Pioneering neuroscientist Rahul Desikan was attacking ALS. Then ALS attacked HIM.

Love, Science, and Facing Down Death

By Sara Rimer

NICK OTTO

Neuroscientist Rahul Desikan (CAS'99, MED'09) and his wife, physician Maya Vijayaraghavan (MED'06). He describes her as Wonder Woman.

On a bright July morning in San Francisco,

neuroscientist Rahul Desikan sits in front of a computer, at the long wooden table in his living room, which doubles as a home office.

Sunlight streams through the windows as Desikan waits for three students from his lab team. Atop a bookshelf is a photo of a strapping six-foot-one Desikan hiking with his wife, Maya Vijayaraghavan (MED'06), in Alaska's snow-capped mountains. Another photo shows him beaming, his four-year-old son—the older of his two children—on his shoulders.

In addition to being a clinician and a University of California, San Francisco, assistant professor of neuroradiology, Desikan (CAS'99, MED'09) is a pioneering researcher with collaborators all over the world. He and his team are combining imaging, biostatistics, and mountains of genetic and health data in their quest to understand the causes behind the most devastating degenerative brain diseases, from Alzheimer's to ALS to frontotemporal dementia.

The people who suffer terribly from these diseases don't have years to wait for incremental breakthroughs—never mind actual cures, which might still be decades away. Desikan, who sits in a wheelchair, is intimately acquainted with such suffering.

He and his collaborators were a month into the largest study ever undertaken of the genetics of amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease, in September 2016, when he began to experience symptoms he recognized from his own research. Five months of tests confirmed his worst fears: he had ALS, the fatal motor neuron disease that attacks the spinal cord, the same disease that killed the great New York Yankee Gehrig at age 41, and defined the life, and death, of the theoretical physicist Stephen Hawking.

Desikan was 38. ALS progressively weakens the muscles, eventually causing paralysis; most people die of respiratory failure within three to five years of diagnosis. There is no known cure for the disease, nothing to stop its advance. Even as Desikan is pouring his life into curing ALS, ALS is stealing the life he had.

"I Fight Every Day"

His wheelchair is pulled close to the table. The disease has already destroyed his ability to walk, use his hands, or hold his head up. He can't embrace his boys or his wife. And in what some friends count as the cruelest blow, Desikan, whose lab partner, Leo Sugrue, describes him as "probably the most extroverted, social person I've ever met," can no longer speak.

As Maya, a physician and a UCSF assistant professor of medicine, works across from him, Craig Cloutier (COM'99, CFA'04), Desikan's best friend since their days at Boston University, gently adjusts the blue-and-white neck pillow that supports his head. Cloutier straps around Desikan's forehead the gyroscopic mouse he uses to search out letters on his monitor's keyboard, and places under his right palm the clicker he presses to tap out sentences, letter by letter, word by word.

With this system, which Desikan and Cloutier improvised together, he continues to publish studies, write grants, and communicate with the world. It's a laborious process. This brilliant researcher who used to type complete papers on his cell phone now needs three hours to tap out half a page.

"The disease shows relentless progression," Desikan emailed friends and colleagues in October. "I have strength only in my fingertips. The irony is that…I'm doing the best work I've done thus far. Like Sisyphus, I fight every day knowing that I'll never win. Yet I can't stop fighting."

Cloutier recalls that 20 years ago he and Desikan drove through the streets of Boston in a friend's Lexus, moonroof open to the sky. Desikan, triple majoring at BU in biology, neuroscience, and the classics, would stand up in the car channeling Austin Powers and shout, "Groovy, baby!" into the night.

In those days the two traveled the world together. Now, they're making one final journey. At 40, Desikan is racing to score a measure of victory against ALS before it kills him. Cloutier, the man Desikan calls his brother, has moved from Manhattan to San Francisco to help him do it—"sometimes," as Desikan puts it, "just holding me during times of unimaginable sadness."

"His mind is more clear than ever," says Cloutier, who had been the art director of a Manhattan industrial design firm and is now living with his girlfriend, Olivia Norrmén-Smith, out of their camper van. "He has all these ideas. It's like he's flying."

The story of Rahul Desikan's disease is as much about friendship, love, and science as it is about loss and death.

Desikan wrote in an April 2018 email to Cloutier and other friends, "Your love is my savior, not some bs god in heaven.

"Our humanity is all we have and no disease or god can take that away. I'm the living proof."

ONLINE: *Watch a video of Rahul Desikan speaking about his disease during a talk on his research at the University of California, San Francisco, in June 2018, and hear a musical composition he created for his wife, at bu.edu/bostonia.*

Team Desikan

As a scientist, meanwhile, he is using his own disease as data to advance his team's research—work he hopes will help lead to treatments, diagnostics, and maybe even a cure for ALS and other degenerative brain diseases. "I am my own petri dish," he told an audience at UCSF in June 2018.

Told them, that is, through his machine voice, which he activates with software that converts his text into spoken words.

If he can secure more funding—and if he has the time—he could make an enormous impact in the battle against ALS and other brain diseases, his colleagues and mentors say.

His colleagues, who along with Cloutier and his students have become part of his extended family, are organizing a fundraising campaign for him and his team. Cloutier is designing the website and acting in the fundraising effort as the point person for Desikan's tight circle of friends from BU. Desikan's sister,

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Vasudha, has moved from Los Angeles to San Francisco to help her brother and is pitching in.

Chris Hess, chair of the UCSF radiology department, wrote in an online pitch: "Rahul Desikan and his research group are poised to answer what I consider the fundamental question of neurodegenerative disease—who is at risk?"

Andrew Budson, a BU School of Medicine professor of neurology, was a mentor to Desikan when he was a College of Arts & Sciences premed student. They have kept in touch. Budson says that Desikan could "catapult forward by decades" research on ALS. In addition, says Budson, by telling his story—Desikan has been profiled by the *Washington Post*, the *Lancet*, *Good Morning America*, and the ALS Association—he is drawing needed attention to the disease, which could prompt other scientists to focus on it. The 2014 Ice Bucket Challenge, which saw millions of people posting videos of themselves being drenched with ice-cold water to raise money for ALS research, brought in a reported $227 million worldwide for ALS organizations. The money helped lead to the discovery of at least one important new gene in the ALS mystery and accelerated the pace of research on potential therapies. But ALS, like most degenerative brain diseases, Hess says, remains poorly understood and much more funding is needed.

In an email to researchers who might know of funding opportunities, Desikan wrote, "My mind and soul are strong. I am as curious as ever about the brain. I still want to grow as a scientist and push myself every day."

Slowed. But Not Stopped.

At Desikan's home in San Francisco, south of downtown, the doorbell rings. His students, postdoctoral scholars Iris Broce and Chin Hong Tan, and research staff assistant Ryan Nillo, call out greetings as they come up the stairs. Desikan smiles back at them. They sit down next to him at the table and open their laptops. Shortly afterward, Sugrue drops by.

Desikan's wife, Maya, and Craig Cloutier (COM'99, CFA'04), his best friend since their days at BU, are his lifelines.

Desikan is their lab father, says Broce, who wants to be an academic neuroscience researcher like him. "People ask me, 'What's it like to work with him?'" she says. "I tell them, 'He just texted me; I can't keep up with him.'"

Since being diagnosed, Desikan has been an author—often the lead or senior author—of 26 published studies on such subjects as Alzheimer's, Parkinson's, and schizophrenia. In April 2018, in a *JAMA Neurology* study, he announced the discovery of two additional ALS genes and a genetic link between the disease and frontotemporal dementia. This was the work he had begun six months before his diagnosis. In March 2017, in a breakthrough *PLOS Medicine* study, he announced that his team had developed a test that combines the effects of more than two dozen genetic variants to identify which

Desikan and Maya, in 2014. The two met at BU. "I knew on our first date we would be married," he says.

older individuals are at highest risk for Alzheimer's. In subsequent studies, Desikan showed that the test, called a polygenic hazard score, or PHS, would be useful for designing clinical trials.

Desikan is moving his head, navigating the keyboard on his screen with the cursor. With his neck muscles severely weakened by ALS, it can be a struggle just to move the cursor. Sometimes it gets stuck; Cloutier frees it. Slowly, words begin appearing on the screen.

These team meetings have become routine, and even with the pauses while Desikan is tapping out words, there is an easy back-and-forth among the group. The students watch the screen, waiting for Desikan's feedback ("this is Iris's work, it's new and super cool…"), his next big idea—or his next joke.

Desikan activates the text-to-voice function when he wants everyone's attention. His students are used to his pleasantly robotic machine voice. It's called Alex. They make fun of Alex when he gets a word wrong. Desikan uses Alex as a kind of straight man.

> "The irony is that I'm doing the best work I've done thus far. Like Sisyphus, I fight every day knowing that I'll never win. Yet I can't stop fighting."

Sugrue is explaining how Desikan uses massive sets of genetic data "to ask questions that, hopefully, no one's asked before" about how environmental factors might interact with a person's "complicated genetic framework" to trigger ALS and other brain diseases.

The voice of Desikan, speaking through Alex, fills the room: "This is why I love Leo. We have mind meld."

Sugrue's response: "It must be that Rahul Desikan implant I have."

Everyone cracks up, Desikan among them.

"This is a lab," says Sugrue. "Rahul is in the cockpit, navigating the data. People think, ALS, game over. But Rahul is working, he's producing. It's hard to understand until you see it."

Speaking again through Alex, Desikan says, "These are my kids and I love them. I want them to be great scientists. In the time I have left, I want to help people like me who have neurodegenerative diseases and make sure these guys are set."

Learning How Beautiful the Brain Is

Desikan's family emigrated from New Delhi to Queens when he was a boy. He graduated from the celebrated Bronx High School of Science and won a scholarship to BU, where, on top of his triple major, he feasted on subjects ranging from ancient Hindu texts to American politics to Frank Sinatra.

Desikan cracked up his friends, and even his professors, with his imitations. One minute he would channel Bill Clinton, with his Arkansas drawl, the next a globe-trotting disc jockey. He's also a music lover, and had cultivated a talent for deejaying. "Rahul would just walk into a club and say he was an international DJ," says his friend Anukool Lakhina (CAS'01, GRS'01,'07). "He would put on this British accent. He'd say, 'I just flew in from London, I was in Tokyo.' People would be like, 'Wow, c'mon in.'"

But if music was his love, science was the passion he would make his life's work.

Recalling his time at BU, he taps out on his computer: "I first learned from Budson how beautiful the brain is." As a junior, he became a research assistant to Budson, then a Harvard researcher at Brigham and Women's Hospital studying memory distortions in Alzheimer's patients.

Budson and Desikan bonded over a shared desire to understand "how disruptions in the brain affect patients," Budson says, and over "the larger philosophical questions of how are we as human beings able to perceive and emote and experience beauty and love."

After graduating from BU, Desikan began working with Harvard researchers Bruce Fischl (GRS'96) and Anders Dale, and with Ronald Killiany, a MED associate professor of anatomy and neurobiology, on what would become the Desikan/Killiany Atlas, used by researchers worldwide to label and measure parts of the brain through imaging and to track the effect of therapeutics.

"He wasn't scared off by problems along the way," Fischl says.

Like when, on the first try, he flunked his medical boards.

Cloutier still laughs about what happened next. He and Desikan went into seclusion. They rented an unfurnished apartment in Somerville. Their friends called it the monkery (Cloutier had spent time in a monastery in Japan). They called each other monks. They worked out, meditated, and studied.

Desikan took the test again—and passed.

Shortly thereafter, he and Maya went on their first date. Her family, too, had emigrated from India. In 2008, they went back there for their wedding.

"I Have Made Peace with My Disease"

"Everything was in place for Rahul," Sugrue says. In September 2016, Desikan landed a faculty position at UCSF, with his own lab, and began his big ALS study.

A few weeks later, his voice became nasal. He felt weakness

COURTESY OF RAHUL DESIKAN

Facts about ALS

Amyotrophic lateral sclerosis (ALS) is a rapidly progressive and fatal disease, attacking nerve cells in the brain and spinal cord that control voluntary movement. It is not contagious.

It is estimated that more than 20,000 people in the United States are living with the disease at any given point.

Although the disease can strike at any age, symptoms most commonly develop between ages 55 and 75.

The average life expectancy for a person with ALS is two to five years from diagnosis. However, the disease is highly variable and about 10 percent of those with ALS survive for 10 or more years.

The majority of ALS cases (90 percent or more) are known as sporadic, which means they occur randomly with no clearly associated risk factors and no family history of the disease. About 5 to 10 percent of all ALS cases are familial, which means a person inherits the disease from their parents.

For unknown reasons, military veterans, particularly those deployed during the Gulf War, are about twice as likely to develop ALS.

in his left arm when he was bathing his older son, and twitching in his fingers.

"It was terrifying," says Maya. "I had just had a baby. We had just moved into this house."

When Desikan confided his fears to colleagues, they told him he was probably just tired. ALS is more often diagnosed in people in their 50s and 60s, not their late 30s.

At his UCSF talk in June he spoke of his initial despair. "I gave up," he said, speaking through Alex. "The irony was too much to bear." He turned his data over to collaborator Celeste Karch, a neuroscientist at Washington University School of Medicine. Months later, Desikan changed his mind and resumed his work with Karch.

"Now I have made peace with my disease and really want to make a dent in ALS," he said.

More than 5,600 people in the United States are diagnosed with ALS each year, according to the ALS Association, and the disease is slightly more common in men than women. Desikan is not in the small percentage of people whose ALS is familial, caused by inherited genetic factors. "I didn't have the classic risk factors, like older age or traumatic brain injury," he told his audience. "I had none of the known, rare ALS variants."

The research of Desikan's team suggests that many genes make up the architecture of ALS, and that environmental factors may trigger the disease in people whose genetic framework puts them at risk. Desikan theorizes that this may be what happened to him.

He ended his talk by thanking Sugrue ("my lab husband"), Hess ("for continuing to believe in me"), his postdocs ("they are my hands"), his two caregivers, Cloutier ("my best friend, who moved cross-country for me"), his sister and parents and in-laws, and "most importantly, my wife, Maya, who is Wonder Woman, and my two sons."

Heracles and Theseus

It is the day after his session with his students. Desikan is at his computer. Cloutier sits nearby. Maya joins the conversation while juggling calls. Their sons are in day care.

In the windowsill behind Desikan a red-and-white orchid is in bloom, a gift from him to Maya for their 10th anniversary, in March 2018.

Maya and CC, as Desikan calls Cloutier, are his lifelines. They help him in and out of the bathroom. They stretch his arms and legs. They get him to the beach, wheelchair and all. When Desikan needed help peeing the other night, Maya inserted a catheter. ("ALS," Desikan quips, "the gift that keeps on giving.")

The disease isn't waiting. He recently began using a breathing machine at night because he can no longer take deep breaths.

Now, he types, "You should ask Maya and CC why they do what they do for me."

They shrug off the question.

CRAIG CLOUTIER

Desikan at his home in San Francisco with his lab partner, Leo Sugrue (from left), and the members of their lab team, Iris Broce, Ryan Nillo, Maria Olaru, Chin Hong Tan, and Yi Li.

"I've always loved being with him," she says. "I still do."

Cloutier says, "He'd do the same for me."

Desikan still pours his feelings into his music. He creates compositions, mixing classical Indian music, Pat Metheny, jazz, and more. One recent piece is dedicated to Maya, another to Cloutier.

He's been finding solace in Greek classics and thinks about the lessons of his favorite Greek play, *Heracles*, by Euripides. "I was like Heracles," he types. "I was bound for academic greatness. The need for success consumed me. Then tragedy struck. CC and Maya are like Theseus. They lifted me up, without judgment. They showed me that life is family and friends. They saved me. Before I thought the divine was in God, but now I've learned that friendship is divine."