The Resilient Brain

Chantal Abbey re-learned skills as basic as walking and talking while at the UCLA Neurological Rehabilitation Unit in September 2002. She has no recollection of the experience.

On August 15, 2002, Abbey was driving north on Sepulveda Boulevard not far from UCLA when a car headed in the opposite direction veered toward her, its driver asleep at the wheel. The head-on collision left the 27-year-old actress in a coma with a fractured wrist, lung trauma, bleeding into the brain and diffuse axonal injury—damage to the axons of nerve cells across the brain’s various structures.

A tube was surgically placed into the right lateral ventricle of Abbey’s brain to drain excess spinal fluid and decompress the brain when necessary. The coma lasted a little more than two weeks. When she left intensive care and was first admitted to the rehabilitation unit, Abbey spoke only her last name in response to any question. “She became restless and distracted by anything that moved, or by any sound,” says Dr. Bruce Dobkin, professor of neurology at the David Geffen School of Medicine at UCLA and director of neurological rehabilitation at UCLA Medical Center. Moreover, adds Dobkin’s staff employed in an effort to “retrain” her injured brain. Her first concrete post-accident memory is of a day in early October when the unit’s therapists were teaching members of her group how to tie their shoes. “I was very angry that I was there, because I didn’t yet grasp that I had been in a serious accident,” Abbey says. “Then, when we were outside, they untied my shoe and asked me to re-tie it and I couldn’t. It finally hit me, and I became very emotional. I remember thinking, ‘I was an honor student, I have a college degree, and now I can’t tie my shoe?’”

Patients such as Abbey who recover from an acute brain injury provide dramatic illustrations of the organ’s ability to adapt, and are helping to illuminate the processes of learning and memory. Powerful new tools are giving neuroscientists unprecedented views to observe these processes in the brains of humans, through functional magnetic resonance imaging (fMRI); and in animals, where real-time recordings are made of individual nerve cells.

“We always knew that learning was a dynamic process, and that somehow it involved a complicated choreography of massive networks in the brain,” says Dr. John Mazziotta, chair of the Department of Neurology at the David Geffen School of Medicine at UCLA and director of UCLA’s Brain Mapping Center. “Now we can see those networks, and we can see some of the ground rules by which this choreography takes place.”

Studies of the normal brain have found that the cortex is compartmentalized into units that perform different functions. But, notes Mazziotta, this fragmentation isn’t absolute. “It’s relative, and it’s constantly changing,” he says. When a person is born blind, for example, the visual cortex doesn’t receive the information it needs to organize. Imaging studies have shown, though, that when that person learns Braille, some wiring takes place in the part of the brain normally associated with vision. “It’s all about the real estate, and as in real estate, it’s location, location, location … and, to some degree, the zoning laws,” says Mazziotta.

Imaging studies of violinists have found that the more accomplished the player, the more cortex is committed to controlling the all-important left hand; similarly, more cortex is devoted to the task in violinists who learned to play earlier in life. “This is an example in which, with rehearsal and increased skill, more and more real estate is devoted to controlling the fine details that go into playing the instrument,” Mazziotta explains. Imaging studies have also shown that as new concepts are learned, large areas of the brain are active; as the information becomes better understood, the amount of these brain regions that are active during recitation of the knowledge shrinks, while other parts of the brain having to do with recall show greater activity.

The brain’s ability to reorganize during learning, known as plasticity, is commonly associated with children. But, while the child’s brain tends to be more plastic than the adult’s, Mazziotta points out that the mechanisms to learn are active at all points in life—and that the more they are used, the better they perform.

Looking at living neurons in the brains of animal models, researchers are able to glean additional insights. Dr. Carlos Portera-Cailliau, assistant professor of neurology and neurobiology, notes that in recent years, a combination of advanced microscopic imaging methods and the use of fluorescent probes has enabled neuroscientists to observe changes that take place in the living cells of the intact brains of mice during normal development and in disease.
Chantal Abbey was taught to “retrain” her injured brain following an auto accident.
Using a green fluorescent protein to follow certain neurons in the brains of young mice, scientists such as Portera-Cailliau are in a position to study the changes that take place following a stroke, when the nerve-cell growth processes are lost in a portion of the brain but others begin to move into the damaged area to compensate. “Depending on an animal’s experience as it explores its environment, the brain will grow differently,” Portera-Cailliau notes. “The brain is very plastic early in development, which is why children who suffer a stroke will recover almost completely their function. That plasticity is important for learning, but also for recovering after lesions.”

It follows, then, that the more plastic an adult’s brain, the more successful the learning after brain injury. So Portera-Cailliau’s goal is to determine the molecular mechanisms that facilitate this rewiring following the insult. Such information might point the way toward therapeutic targets and, potentially, drugs to speed recovery of the adult brain after stroke, trauma or other injury.

Functional MRI studies reveal changes in the brain in response to training with walking. Dobkin and colleagues have shown, for example, that intense physical exercise can play an important role in restoring the brain and spinal cord after serious injury. In a study in which spinal-cord-injured patients walked with assistance on a treadmill, they found that the greater the load on the legs, the higher the muscle activity. Moreover, the spinal cord’s output, as measured by muscle activity, was synchronized with the step cycle, suggesting that a “rewiring” was occurring. In the laboratory of Dr. Fernando Gomez-Pinilla, professor of neurosurgery at the David Geffen School of Medicine at UCLA, researchers have found that exercise affects molecular systems important for maintaining neural function and plasticity; specifically, it promotes increased output of brain-derived neurotrophic factor, a protein that causes certain types of nerve cells to survive and grow, particularly at the level of the synapse, where most learning takes place. According to new research, brain-derived neurotrophic factor helps translate the action of training and experience into molecular events that support cognitive function and functional recovery. In follow-up animal studies, Gomez-Pinilla’s group has found that exercise after brain injury helps the recovery process, and that it may also enhance the synaptic plasticity in the normal brain.

As a neuropsychologist working in UCLA Medical Center’s Neurological Rehabilitation Unit, Dr. Susan Bookheimer, professor of psychiatry and biobehavioral sciences, has focused on assessing brain-injured patients to understand how different lesions can affect brain function differently. To Bookheimer, among the most interesting results from fMRI studies is the understanding that contrary to what was previously assumed, the task of absorbing new information is not confined in the structure of the brain known as the hippocampus. “That remains true for explicit memories,” Bookheimer notes, “but it turns out that a lot of learning is unconscious, and is based on our habits and experience.”

This “habit learning,” taking place through many repetitions, is not limited, as once thought, to motor behaviors. Researchers have found that the basal ganglia portion of the brain can be the site for conceptual learning that is not explicitly taught—from understanding social cues to language skills and a general familiarity with one’s environment. “This knowledge about another region of the brain that contributes to learning is very exciting because it gives us an entirely new avenue for remediation following an injury,” Bookheimer says. Studies have also indicated that the hippocampal and basal ganglia memory systems are mutually inhibitory—the more one is used, the more the other is inhibited. This finding suggests that understanding the nature of an individual patient’s memory and learning impairment provides valuable guidance in the design of efforts to rehabilitate that patient.

As head of the UCLA Neurological Rehabilitation Unit, Dobkin leads a team that begins working with brain-injured patients after the acute period has ended. It’s not uncommon for his patients to have no memory of the two-to-three-week period before their transfer to his unit. “By the time they’re leaving, they often will associate only me with their treatment,” Dobkin says. “When they thank me, I point out that there were many others who took care of them during that acute period, including neurosurgeons, ICU doctors and nurses. That can make the patients anxious, because they don’t remember any of that.”

The retrograde amnesia that many brain-injured patients experience—losing memory of events that occurred for a period of time typically ranging from hours to days or weeks before the injury—reinforces what neuroscientists are learning about the fragility of memory. “Information that isn’t fundamentally important to you, or doesn’t have emotional content, is easily lost,” Dobkin says. “That’s why the ordinary things that happened in the days or weeks immediately preceding an injury may disappear.”

This fragility is by no means limited to brain-injured patients. “A lot of people worry about dementia when they start losing their keys,” Dobkin notes. “That’s not a sign of dementia; it’s probably just the fact that where you placed your keys wasn’t important, wasn’t a focus of your attention. A
memories can also be easily altered as they are intertwined with recollections of other events. “Our factual memory isn't as reliable as we'd like to think,” Dobkin says.

Learning and memory are more complex than scientists previously suspected. The mechanisms involved in rote learning of facts or events differ from those involved in skills learning, such as playing the piano or hitting a baseball. We have memories of the past, as well as prospective memories—keeping plans or appointments in mind.

As they develop a better understanding of the role of chemical messengers in solidifying memories, Dobkin and his colleagues are laying the groundwork for therapeutic strategies to strengthen the memory in brain-injured patients through electrical stimulation or individually tailored medical regimens. In his studies of patients who are relearning how to walk, Dobkin has shown through fMRI that the brain changes as the skills are practiced. Dobkin is using imaging studies to test a variety of learning strategies in brain-injured patients undergoing rehabilitation. “Right now, we can’t predict which patients will benefit from particular approaches,” he says. “By relating one study to the next, we hope to be able to better predict which paradigm will be most likely to work for individual patients.”

The scientific proof that brain-injured patients will do better because of particular interventions designed to help them learn isn’t yet there, Dobkin says. “The problem is that 15 years ago, strategies were based on theories that had nothing to do with how the brain works,” he explains. “A variety of drug and training approaches is just starting to be tested that build upon neuroscientific data.”

In working with brain-injured patients, Dobkin and his staff seek to optimize reinforcement. “We try to just give them one thing on their plate, without a lot of distraction, so that they can focus,” he says. “Then we try to get them to use their vision, hearing, touch and movement to understand the relationship between what it is we want them to learn and how they’re going to retain that information.” As motor skills are practiced—feeding oneself, for example—the nerve cells in the brain related to that function are reinforced. To help patients with prospective memory, they’re encouraged to keep notes. “At first you might not remember to look at the notes, but gradually you learn to write down anything important, and to check every hour to make sure you’re not missing something,” Dobkin explains.

As their recovery progresses, patients are encouraged to follow a news story that interests them—reading about it, watching or listening to coverage, and discussing it with friends and family members. Medications for improving attention by increasing one of several neurotransmitters can be useful to augment the learning process, Dobkin adds. But the most important aspect of the rehabilitation process is practice. “Patients who are the most motivated—who don’t just wait for the one hour they spend with the therapist three times a week, but constantly rehearse and try to strengthen the connections—tend to do the best,” he says.

A year and a half after her accident, Chantal Abbey started graduate school, enrolling in a California State University, Northridge program to earn her teaching credential. “For the most part, I feel like my memory has recovered 100 percent,” she says. “But school is definitely more of a challenge. I don’t memorize things as easily as I used to.”

She still writes everything down and relies heavily on her day planner. “My life is very different from how it was before the accident,” she says. “I was never the type of person who had to be really organized, but now that’s the only way I can function. I never used to worry about change, but now I need my routines.”

Other than that, she feels like herself. The flatness that characterized her personality in the months after the accident is long gone; her old sense of humor finally returned.

“There’s this remarkable adaptation that can occur, as long as the brain injury isn’t too profound,” says Dobkin. “That plasticity is based on a lot of things we don’t know about for sure, but that have to do with the ability of spared pathways to increase their activity in a way that compensates for the damaged areas. It has to do with how fundamental mechanisms of learning restore themselves. The skills training that we gave Chantal, and that her family gave her, and that she continued to reinforce, all presumably acted on these adaptable systems and helped to restore function.”