Is Alzheimer's treatment of injecting stem cells into the brain a breakthrough or quackery?

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More than eight years after he realized something was wrong, after, as he described it, "My brain went ...

"What's the word? ... Foggy," Jack Sage finally said after several seconds of silently coaxing his synapses to fire.

More than eight years after his brain went foggy, four years after he was diagnosed with Alzheimer's disease and two years since he began an innovative and extremely invasive therapy, Sage said he is being flooded by memories that seem new, or, at the very least, feel easier to retrieve. His daughter, Kate, thought Sage had suddenly begun to open up about his past because he knew his time was growing short.

"He should not know who I am at this point," Kate said.

His doctor, Christopher Duma, hopes Jack Sage goes down in history as the one-man turning point in the treatment of Alzheimer's disease, while others are skeptical about what Duma has done to Sage's brain. Everyone agrees that Alzheimer's disease is an exploding problem.

The California Alzheimer's Disease Data Report from 2009 projected a 67 percent increase between 2015 and 2030 in residents in Los Angeles, Orange, Riverside and San Bernardino counties living with Alzheimer's disease - up to 498,137. The same report references a study, between

2000 and 2004, in which 58 percent of the deaths among people 65 and older in California were attributed to Alzheimer's disease.

The Alzheimer's Association reported that 610,000 Californians 65 or older had the disease in 2016, and it estimated increases to 690,000 by 2020 and 840,000 by 2025.

On a cool recent night, Sage, a handsome, fit, 82-year-old, sat next to his wife Gloria talking about his children (It is significant that Sage remembers their names James, 46, Kate, 50, and Kelly, 56), recalling when he and Gloria moved into the Newport Beach house with a view of the Pacific Ocean (1990), laughing about their first date at the Bel-Air Country Club (1979), recounting his years as a labor negotiator and executive for Del Monte, Allied Chemical and Continental Airlines (1970s and '60s) and going all the way back to the jack hammering he did in the nickel mines (mid-1950s) in Northern Ontario, Canada.

At this point in his illness, his doctor said he should be having more trouble remembering the perilous tunnels of the Sudbury nickel mine.

"You drill into the granite," Sage said. "You put dynamite in the rock. You dynamite it. Then you shovel out what's left."

And mining, you might say, is what is happening in Jack Sage's brain.

Sage's series of recollections, including his exploits on the golf course in Indian Wells where he has a second home and plays several days a week flashbacks representing the three main components of long-term memory: semantic (recalling the meaning of words), episodic (recalling autobiographic milestones) and procedural (recalling how to accomplish tasks) prompted a grin from Duma, the brain surgeon who, for $10,000 per treatment and without insurance coverage, cut a hole in the back of Sage's head and injected a stem cell serum that had been sucked

out of Sage's love handles.

Is this the Alzheimer's breakthrough the world has been waiting for? Or, is this unproven medical procedure what University of Minnesota bioethicist Leigh Turner calls "quackery and flimflam?" Is this an unsafe, money-grab - it is being conducted outside the approval process of the Food and Drug Administration - preying on the most vulnerable among us?

Turner has written extensively and critically about the Cell Surgical Network (CSN), for which Duma, whose home hospital is Hoag in Newport Beach, is listed as a network physician. The CSN promotes "the stem cell revolution," which its literature claims, is an appropriate treatment for people suffering from a variety of inflammatory and degenerative conditions in other words, for cancer, diabetes, bad knees and hips as well as multiple uses in cosmetic surgery.

"You don't just start dumping things into people's brains," Turner said. "The problem is people may spend a lot of money and find there is no benefit. He (Duma) is exposing people to serious harm. Fat cells don't belong in people's brains."

Sage is the first patient in Phase I of a clinical study officially called "Intracerebroventricular injection of autologous abdominal fat-derived, non-genetically altered stem cells." Sage was the first Alzheimer's patient anywhere to have his own liposuctioned cells injected directly into his brain. He has received eight injections (about two months apart) since November 2014.

Duma quickly offers a qualifier. It is far too early to tell if what he has done to Sage will indeed change the world. He said Sage and, later, 19 other patients have not been harmed by the procedure, and that - safety - is the only criteria in Phase I. Whether the treatment is effective is a

question for Phase II, for which Duma is hoping to attract private funding. Also, he wrote a letter to the national Alzheimer's Association asking for $700,000 to continue his work. He was instructed to apply officially later this year. If he gets the grant, the fees for his patients would be waived.

Early in the process, Duma is excited by Sage's results.

Sage's most recent cognition scores have risen from 45 on the 100-point Memory Performance Index in March 2015 to 54 in September 2015. The volume of his hippocampus - the memory center of the brain - has grown from the fifth percentile before his first treatment to the 28th percentile after his fourth treatment to the 48th percentile after his eighth treatment.

"My golf game is getting better," said Sage, who, heart permitting, plays several times per week. Sage's brain isn't his only problem. He has a long history of heart ailments that have required the insertion of 12 stents to keep his arteries open.

"You can't make a global conclusion based on one patient, but it's a huge turning point," Duma said with the confidence of someone who probes brains for a living.

Duma is somewhat of a maverick in the medical world, a brain surgeon who regularly shuns a scalpel for the gamma knife, a futuristic laser for removing brain tumors. He is known outside the operating room for playing keyboards in bands that specialize in 1970s-era covers of groups such as Genesis, Yes and Emerson, Lake and Palmer. As a child, he was a classmate of John F. Kennedy Jr. at The Browning School in New York City. "We called him John John," Duma said.

Duma realizes he will face opposition to his stem cell/brain injection

therapy. But, as in all breakthroughs, someone has to be first.

"I could have harmed people," he said. "I took an enormous leap."

NOT MUCH HOPE

Alzheimer's patients don't get better.

They get diagnosed, lose their dignity and die.

The speed at which death occurs is the only variable.

In the depressing world of Alzheimer's treatment, Sage and Duma represent equal parts hope and skepticism. The Orange County Register contacted universities and research centers across the country, including Stanford, Harvard, Duke, Florida International, UC Davis, and some of the interview requests were denied while other calls were not returned. Very few medical experts want to talk about the combination of stem cells and Alzheimer's disease, apparently because they know so little about it.

"An Alzheimer's patient improving because of therapy? I'm hopeful it's true. I'm hopeful it's true for all patients," said Joshua Grill, the co-director of the Memory Impairments Neurological Disorders (MIND) institute at UC Irvine. "We are in dire need."

But, Grill continued, "One study does not a revolution make. I've never read anything about this (Duma's work), and I don't know what science is behind it."

Dean Hartley, Director of Science Initiatives at the Alzheimer's Association, knew about Duma's work.

"This is new territory," Hartley said. But with one patient, "No, you cannot say this is a game-changer."

Hartley said many studies fail at the Phase II level, where more and more people are exposed to the therapy.

Still, Hartley said Duma's work is encouraging.

"We want to see things like this happen," Hartley said.

It's not as if Duma is conducting his research in secret. He spoke about his study in public forums twice last year - Sept. 28 at the Congress of Neurological Surgeons in San Diego, and Oct. 1 at the International Society for Cellular Therapy in Memphis.

Duma said he is nearly finished writing a paper about his work that he hopes will be published in a peer-reviewed journal.

THE STEM CELL IDEA

In 1993, Christopher Duma was working at Good Samaritan Hospital in Los Angeles when he and his colleagues began injecting stem cells into the brains of patients with Parkinson's disease. They were making some progress, he said, but politics intervened. Some of the stem cells they were using came from aborted fetuses. Pressure from anti-abortion groups shut that program down.

Fifteen years later, Duma was assisting plastic surgeon Michael Elam on a face-lift on a Parkinson's patient when Elam said, "We need to talk about stem cells."

Elam introduced Duma to Drs. Mark Berman and Elliot Lander, the founders of the Cell Surgical Network.

Berman and Lander had been separating stem cells from fat by using a centrifuge (which they own the patent for) and injecting them into knees and hips and other places where injuries had occurred. Their work had passed an Institutional Review Board after 1,524 patients were treated with no adverse effects, Berman said.

"If you want to repair an injury," Berman said, "the best tissue is the stem cell."

In 2013, Duma suggested a new target for stem cell therapy: the brain.

Duma, with Berman, Lander and Elam as co-authors, tried to begin a study of brain/stem cell injections. But their first attempt at Institutional Review Board approval was denied because they hadn't done animal testing. So they got Dr. Oleg Kopyov at Cal State Northridge to conduct tests on rats.

With the help of Kopyov's work, Duma got Institutional Review Board approval. They chose not to take the usual next step - FDA approval.

The Institutional Review Board "was expecting us to go through the FDA," Lander said. "But there are hundreds of obstructions." The FDA approval process usually takes between eight and 12 years, according to the online journal Medscape.com.

Duma said stem cells present a "quandary" for the FDA because "stem cells are not a drug, and they're not food." Clinics that take stem cells out of the body and put them back in without additives argue that they are exempt from FDA mandates.

"We have been harvesting fat from abdomens and putting them in the brain during brain surgeries since the 1920s," Duma said. "We do it nearly on every case for pituitary tumors, acoustic and skull base tumors

and for conditions of spinal fluid leakage ... since the 1920s. If the FDA ruled that harvested autologous fat cannot be used in the brain, then it would change nearly a century of neurosurgical standard of care."

Someday, Duma said he hopes the FDA will recognize his work.

The work can't wait, he said.

THE BRAVE ONE

In August 2013, Jack Sage staggered into the office of Dr. William Shankle in Newport Beach.

Shankle, a renowned expert in cognitive disease - he is the author of the Memory Performance Index that is used around the world - diagnosed Sage with two problems: Alzheimer's disease and hydrocephalus (fluid on the brain). Sage needed a shunt in his brain to drain the fluid and relieve the pressure.

So Shankle walked him down the hall (their offices are yards apart on the same floor in the same building) and introduced Sage to Christopher Duma, medical director of Hoag Hospital's Brain Tumor Program, and the surgeon who would put in the shunt.

Duma remembers that first meeting. Sage was in "straight-line cognitive decline," Duma said.

Shankle would not grant an interview about Duma or his treatment. Shankle said he is wary of "hocus pocus about Alzheimer's disease" without saying that Duma has done anything wrong. More than a decade ago, Shankle tried a surgical stem cell therapy on patients. He removed patients' stem-cell-rich omentum, a fatty sheath covering the abdomen, cut open their skulls and stretched the omentum directly on their brain.

Four of the six patients he studied had serious complications from the surgery.

The patients improved in cognitive tests, but the surgery was too much for them.

"The method of delivering the treatment was radical (surgical transposition of the greater omentum to the surface of the brain while keeping the blood supply intact)," Shankle wrote in an email. "After showing that it really works, my goal was to never do the surgery again but find a different way of delivering these critical factors less invasively."

Sage was the patient Duma had been waiting for.

"Jack was a man who was doomed," Duma said. "He looked like classic Alzheimer's. He had no ability to follow a train of thought. He was asking and re-asking the same questions. People like Jack are there, but they're not there."

Sage was perfect for Duma for other reasons. He has always been a fitness nut - cycling, tennis, golf, skiing and 10K runs were all part of his lifestyle. Kate Sage said he has been ordering salmon and spinach for dinner at restaurants for years.

"Jack is the experimental model," Duma said. "He is the brave one."

During two years of treatments, Sage has either maintained or slightly improved his cognitive health. He had a major heart attack in 2016, making his brain less of a cause for concern than his heart.

Kate said she doesn't know if Duma's treatment is working.

"It's hard for me to say this is miraculous," Kate said.

She said she doesn't worry about his brain as much anymore.

"He's going to drop dead with some kind of a heart thing," she said. "He's not going to lose his memory."

JACK SAGE

The tragedy of Alzheimer's disease is that it not only steals the history that makes us who we are. It takes our skills, our beliefs, our independence, our ability to love.

So far, Jack Sage is still Jack Sage. Obviously, he doesn't know if he would be the same without Duma's treatments.

"I can tell I'm getting better and better," Sage said. Is that pure optimism? The Placebo Effect?

In January, Jack Sage's driver's license came up for renewal. He said he's able to remember driving directions without problem. He still navigates the route from his home in Newport Beach to his other home in Indian Wells. But, he was required to pass the written test, and Sage feared he wouldn't be able to remember the complex rules of the road.

"I was worried," he said.

But he passed, and his license was extended five years.

His improved memory, he said, sometimes catches him by surprise.

"These memories come up when I don't even think about it," Sage said.

Sometimes, the memories take Sage places he doesn't want to go.

When he worked in the nickel mines in the 1950s, he and his first wife had a son.

"His name was Mark," Sage said, speaking slowly as if the memory was bubbling up from depths he didn't want to consider. "We rented a house with a playroom. My wife went shopping, and I was upstairs ...

" ... I was working on my school work for McMaster University ...

" ... Mark fell ...

" ... we had a drainage basin inside the house ...

" ... when I got to him, he was gone ... "

Sage stopped talking as if flooded by new emotions over the death of his son.

"We were distraught," he said. "It was tough times for years."

In the murky world of Alzheimer's therapy, Jack Sage is still mining.

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