow and shoulder, to interrupt the beam of light, he experienced an intense electric shock that lasted up to 3.5 seconds. This type of behavioral conditioning is called *avoidance conditioning*; it uses what B.F. Skinner (the psychologist who first systematically described it) termed "primary negative reinforcers," such as loud noise or electric shocks, to teach an organism new patterns of behavioral response. As Skinner put it, "A negative reinforcer strengthens any behavior that reduces or terminates it." Conditioning of this sort was widely used in animal (and even human) research in the 1960s and 1970s, the period of Skinner's greatest influence.

In the training paradigm Taub used, the conditioned stimulus was the buzzer. Because it was paired with a primary negative reinforcer (the shock), it became, in Skinnerian lingo, "a conditioned negative reinforcer." The conditioned response or "operant behavior" to be performed to avoid the shock was flexing the deafferented arm. Each training session lasted twenty trials. The entire training series, Taub said, "was to be of long duration, if necessary." In fact, it would typically require more than nine weeks of testing, five days a week, spent conditioning and conditioning the animal through electric shocks. Within a few weeks Taub had collected results that threatened a key finding of the Sherringtonian canon. "What do you know: the monkeys with the deafferented arms could learn new conditioned responses," he recalls more than thirty years later. To avoid the shock, the monkeys could move their deafferented arms.

Taub had another way to motivate the monkeys. In the second set of experiments, he and colleagues put six monkeys in straitjackets to restrain their good arm. This made the monkeys very upset—they either struggled obsessively to wriggle out of the constraint or refused to move at all. Nevertheless, five of the six animals got the point: they figured out that if they wanted to reach the food placed outside their cage, they would have to extend the deafferented arm. Two of the six also used their bad arm to support themselves, to move around "in the limited confines of their cages," as Taub put it, and even to feed themselves a peanut. "If you use simple restraint of the unaffected limb, within a couple of hours the monkeys will begin using the affected limb," Taub says, looking back on his results. "The use of that limb is clumsy, but it is permanent. This demonstrated unequivocally that the

Sherringtonian reflexology position was incorrect." Clearly, volitional movement did not require sensory feedback.

"I couldn't imagine the incredible response when we began publishing in the early 1960s," Taub recalls. His discovery that sensory feedback is not necessary for movement contradicted the position of a professor of his, one of the Columbia psychology department's leading researchers. Taub was about to experience the first, but far from the last, consequence of bucking the conventional scientific wisdom. When it came time for him to defend his proposal for his doctoral thesis, the professor whose views his work undercut showed up at an event usually attended only by the student's thesis committee. "He was very angry," Taub recalls. After debating Sherringtonian reflexology with Taub, the professor stormed out. Soon after, Taub learned that he had failed a course (taught by the same professor) required for his Ph.D. because he had not taken the final. He had expected to receive an incomplete, which could usually be converted into a grade as soon as a student took the exam. Instead, the professor told Taub he had failed—because of his "insolence."

In 1962 Taub transferred to New York University. He continued his deafferentation work, under an NIH grant to the senior scientist in the group, A. J. Berman. Within a few years they found that monkeys could flex the fingers of a deafferented arm if properly motivated. To provide the motivation, Taub strapped a monkey into a restraining chair and taped a fluid-filled plastic cylinder into its bad hand. If the monkey squeezed the cylinder within a given amount of time, nothing happened to him; if he failed to do so, he received an electric shock. Just as the monkeys conditioned to break a light beam after hearing a tone did, these monkeys, too, learned (eventually) to grasp the container in order to avoid an electric shock, Taub reported in 1966.

By 1968 he had concluded that a monkey will not use a deafferented arm if it can get along reasonably well with the other three limbs, especially since trying to use an arm without feeling can lead to uncoordinated movement, falling, and dropping food. The monkey succumbs to what Taub dubbed *learned nonuse*. But conditioning (getting an electric shock if it doesn't use the bad arm) and restraint (leaving the monkey no choice if it wants to eat or walk but to use the bad arm) force it to use the arm or to be subjected to electric shock or go hungry. The motivation to use the limb is increased, so the monkey uses it. "With specific training," Taub concluded, "deafferented monkeys can learn to perform almost any sequence of movements of which a normal monkey is capable, except the most precise."

Something else was happening. Animals with two deafferented arms behaved quite differently from those deafferented of a single arm: the bilaterally deafferented monkeys were able, soon after surgery, to use both arms to grasp, walk, and climb, Taub and Berman reported in 1968. This counterintuitive result—the more crippling the surgery, the better the monkey did—was, Taub decided, "one of the central enigmas" in the field. Somehow, a smaller lesion (single limb deafferentation) was

producing worse crippling than a lesion twice the size. When a single limb is deafferented, the monkeys don't use the arm; when both limbs are deafferented, the monkeys exhibit almost normal movement. This, Taub decided, was "a paradoxical inversion of results."

Twenty years later, Taub still professes shock at the reaction his results elicited.

I am a psychologist, and was just calling the data as I saw them. I had never gone to school in neuroscience so I had no idea what the violence of the reaction from the traditionalists would be. But the people in control of neuroscience then were all students of Sherrington [who had died in 1952]—people like Sir John Eccles and Ragnar Granit [who won Nobel Prizes in 1963 and 1967, respectively]. They were very upset. I was invited to give a colloquium at NIH and Granit was there. He spoke English [in addition to his native Finnish] reasonably well. But at the end of my talk he got up and began to question me; he got so angry that at first his face got incredibly red, and then he lost his English. He denied that Sherrington had ever said what I said he said, or believed it that strongly. I said okay, but really, it was so obvious, there was a reason the position was called Sherringtonian reflexology…. These people really despised me. I couldn't imagine where all this emotion was coming from. Not that I was an easy person. I grant that I was a very difficult young man. I was very insecure, and that translated into unconscious arrogance, and I was certainly convinced of my interpretation. People didn't like me; I was going up against all these distinguished people. I didn't have any mentors of my own, since I was in behavioral psychology rather than neuroscience. And that's probably why I was able to do the research that I did, because I had no preconceptions.

In 1970 Taub finished his Ph.D. thesis in experimental psychology, "Prism Adaptation and Intermanual Transfer: An Application of a Learning Theory of Compensation for Sensory Rearrangement." (The thesis described how monkeys whose view of the world was skewed as a result of looking through a prism could still direct a deafferented arm to a target, even though the prism made objects appear displaced.) In the fall of 1969 he had been offered a research job at the Institute for Behavioral Research in Silver Spring. There Taub decided to continue his deafferentation experiments, focusing on which movements would or would not be impaired after sensory deprivation, and under what conditions.

At IBR, Taub carried out numerous variations on the deafferentation experiments that would change neuroscience. From the first, he observed that immediately after surgery a deafferented monkey gets by with only its good arm. That made sense, for recovering function in a deafferented limb requires time. Unless the experimenter intervenes to induce use, "the monkeys never learn that, several months after the operation, the limb has become potentially useful," Taub explained. Putting the good arm of unilaterally deafferented monkeys in a straitjacket for nine full weeks after the surgery, he found, overcame this learned nonuse. The monkeys continue to use the deafferented limb after being freed from

the restraint. All the animal needed was some motivation to prevent him from coddling his deafferented arm. Depriving monkeys of the use of their one good arm, or subjecting them to electric shocks until they learned to use the bad arm, did the trick. "Everything we did," Taub said more than twenty years later, "was to answer an important question." Eventually, monkeys could use their bad arm to climb to the top of an eight-foot bank of cages, as well as climb laterally and pick up raisins.

One problem was starting to crop up, however. "Deafferented monkeys have a tendency to sustain severe damage to their affected extremities, frequently as the result of self-mutilation," Taub reported in 1977. "This tendency toward injury, self-inflicted or otherwise, constitutes one of the major difficulties in carrying out deafferentation experiments with monkeys." "Difficulties," he would find out, was putting it mildly.

So far, all of Taub's experiments had been carried out with adolescent monkeys, who of course had been using their limbs for years before Taub severed their sensory nerves. That raised a key question: was somatic sensation early in life necessary for developing normal coordination? How early could an animal lose sensation to a limb and still learn, or relearn, to use it? Were certain movements hard-wired into the brain, or did they require the sensory feedback that Sherrington posited? If the latter, how much sensory feedback was necessary—days, or weeks, of movement in utero? To answer this, in the early 1970s Taub began to deafferent monkeys on the day of their birth. Amazingly, their ability to walk, climb, and reach was as good at three months as that of monkeys that had not been operated on.

The next logical step was to deafferent fetal monkeys. In 1975, Taub and colleagues at IBR performed the delicate surgery outside the womb, with the fetuses in a warm saline solution bath, and then returned the tiny things to the uterus. Unfortunately, the experiment had a high mortality rate: in one batch, six out of eleven fetuses died. Not even the survivors fared well. All were quadri-paretic; the best-off could stand for a few moments, but do little else. Their impairment worsened; one died; and the rest were "sacrificed" at five to twelve months of age. But the reason for their immobility, Taub learned when he autopsied the animals, was that the surgery had made the fetuses' vertebrae flare in such a way as to damage the spinal cord. After using a different surgical procedure to deafferent fetal monkeys, Taub found that (in the two monkeys that survived) the deafferented arm was impaired but not useless: the monkeys supported themselves, walked, and reached with it. Volitional movement, Taub concluded, was not dependent on sensory feedback; rather, it was preloaded into an animal's brain like Windows XP on a laptop.

In the late 1970s, Taub began an experiment designed to test his hypothesis of learned nonuse directly: he restrained the deafferented arm of his monkeys for three months after surgery. This way, a monkey would never learn that the limb was useless during this period; it would simply assume that the restraint was holding it hostage. Taub also restrained the animal's good arm, so the monkey

would not become adept at living one-handed, carrying out its daily activities with a single forelimb. So for three straight months, monkeys were strapped into straitjackets, with their arms crossed over their chest, pinned to the side of their body, or tied behind the back. The limb position was changed every other day.

Almost as soon as the restraints came off, the monkeys managed to use the deafferented limb.

Taub had demonstrated the phenomenon, and the power, of learned nonuse. In the immediate aftermath of an injury, the animal learns to avoid using the affected extremity, because doing so gives the monkey only "negative feedback" when it attempts to walk, climb, or grasp with the arm. That is, those attempted movements are clumsy or ineffectual. At the same time, the monkey learns compensating moves that are, in stark contrast, successful and rewarding: it works around the injury, much as stroke patients with a useless arm learn to do. The combination of negative feedback if he tries to use the affected extremity and reward if he develops compensatory moves suppresses use of the affected extremity. Although the condition is normally permanent, Taub had seen hints in the Silver Spring monkeys that learned nonuse of the affected limb could be reversed by restraining the intact limb so the monkey was compelled to use the deafferented arm. "The simplest method for evoking purposive use of a single deafferented limb is prolonged impersonal restraint of the intact limb," Taub concluded. Failure to use a deafferented limb reflected learned helplessness, not a motor incapacity. It was 1980.

In a chapter he wrote for a book that year, Taub argued forcefully that his work with deafferentation pointed the way toward testing whether learned nonuse accounted for a stroke patient's inability to use an arm, and he laid out a training procedure to overcome it. He emphasized that motivation was crucial but allowed that the electric shocks he used with the monkeys would probably not be necessary in stroke patients. (Praise, and perhaps tokens good for privileges or favorite foods, might be adequate, he suggested.) "I had had these data for 10 years, yet I never before thought of applying learned non-use to stroke rehabilitation," Taub recalls. "In neuroscience then, you just didn't think of applications to human beings. It didn't occur to anybody."

Actually, it did occur to one person. In 1967 Larry Anderson visited Taub's laboratory at the Institute for Behavioral Research. There, he observed some of the conditioned-response experiments with the monkeys and asked Taub whether he thought something similar might work in stroke patients. "I said sure, try it," Taub recalls.

Anderson did, with three stroke patients. He tied down the unaffected arm of each patient, leaving only the "paralyzed" arm free. Anderson then sounded a tone. Patients who failed to move the seemingly immobilized arm at this signal received a mild electric shock. Amazingly, the stroke patients learned to move an arm that they had thought they would never use again. For one of the patients, this

demonstration led to a significant improvement in the life situation; for two of them, without follow-up therapy, the demonstration did not translate into real life.

Anderson's boss decided to scale up the experiment and recruited twenty-four stroke patients. Immobilizing the good arm, and motivating patients to use their "useless" arm, produced substantial improvement in all twenty-four. "There are those two papers in the rehab literature," Taub says,

but they were so far out in left field that I don't believe there has been a single reference to either except in my own articles. It was as if they had never been written. They were just too different from the traditional view of what is feasible and appropriate for treating stroke patients. For myself, I was fully engaged in working with monkeys, and my plate was full. I was a pure scientist, and you didn't do that then—rush to apply a finding in basic science to medicine. The message in the field was that if you were not doing pure research, you were tarnished. It took me so long to think about applying the monkey results to stroke patients because one just didn't think along those lines. It was only 10 years later that it occurred to me to try this in stroke patients.

That was the radical proposal in his 1980 paper. He was a year into this work when Alex Pacheco asked whether Taub could use some help around the lab.

The month after the September raid, the National Institutes of Health suspended the rest of Taub's grant. The decision reflected a simple political calculus: although the agency knew that to withdraw funding from a researcher embroiled in a controversy—indeed, a court case—over his use of lab animals would ignite the wrath of many in the biomedical community, NIH also recognized that it would otherwise have been impossible to maintain its credibility with the public and Congress. Throughout the saga of the Silver Spring monkeys, NIH would be caught in a crossfire between its core constituency—biomedical researchers—and the public.

At Taub's November 1980 trial, Pacheco testified that cages were cleaned only infrequently, that cockroaches had the run of the lab, and that if caretakers failed to show up, the monkeys could go two or three days without food. He testified to the animals' self-mutilation, describing how Billy chewed off eight of his ten fingers and Paul tore off all five fingers of one hand. Courtroom exhibits featured gruesome photographs of the macaques with chewed-off fingers and bandaged arms. Five of the nine deafferented monkeys had mutilated themselves; open sores drained the length of their arms. Several had bone fractures; one suffered from osteomyelitis. Defense witnesses, and Taub himself, testified to the scientific merit and promise of his work and argued that deafferented monkeys are notoriously difficult to care for: with no feeling in the limb, they treat it as a foreign object, mutilating it and chewing off digits. The main point, and the only fair indicator of whether conditions in the lab were acceptable, argued the defense, was that the monkeys were healthy. As for the feces and other filth, they argued, monkeys are well known for fouling their cages.

"Nobody ever saw the conditions that Pacheco photographed," Taub maintains; he had long been convinced that Pacheco staged at least two of the photos introduced into evidence.

In the long history of researchers' administering electric shocks to animals, operating on them without anesthesia, and, of course, "sacrificing" them by the truckload, Taub had the distinction of being the only scientist ever hauled up on criminal charges for what he had done. People were aghast to learn that, as part of the experiment, day-old monkeys had their eyelids sewed shut. Yet when Harvard's David Hubel and Torsten Wiesel did the same to newborn kittens, as described in the previous chapter, their research won them a Nobel Prize. Many scientists therefore viewed Taub as a victim. They aided his defense in the belief that an unfavorable verdict would be the leading edge of a drive by antivivisectionists (the term most scientists preferred to "animal rights activists") to outlaw all animal experiments. Supporters such as Edward Coons, Jr., of NYU, Neal Miller of Rockefeller University, and Vernon Mountcastle of Johns Hopkins University raised more than $2,500 for Taub's defense; they believed that he had been set up and that NIH's suspension of his grant reflected nothing but a cold political calculus. Yet the biomedical community was clearly fractured by the case of the Silver Spring monkeys. NIH officials, writing in *Neuroscience Newsletter*, noted that deafferented monkeys kept at NIH "have not developed lesions comparable to those in five of the nine deafferented monkeys from IBR…. [F]ractures, dislocations, lacerations, punctures, contusions, and abrasions with accompanying infection, acute and chronic inflammation, and necrosis are not the inevitable consequences of deafferentation." Their animals, implied the NIH officials, had been given proper, humane care—unlike the Silver Spring monkeys.

In late November 1981, a district court judge found Taub guilty of six counts of failing to provide veterinary care for six monkeys (Paul, Billy, Domitian, Nero, Big Boy, and Titus) who had, among other injuries, massive scar tissue on their open wounds. The judge dismissed the other 113 counts. Taub was defiant throughout. He insisted that the animals had suffered no pain and after the verdict declared, "What has happened to my work harks back to the Middle Ages, and to the period of religious inquisition, when scientists were burned at the stake." The $3,000 fine the court imposed belies the true price that Taub paid. His NIH grant would never be reinstated; he lost his job at IBR; his research came to a standstill. He would spend several years trying to write up his work on deafferentation, under a $20,000 grant he received from the Guggenheim Foundation in 1985.

Taub appealed the verdict to the circuit court in Rockville, Maryland. A jury there cleared him of all but one misdemeanor count of animal cruelty on July 2, 1982, sustaining the conviction only for Nero, whose arm had required amputation after the raid because it developed a massive infection. Two months later, Judge Calvin Sanders ordered Taub to pay the maximum fine, $500, but added, "I hope and trust this will not deter you from your efforts to assist mankind with your research." On August 10, 1983, however, the Maryland Court of Appeals unanimously

overturned that one-count conviction, ruling that a federally funded researcher was not subject to state laws on animal cruelty. Taub described himself as "delighted to be exonerated…delighted on behalf of science." Two weeks later, as he addressed the American Psychological Association's annual meeting in Anaheim on "Tactics of Laboratory Attacks by Anti-Vivisectionists," nearly 200 animal rights demonstrators burned him in effigy.

As for the monkeys, their saga was far from over. Immediately after their seizure they were housed in the basement of the home of a PETA member in Rockville. There, vets cleaned and bandaged the animals' wounds, volunteers groomed them with toothbrushes, and a television was installed so they could watch soap operas, which they seemed to love. Just days after the seizure, however, a judge ordered the monkeys returned to Taub's lab, where a court-appointed vet would supervise their care. After mysteriously vanishing for several days (no one ever owned up to kidnapping them, but after prosecutors explained to Pacheco that they could not make a case against Taub without their star evidence, the monkeys reappeared), the seventeen monkeys were trucked back to IBR. Their stay was brief, however. Six days after, Charlie was found dead in his cage, apparently of cardiac arrest suffered after surgery to repair damage he had sustained in a fight with Nero. The judge was singularly unamused at this turn of events. That day he reversed his order and ordered the sixteen surviving monkeys sent to NIH's primate facility in nearby Poolesville. NIH took custody even though the animals remained the property of the Institute for Behavioral Research, an arrangement that would cause problems.

PETA sued in U.S. District Court to have the monkeys transferred from Poolesville to a primate sanctuary called Primarily Primates, in San Antonio, Texas, but the court ruled that PETA lacked legal standing. In 1986 PETA persuaded Representative Robert C. Smith of New Hampshire and Representative Charlie Rose of North Carolina to draft a petition calling on NIH to send the monkeys to the sanctuary; 252 members of the House signed it. (Smith even offered to buy the monkeys himself.) Pundits weighed in; James J. Kilpatrick wrote that the monkeys "deserve a break that the law won't give them…. Why can't a just and humane court…let the monkeys go?" In a letter, James Wyngaarden, the director of NIH, promised that he would indeed allow the monkeys to be moved from Poolesville; he also promised, "These animals will not undergo invasive procedures for research purposes." Any experiments, he continued, would occur only after their "natural death." On June 13 of that year Wyngaarden repeated his promise in testimony before Congress: the animals would never again undergo invasive procedures as part of research. By this time, investigating panels from the Society for Neuroscience, the American Psychological Association, and the American Physiology Society had all cleared Taub of animal cruelty charges. The Society for Neuroscience even contributed $5,000 toward Taub's legal bills.

Whatever promise animal rights activists thought they had wrested from Wyngaarden, the Silver Spring monkeys were not moved to a sanctuary. NIH had

begun to feel the wrath of the biomedical community—its constituency—over the perception that it was caving in to "antivivisectionists." In 1984, researchers at the University of Pennsylvania had been caught, on videotapes that PETA stole, dangling baboons by crippled hands, even propping up one trembling, brain-damaged baboon, turning the camera on him, and asking in voice-over, "Look, he wants to shake hands. Come on…he says, 'You're gonna rescue me from this, aren't you? Aren't you?'" That was too much even for NIH. The following summer, the secretary of health and human services (HHS) ordered the Penn lab shut down, an action that triggered a flood of furious calls and letters from scientists to NIH. In retrospect, it seems very likely that the firestorm over the Penn closing and other perceived cave-ins to animal rights activists "sealed the fate," as the *New Yorker* put it, of Billy, Sarah, and the other Silver Spring monkeys. NIH was accused of pandering to "animal lunatics" and was feeling the bitter backlash of a scientific community convinced the agency had sold out one of their own. NIH was going to take a stand in favor of using animals in biomedical research, and that stand would be on the Silver Spring monkeys.

So over a June weekend in 1986, the NIH assistant director, William Raub, contacted two of the country's leading primate facilities, Yerkes Regional Primate Center in Atlanta and the Delta Regional Primate Center, located across Lake Ponchartrain from Tulane University's main campus in New Orleans. Yerkes wanted no part of the symbol-laden animals. But Delta's director, Peter Gerone, was game. On June 23, the fifteen surviving monkeys (Hard Times had been euthanized at Poolesville in 1982) were moved to Delta, deep in the tranquil woods of Covington, Louisiana, surrounded by magnolias, sweet gums, and pine trees. Within a week of the animals' arrival, protesters were blocking the entrance road. Alex Pacheco felt betrayed; he had made arrangements for the monkeys' transfer to Primarily Primates, going so far as to outfit a mobile home as an animal clinic where the animals could be cared for. Instead, the monkeys were housed at Delta, in double-decker stainless steel cages that lined the walls of a nine- by twelve-foot concrete-block room. Brooks died a few months after he arrived; five of the control monkeys—Chester, Sisyphus, Adidas, Hayden, and Montaigne—were sent to the San Diego Zoo in the summer of 1987. That left Sarah, plus the eight male macaques that had undergone deafferentation—Augustus, Domitian, Billy, Big Boy, Titus, Nero, Allen, and Paul. Gerone refused to allow anyone from an animal rights group, or even newspaper reporters and photographers, to see the animals.

Although PETA continued pleading for the monkeys to be moved to a sanctuary, in April 1987 the Supreme Court upheld lower court rulings that PETA lacked legal standing to sue for custody. The following month, less than a year after taking custody of the animals, Gerone recommended that eight be put to death as "the humane thing to do." PETA and its allies were outraged. Newkirk charged that the monkeys "had been through hell and back" and deserved to be with "people who care about them." NIH rebuffed the requests throughout 1988—for it had been presented with an intriguing proposal.

In connection with a paper sent to the *Proceedings of the National Academy of Sciences* on February 22, 1988, the neuroscientists Mortimer Mishkin and Tim Pons of the National Institute of Mental Health suggested that the Silver Spring monkeys perform one last service for science. When humane considerations require that one of the animals be euthanized, they said, let scientists first examine its brain in search of evidence that the cortex had reorganized after twelve years of being deprived of sensory input from one limb or more. The Silver Spring monkeys, which had been deafferented when they were three or four years old, were a unique resource, the scientists argued. As NIH's William Raub told a reporter, "The Silver Spring monkeys were the first animals ever…in which so large an area of the brain—namely, the region corresponding to the map of an entire forelimb—had been devoid of its normal sensory input for as long as a decade." Throughout the 1980s and even earlier, as we'll see in the next chapter, scientists had been documenting cortical remapping in the brains of adult primates. *Cortical remapping* is what happens when an area of the brain that once processed sensation from, say, a thumb now processes input from a finger. In earlier studies, Pons and Mishkin found that the brains of seven macaques had been remapped in that the cortical representation of the hand had been taken over by the foot. But the remapping generally being reported by other studies was minuscule: the distance between the old representation and the new was usually on the order of only a couple of millimeters. By examining the brains of the Silver Spring monkeys, Pons and Mishkin hoped to determine whether cortical remapping occurred to a greater extent than anyone had previously reported.

NIH, of course, was not stupid enough to call for the monkeys' deaths in order to let scientists saw open their skulls and examine their brains. Instead, the institutes decided that when the animals became so ill that they had to be put down, then scientists could—with the animals under deep anesthesia—examine their brains, just before the animals were sacrificed. On July 1, 1988, William Raub wrote that the monkeys "are likely to require euthanasia eventually and that some almost surely would reach that stage this year." NIH had therefore prepared a plan, he wrote: the deafferented animals would undergo a procedure, while still alive but before being anesthetized, in which scientists would remove part of their skull and probe their brain for signs of cortical reorganization. Only after this would a monkey be euthanized.

Alex Pacheco and PETA were livid. Even Representative Rose wrote, in a scathing letter to NIH, that experimenting on the animals would be "a very serious violation of a commitment to me, to the Congress and to the public." The (first) Bush administration received thousands of letters protesting the decision; the first lady alone got 46,000, apparently from people who thought this kindly looking white-haired grandmother would intervene on behalf of the crippled monkeys. In 1988, animal rights groups successfully sought a restraining order prohibiting euthanasia if the brain surgery were to accompany it. By this point, Pacheco so mistrusted NIH

that he suspected they would find any excuse to kill the animals in order to carry out the brain experiments.

Just when it seemed that matters could not get any worse, in the winter of 1989 Paul began to die. He started chewing apart the arm that had been deafferented; there was, of course, no feeling to signal him to stop. (Experience had shown that animals quickly maul any protective covering.) He actually cracked the bones in his hand. After the Tulane vets amputated half the arm and put him back in his cage, Paul stopped eating. Although the caretakers tried to soothe him, rubbing his back and offering him treats like peanut butter and sliced bananas, he refused all food. He began ripping apart his stump; gangrene streaked what remained of the limb. On the Fourth of July, vets amputated the rest of the arm at the shoulder. Even with force-feeding, Paul wasted away, finally dying on August 26, 1989, on the floor of his cage, with his head tucked beside the only arm that scientists had left him. He weighed seven pounds, compared to his original twenty. Throughout the ordeal, PETA had refused to acquiesce to euthanasia, convinced that Tulane's description of Paul's condition was an exaggeration, if not an outright lie.

Then it was Billy's turn. Although he had two deafferented arms, he managed to scoot around his cage with grim determination. But his odd locomotion caused pressure wounds on the backs of his hands and made his spine curl. After developing a bone infection that failed to respond to antibiotics, he was reduced to huddling in a corner. Tulane asked PETA for permission to put Billy down, to spare him the tortured and drawn-out death that Paul had suffered. Although PETA's own vet agreed that Billy should be euthanized, Pacheco rejected the advice. He didn't believe Billy was suffering, or about to die, especially since Tulane refused to allow him or anyone else from PETA to see for himself. By this time Billy's spine was fused in a curve and he was immobilized. "We had a crisis at Christmastime," said Peter Gerone, who directed the primate lab at the time. "He stopped eating." Although the International Primate Protection League, citing a state animal-protection statute, asked for and received a temporary restraining order from the U.S. District Court for the Eastern District of Louisiana that held up experiments on the seven surviving monkeys, on January 10, 1990, Tulane won an order from the U.S. District Court of Appeals allowing scientists to carry out the brain experiment before euthanizing Billy.

On January 14, 1990, Billy became the first of the Silver Spring monkeys to undergo neurosurgery before being put to death. After anesthetizing him with ketamine hydrochloride, neuroscientists led by Pons and Mishkin administered a mixture of isoflurane gas and oxygen, a deep anesthetic. Placing his head in a frame to hold it steady, the scientists drilled through the skull covering the cortex opposite the deafferented limb. Then, using tungsten microelectrodes, they recorded from brain areas approximately 0.75 millimeter apart across the region of the somatosensory cortex, to measure the activity that occurred in Billy's brain when they gently stroked different parts of his body with a camel's-hair brush or cotton swab. The goal was to determine where, in the somatosensory cortex, the

brain processed each sensory input. In particular, the researchers hoped to determine whether the region of the somatosensory cortex that had originally received sensory input from Billy's arms, but that had been deprived of this normal input for more than twelve years as a result of the deafferentation, had changed. In macaques, earlier studies had established, the arm representation in the somatosensory cortex lies between the representation of the trunk and the representation of the face. The representation of the chin and lower jaw abuts the representation of the hand. In Billy, the zone representing the fingers, palm, lower and upper arm of the deafferented limb, remember, was not receiving any sensory input. It would not be far off to call this "deafferentation zone" the zone of silence: it was a radio dish tuned to a station that was no longer broadcasting.

Or so everyone thought. But when Pons took electrical recordings from the deafferentation zone, he found that the entire region "responded to stimulation of the face." Touching or brushing Billy's face, or even gently moving his facial hair, produced vigorous neuronal responses in the supposedly silent zone. Apparently, having waited so long for signals to arrive from the arm and hand, this region of cortex had done the neural equivalent of moving its antenna slightly to pick up signals from a different transmitter altogether. The cluster of neurons in the somatosensory cortex that responded to stimulation of the face had pushed so far into the once-silent zone—which originally received inputs from the deafferented arm—that it abutted the somatosensory representation of the monkey's trunk. Indeed, all 124 recording sites in the "silent zone" now responded to light stimulation of the face. After the experiment, Billy was given an overdose of pentobarbital and put to sleep.

That month, an editorial in the journal *Stroke* argued against the relevance of such animal work to humans: "Each time one of these potential treatments is observed to be effective based upon animal research," it said, "it propagates numerous further animal and human studies consuming enormous amounts of time and effort to prove that the observation has little or no relevance to human disease." But Louis Sullivan, then secretary of HHS, glimpsed in the experiment a ray of hope for brain-injured people: "The investigators entered uncharted territory when they studied the brain of the first of the [Silver Spring] primates to be euthanized for humane reasons," he declared. On July 6, 1990, Augustus, Domitian, and Big Boy were also experimented on and then euthanized. An appeal by PETA to the Supreme Court, asking the justices to block the euthanasia of Titus and Allen, was denied on April 12, 1991. Titus was put to sleep at 2:00 P.M. that day. Allen was put under deep surgical anesthesia as part of a four-hour experiment; he never awoke.

The researchers reported their findings from four monkeys in the journal *Science* in June 1991. (Taub's name was also on the paper, but only because he had overseen the original deafferentation experiments more than twelve years before.) They found, they said, that the deafferented region, which included primary somatosensory maps of the fingers, palm, arm, and neck, was not the

nonfunctional desert they expected; rather, the entire zone had responded when the researchers brushed the animal's face. "Deafferentation zone," then, was a misnomer: although part of the monkeys' somatosensory cortex had been deprived of its original afferent input, from the arm, over the course of the previous dozen years it had been innervated by neurons from the face—specifically, the part of the face from the chin to the lower jaw. The part of the cortex that usually received sensory input from the monkey's arm did not simply go out of business. Instead, neuronal axons from adjoining cortical regions had grown into it. The result was a rezoning of the monkey's somatosensory cortex. Virtually the entire hand region, measuring 10 to 14 millimeters across, had been invaded by neurons of the face area. Like an abandoned industrial neighborhood that has been rezoned for residential use, the monkeys' somatosensory cortex had been rezoned so that the arm region now received input from the face. The scientists had discovered, they wrote, "massive cortical reorganization" that was "an order of magnitude greater than those previously described." Pons made it clear why they were able to discover what they did. "It was, in part, because of the long litigation brought about by animal-rights activists that [made] the circumstances extremely advantageous to study the Silver Spring monkeys," he told the *Washington Post*.

All these years later Taub, who had been hired by the psychology department of the University of Alabama at Birmingham (UAB) in 1986, makes an admission. "Nothing was lost to science" as a result of the raid on his lab, he concedes. "Just a few years later Mike Merzenich [at the University of California, San Francisco] made the discoveries that we were headed toward." He pauses. "Though I must say, I wouldn't have minded making those discoveries myself." Instead, Taub was unable to conduct research for six years. Journals that once published his work wanted no part of him; agencies that once funded him turned down his grant proposals.

Taub's experiments on deafferentation in monkeys generated two complementary lines of research. One was called *constraint-induced movement therapy*. It grew out of Taub's discovery that animals with bilateral forelimb deafferentation eventually use their limbs extensively, whereas those with unilateral deafferentation—a lesion only half as extensive—have a virtually useless arm. The lack of purposeful movement, Taub concluded, reflected learned nonuse. For more than twenty years, until the 1981 raid on his lab, Taub had sought ways to overcome learned nonuse, motivating his monkeys through hunger or the desperate desire to avoid electric shock to use an arm they were otherwise content to leave hanging uselessly at their side. At UAB he would finally take up the idea he had broached so long ago, in that chapter he had written in 1980, on whether learned nonuse might explain a stroke patient's inability to use a limb, and whether behavioral therapy might overcome it. Taub would not starve, let alone shock, his patients at UAB. He would simply put their good arm in a sling, and their good hand in an oven mitt, so that if they wanted to hold something, or feed themselves, or get dressed, or do the laborious rehabilitation exercises he put them through, they would have to use their "useless" arm. He called it constraint-induced movement therapy, or CI therapy for

short. It was the work with the deafferented monkeys that had demonstrated to him that behavioral intervention might help patients overcome the learned nonuse of a limb affected, for instance, by stroke. In November 1992, a year after the experiments on the Silver Spring monkeys demonstrated massive cortical remapping, UAB granted Taub $25,000 to study whether stroke patients could be taught to overcome learned nonuse of a limb. This is the subject of Chapter 5.

The other avenue of research was more purely scientific. Pons and Mishkin had shown that deafferentation results in cortical reorganization or remapping. The plasticity of the adult brain overturned an entrenched paradigm, opening the door to a greater understanding of the brain's capacities. Cortical remapping became the first example of neural plasticity in the adult brain. As these things tend to do, the two lines of research would meet up again, eventually, when Taub discovered that the brains of rehab patients had changed as a result of constraint-induced movement therapy.

For almost twenty years the Silver Spring monkeys were famous not for what they had done, but for what had been done to them. But, looking back, it is clear that they left a double legacy. Their case prompted revision of the Animal Welfare Act in 1985, requiring that researchers reduce unnecessary suffering among lab animals. It made PETA a force in animal rights: the group went from "five people in a basement," as Ingrid Newkirk puts it, to a national movement. It put biomedical researchers on notice that the rules had changed, that complying with the lenient animal use standards would not be enough to insulate them from the fury of animal rights advocates. "Until the Silver Spring monkeys," says Newkirk, "people thought, yes, animals are used in labs, but there is nothing I can do about that. But then they saw the animals' faces, and their suffering, and realized that there are things ordinary people can do. The animals came out of the lab for the first time, and people saw their suffering. After the Silver Spring monkeys, nothing was ever the same." At Poolesville, which houses more than 1,000 monkeys, animals are now kept in large social groups rather than solitary cages, "since they are social creatures by nature," says J. Dee Higley, who joined the facility in 1989 and studies violence associated with alcoholism. "When I first got here, hundreds of animals were kept in single cages. Now we know that if you keep a primate in a single cage, you are very likely to have an abnormal animal."

But the Silver Spring monkeys also changed forever the dogma that the adult primate brain has lost the plasticity of childhood. Instead, a new paradigm was beginning to emerge.