

One Precious Gift

Families donate brains to answer their own questions—and those of science.

BY JAMIE TALAN

It began in the late 1990s, the change in George Edwards. It's hard to say when his brain began to register the effects of a neurodegenerative disease, says his widow Rachel Hadas, Ph.D., an award-winning poet and the Board of Governors Professor of English at Rutgers University in Newark, NJ.

But looking back, the damage began to reveal itself in the form of odd, uncharacteristic behavior, she recalls. The composer and long-time professor of music at Columbia University was quiet by nature, but he had become disturbingly remote, and apathetic.

Hadas chronicled her husband's brain illness in *Strange Relation: A Memoir of Marriage, Dementia, and Poetry* (rachelhadas.com). The book, published in 2011 by Paul Dry Books, provides readers with a moving account of Edwards' behavioral and cognitive changes.

But the family learned the exact cause of that illness only after Edwards died and an autopsy was performed. By donating his brain to science, they are also helping neurologists learn what to look for in the examination room.

LEAVE OF ABSENCE

Hadas calls the quiet that settled over their apartment on the upper West Side of Manhattan during Edwards' illness "empty silence." He had been an accomplished composer who could spend days perfecting a few dozen seconds of music, an athlete who loved tennis, a father who regularly sat down for a game of chess with his son, and a husband who shared a rich intellectual life filled with music and books.

In the spring of 2002, Jonathan, their only child, graduated and went off to college. Edwards had never been one to waste a second; now, he had taken to sitting in a chair in the living room,

seemingly content in doing nothing.

Hadas recalls a trip in 2003 to St. Louis, MO, to see her half-brother, who had terminal cancer. In a poem, she describes standing at the door with suitcase in hand and watching her husband in the dining room, silent, "like a tree in a yard." He did not even say good-bye to her brother.

Near the end of the fall semester in 2004, she received a call from the chairman of the music department at Columbia. Edwards was not communicating well with students or his colleagues, the chairman said. The recommendation was that he should take a leave of absence.

Hadas made an appointment with a doctor, who examined her husband. The simple question "What year did you get married?" led to a long stretch of silence. Edwards' answer arrived like a question: "1990?" The couple had exchanged vows in 1978.

WHICH DEMENTIA?

Doctors considered two main possibilities: frontotemporal dementia (FTD), a condition marked by behavioral and personality changes and language problems; or the more common Alzheimer's disease (AD),

which begins with lapses in short-term memory and progresses to significant cognitive and behavioral problems. Both are neurodegenerative diseases but involve different areas of the brain. Frontotemporal dementia primarily affects the frontal and temporal lobes of the brain, which play a significant role in decision-making, behavioral control, emotion, and language; while AD primarily affects the cortex, damaging areas involved in thinking, planning, and remembering.

A tentative diagnosis of FTD was made in 2005, when Hadas



COMPOSED Music professor and composer George Edwards, long before the onset of dementia.



first brought her husband to a doctor. By then, Edwards could not—after three decades teaching music theory and composition—manage a classroom. It was only in hindsight that Hadas realized his silence and occasional bursts of anger at home weren't personal.

It was the change in behavior and Mr. Edwards' age—he was 61—that led neurologists to consider FTD. The majority of people diagnosed with AD develop symptoms after 65 and often much later. Early-onset AD is rare and usually associated with a known family history.

Hadas thought FTD was more in keeping with her husband's symptoms. So did the doctors who began treating him. In 2006, she flew out to an FTD scientific symposium at the University of California, San Francisco. After the meeting, she brought her husband to see Murray Grossman, M.D., a professor of neurology at the University of Pennsylvania, Fellow of the American Academy of Neurology (AAN), and leading expert on FTD. The couple wanted to attach a name to the symptoms out of more than curiosity: They have a grown son who may share a genetic risk for either one of these conditions. Both FTD and AD have been linked to specific (and different) genes that put people at risk for the illnesses.

But the examination was inconclusive. Dr. Grossman said the only way to know with certainty whether FTD or AD was the cause of Edwards' symptoms was from an autopsy.

That was when Hadas decided that her husband's brain would be donated to science. (By that time, Edwards was too ill to participate in the decision.) Families can request an autopsy at the time of death without donating the brain, but Hadas wanted to help the cause of research.

Edwards grew progressively worse; by 2007, his exhausted

wife made the decision to place him in a nursing facility. His occasional violent outbursts got him kicked out of several places, and at the time of his death he had only been in what would be the last nursing facility for three weeks.

When Edwards died in October 2011, his brain was donated to the New York Brain Bank at Columbia University, where he had been a patient and had spent much of his adult life teaching. The autopsy revealed he had AD, not FTD.

"I am very, very glad that I did this," says Hadas. "It's good to know exactly what he had."

PREPARING FOR THE BRAIN BANK

On the night of his death in October 2011, Hadas' grief took a backseat to a singular goal to get his body to Columbia's Brain Bank. She had been preparing for this moment for years. Close to midnight, Hadas phoned Arlene Lawton, R.N., a brain donation coordinator at Columbia. Lawton's job is to work with families to ensure that the brain gets to the autopsy lab quickly so it can be prepared for research. She and Hadas had formed a strong bond over the years.

As is the protocol for brain donation, once the brain is removed, the body is sent to the funeral home. By Monday afternoon, in a basement laboratory, portions of Edwards' brain were cut away to prepare for testing. Other tissue was set aside for further study.

The cut sections of his brain were scrutinized. Columbia neuropathologist Jean Paul Vonsattel, M.D., director of the Brain Bank, knew nothing about the life of the 68-year-old composer, but Edwards' brain tissue told at least part of the story: The plaques, tangles, and diffuse changes were characteristic of AD. The pathology looked nothing like the FTD brain, which usually shows a build-up of protein and atrophy in the frontal and temporal lobes.

The Need for Brain Donors

The federal government is stepping into the autopsy business. “The opportunity and the need have never been greater,” says A. Roger Little, Ph.D., senior advisor for the Science Policy Planning and Communications office at the National Institute of Mental Health (NIMH). “For us to understand diseases, we need to understand the people who have them.” The government is pulling together the brain autopsy resources at the half dozen brain banks across the country and creating an infrastructure so that people can donate tissue to these banks no matter where they live. And scientists will also have an easier time getting their hands on samples for research.

Dr. Little’s office received a grant to contract with the brain banks so that tissue can be shared broadly and systematically. “It has not been easy for people to donate brain tissue,” he explains. The NIMH will be reaching out to educate the public on the importance of donating tissue for research. Federal regulators have met mental health advocacy organizations to talk about autopsies and the importance of brain tissue in research. The public will be able to go to a new website that is being designed to educate about brain tissue donation. It will be up and running by the fall.

The brain tissue banks are not only for people with diseases. “There is a huge need for healthy brain tissue for scientists to use as controls,” says Dr. Little. With more tissue, scientists will be able to match age and gender in both diseased and healthy brains.

For more information on brain banks and becoming a donor, visit the National Institute for Neurological Disorders and Stroke website at ninds.nih.gov.

The autopsy results were surprising given that Mr. Edwards showed all of the clinical features of FTD.

By mid-December, a copy of the results with the official diagnosis of AD was sent upstairs to Lawrence S. Honig, M.D., Ph.D., the neurologist who had taken care of Edwards for several years. Dr. Honig read over the report. He picked up the phone to share the news with Hadas and would later send her a copy of the results. “She had been through so much with George,” says Dr. Honig.

WHY DONATE?

There are many reasons why families decide to donate their loved ones’ brains to science. Hadas wanted to know the exact nature of her husband’s disease and hoped his tissue would be used to better understand AD. “It gives his death more meaning,” she says.

Dr. Honig, his last neurologist, believes that Edwards’ brain will help researchers better understand the uncommon symptoms of AD.

“Being able to link the pathology seen at autopsy with the clinical features of George’s disease is so important,” says James Noble, M.D., another of Edwards’ neurologists. Dr. Noble had been struck by Edwards’ mastery of language well into the course of his disease.

With a final diagnosis, Edwards’ tissue was catalogued and banked for research. At Columbia, and in other brain banks, the autopsy data is paired with the clinical records and offered to researchers worldwide.

UNCERTAINTY IN LIFE

Patricia Madonna was 51-years old when she died. Diagnosed at nine with Type I (juvenile) diabetes, her childhood was spent trying to regulate her abnormal insulin levels. At 15, she was diagnosed with anorexia and complained of double vision.

In her senior year of college, the young woman married and within a few years gave birth to two daughters. By then, she had a hard time focusing. She had a number of car accidents, one after another. Her hands started shaking, which increased as the years went on. Her mother, Rita, brought her to dozens of doctors around the country. For many years, the shaking was so intense that Madonna had to be fed.

Soon after a divorce, she moved in with her parents. Over several more years, her hands began to shake again and her legs began to tremble. Madonna’s parents continued to search for a diagnosis. To the family, it looked like a neurologic disease. Her brother, a spinal surgeon, helped identify some of the world’s experts on movement disorders. Madonna’s symptoms suggested multiple sclerosis (MS), but no one was certain. Throughout the decades, MS was repeatedly ruled out because they weren’t the textbook list of symptoms.

In her 40s, Madonna got worse. Her thinking was so unfocused that she could no longer say what season it was. When provided with clues—“Patty, look at the flowers coming up”—Madonna might answer, “Oh, it’s spring,” and laugh uncontrollably. Her cheerful, sweet disposition seemed to ease the blow of the symptoms.

At 49, Madonna experienced a tonic-clonic (grand mal) seizure and was paralyzed on one side of her body. Soon after, she was put into a nursing facility, where her body folded up into a fetal position. She could no longer swallow, and doctors eventually inserted a feeding tube. “But she was aware of everything that was happening to her, trapped in her body,” says Maureen Regan, her sister.

GETTING AN ANSWER

Almost three years later, on a crisp fall morning, Madonna died at Good Samaritan Hospital on New York’s Long Island. It was then that her family decided that they had one last shot at finding out what had caused her symptoms. “We wanted an autopsy,” says Judith Regan, her older sister and a radio show host on SIRIUS.

Maureen Regan had eight hours to find a medical center to do an autopsy. She finally located the number for the New York Brain Bank. Carol Moskowitz, R.N., an advanced nurse practitioner in

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—CAROL MOSKOWITZ, R.N.

charge of brain donations, took the early call. Regan begged the coordinator to take her sister’s brain. The problem, Moskowitz told Regan, was that the program was only accepting brains from patients who had been seen at the medical center, Regan recalls. Madonna’s mother insisted that her daughter was seen at Columbia’s movement disorders center for an evaluation almost two decades earlier, but there was no record of her in the system.

Following Columbia protocol, the pathologist at Good Samaritan Hospital called in a special team to extract Madonna’s brain. By three in the afternoon, the brain had reached Columbia.

After the memorial service for Madonna, Maureen Regan collected her sister’s medical files from their mother, who over 35 years had amassed papers as thick as three telephone books, and headed in to deliver them to Moskowitz.

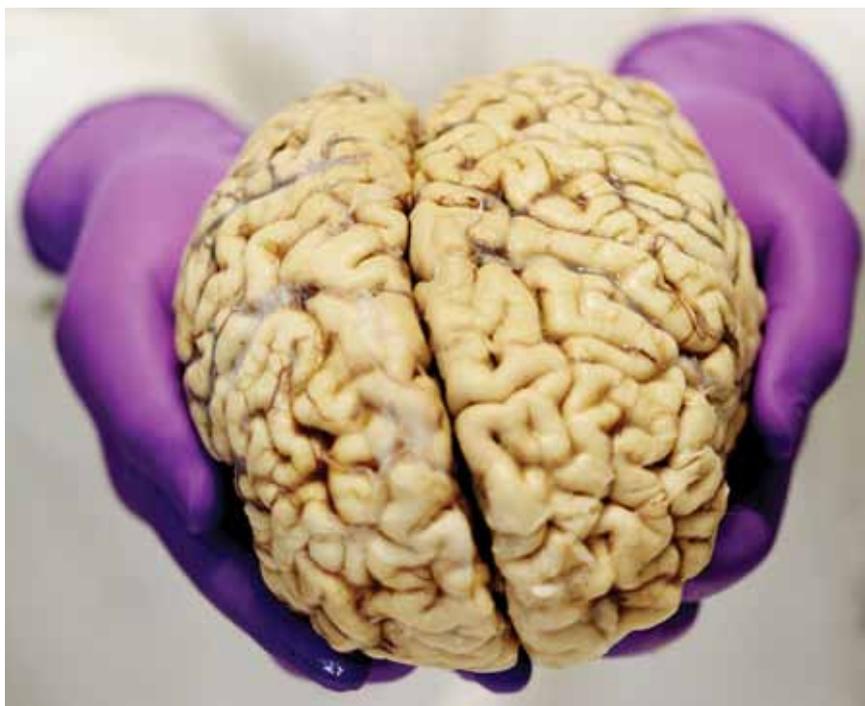
Regan laid out the documents on a large desk in a conference room at the hospital. Somewhere in that documentation, Regan says, was proof that her sister had been a patient at Columbia. As they began talking, Moskowitz was in mid-sentence when she jumped up and headed over to an old card file. Before electronic records, Moskowitz kept handwritten index cards on patients they had videotaped for evaluation.

“Just a second,” Moskowitz said. She thumbed through the names. And there she was, Patricia Madonna, complete with a video of her as a young adult, trembling and barely able to walk. At the time, doctors at the movement disorders clinic ruled out MS.

In life, doctors struggled with a lack of laboratory evidence—blood tests, spinal taps, and brain scans—in support of MS. In death, the diagnosis was obvious: “Demyelination of brain, extensive, focal, in cerebral white matter, gray nuclei, pons, brain stem, cerebellum and optic chiasm, consistent with multiple sclerosis,” the autopsy report stated.

Two of the doctors who later signed off on the pathologist’s autopsy report had been the very ones who ruled out MS in Madonna.

“The final diagnosis gave our family a bit of peace,” says Maureen Regan. “It was a relief to finally know what was wrong with my daughter,” adds their mother. “Maybe it will help us or help others.”



HELPING DOCTORS IN THE EXAM ROOM

A lot of work goes into preparing and procuring brain tissue and making it available for research, which is the ultimate goal of a brain bank. While Columbia and other brain banks will take donations of diseased brains from other parts of the country, Moskowitz says, the tissue must come with good medical records, including videos and cognitive testing.

At Columbia, neuropathologist Dr. Vonsattel has led the way to formalize protocols for brain donation. He would love to see a national brain banking system, he says: It is an expensive process, but one that yields a lot of important information about the diseased brain.

As for George Edwards and Patricia Madonna, their brains will continue to teach doctors what to look for in examination rooms. At a recent meeting, more than a dozen doctors sat around a table and watched videos of Madonna that had been taken decades earlier. Her clinical history was shared, and then they were asked to vote on a diagnosis. One of 15 doctors said it was MS. Then, Dr. Vonsattel described the changes in the woman’s brain, which were characteristic of MS.

“Most people say that donating a loved one’s brain makes a big difference,” says Moskowitz. “They do it because they want to know what their loved one had and help unravel the puzzle of neurologic diseases for others.”