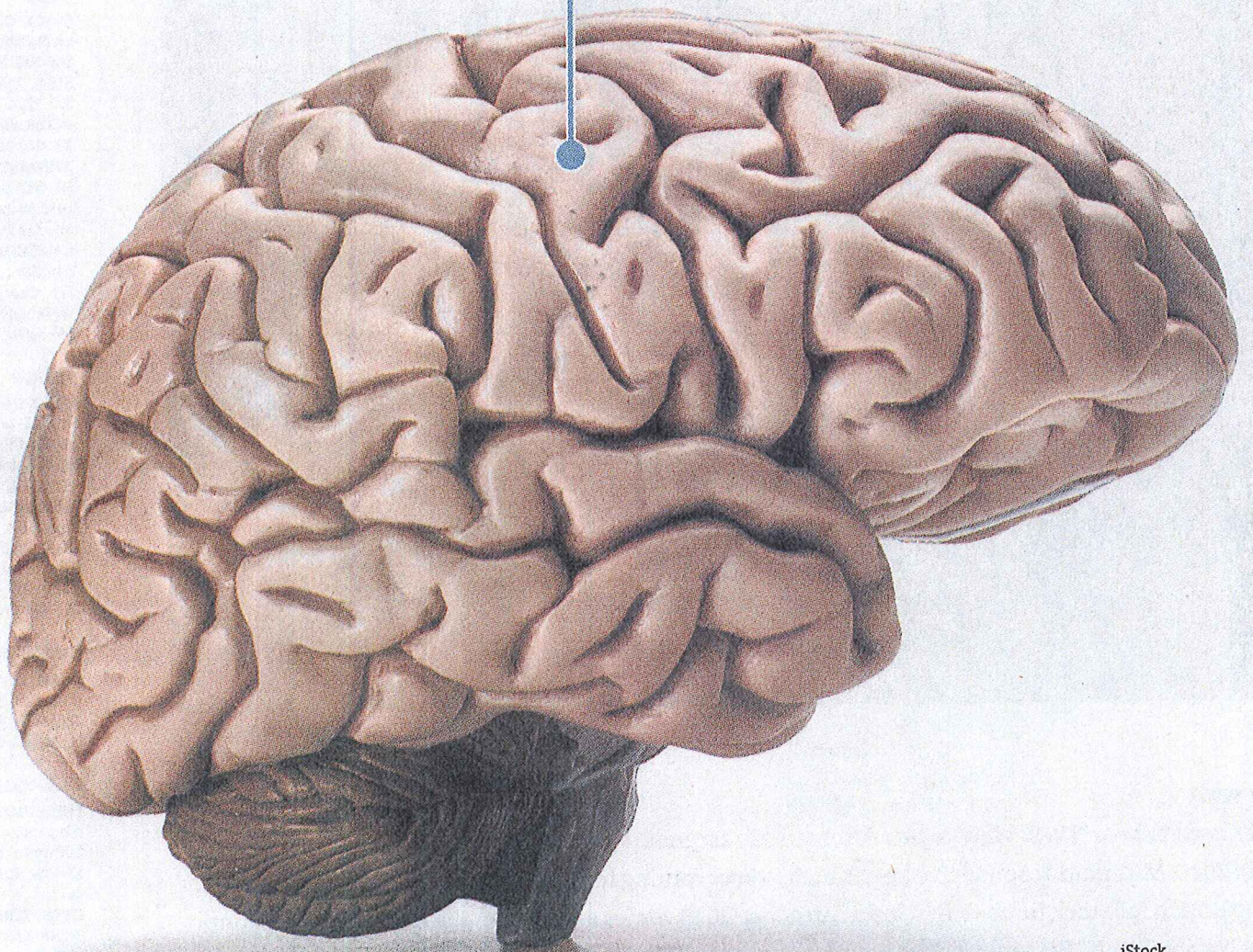


VARIETY

BRAINSTORMING A NEW APPROACH TO ALZHEIMER'S



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A St. Paul researcher has spent decades trying to help dementia patients, his family and, perhaps someday, himself.

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By SHARYN JACKSON
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William H. Frey II keeps photos of his meals on his phone: the salmon and peas he ate for lunch; the pile of spinach and potatoes. They are his medicine.

Although he's at the center of a potentially game-changing discovery in the treatment of Alzheimer's disease, Frey, 68, is treating himself preventively with a healthy Mediterranean diet and lots of exercise. He knows what's at stake; he has lost at least a dozen family members to related brain disorders.

When he started Alzheimer's research in 1977 at what is now Regions Hospital in St. Paul, no one in his family had dementia. But then his grandparents got sick. And his aunts and uncles. And his father. His work became personal.

For nearly four decades, the Atlanta native has devoted his career to solving a fundamental puzzle of dementia: how to undo the damage it wreaks on memory.

By amassing one of the largest collections of brains for dementia research in the country, he positioned the HealthPartners Center for Memory and Aging, of which Frey is senior research director, to become pivotal in the effort to ease Alzheimer's symptoms and to understand a frightening disease that is rapidly on the rise.

Now, 27 years after Frey made a groundbreaking discovery, a new treatment is undergoing a clinical trial in St. Paul that could help not just Alzheimer's, but Parkinson's, stroke, traumatic brain injury and, potentially, countless other issues, from mood swings to cravings.

It works by spraying a mist of drugs through the nose directly into the brain, bypassing the blood-brain barrier that essentially keeps whatever is in the bloodstream away from the central nervous system.

Frey and his colleagues are running the largest and longest study of its kind on the treatment, with 90 patients using it over six months. A larger, federally funded study also is in the works.

"We're hopeful that this is going to get out there to help people" in as little as four years, Frey said.



William H. Frey II, Ph.D.

Born: 1947 in Atlanta.

Job: Senior research director at HealthPartners Center for Memory and Aging.

Brushes with fame: Appeared in People magazine, on "20/20" and was interviewed by Walter Cronkite for his 1985 book on the mystery of tears.

Quirk: Texts his grown children pictures of the healthy food he eats.

His colleague Dr. Michael Rosenbloom, the study's principal investigator, estimates it could take a little longer, perhaps 10 years, to land in pharmacies, but he's no less optimistic about the treatment's ultimate potential.

"This is something that's revolutionizing not just how we treat dementia," he said, "but it could potentially revolutionize how we treat neurological disorders."

A novel approach

For decades, Alzheimer's research was most commonly relegated to the study of amyloids, or protein fragments, which clump together and prevent the brain from working properly.

"Unfortunately, that line of research has not given us as many useful treatments as was hoped for," said Terry Barclay, past chairman of the Alzheimer's Association's local medical and scientific advisory council, and a neuropsychologist involved in the study at HealthPartners.

With relatively few treatments on the market today, many of which cause intolerable side effects in patients, a new method is needed, Barclay said.

Frey's mist treatment was a revolutionary idea when he discovered it in 1989, but he wasn't exactly lauded for it. "People had a hard time believing there would be a way around the blood-brain barrier," he said.

It took him eight years to patent his invention. "The patent office argued that it was a



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Researcher William H. Frey II in his lab at Regions Hospital in St. Paul.

crazy idea, that it couldn't possibly be true, even though we had the data."

He pressed on with his work, and after scientists in other parts of the world caught on, he won his patent in 1997. In 2001, he developed a specific treatment using his intranasal method: sending insulin into the brain.

Some scientists liken Alzheimer's to "diabetes of the brain." The ability to remember is powered by energy, which comes from glucose, or blood sugar. But brains with Alzheimer's are unable to process glucose; they are, said Frey, "starved for energy." Insulin helps diabetics process glucose in the blood. By getting insulin into the brains of patients with Alzheimer's, Frey found, energy could spike, improving memory in just 15 minutes without altering glucose levels in the blood.

"This is a totally novel, completely different way of approaching the disease through a different pathway," Barclay said of Frey's discovery. "There is a ton of excitement."

And Frey, who can talk animatedly for hours about his work, is the force behind that excitement, his colleagues say.

"Bill's a very dedicated pioneer," Barclay said. "He's been a really outside-the-box thinker, and despite lots of criticism from people in the field, has maintained his focus."

Frey gets some of his focus from yoga, which he got into about a year ago. He likes that it's aerobic, but he is particularly attached to the "mindfulness" aspect as a way of reducing stress — one of the ways he can care for a brain that may have inherited something he doesn't want.

"When you realize you have a significant family history for these disorders, then you become very interested in doing what you can do to reduce your risk," he said.

Once he understood what his family medical history was saying, his connection to his work became personal. At the same time, the aging of America made his work more urgent.

As the baby boomer generation ages, and with Americans living longer due to advances in medical technology, the number of people with Alzheimer's is expected to grow by 40 percent by 2025; by 2050, there could be 16 million people living with it nationwide, with almost a million new diagnoses each year.

"I've seen firsthand the consequences of having someone you love and care about get Alzheimer's or get Parkinson's and die from it." That tragedy, he said, "is highly motivating to me."

Tackling football's problems

While Frey was fighting for the recognition of his intranasal delivery discovery, he gained fame for something else: tears.

His 1985 book, "Crying: The Mystery of Tears," got him interviews on all the major broadcasters, and a profile in People magazine ran a photo of him teaching taekwondo at the University of Minnesota. The book explored why humans are the only animals to cry tears; he hypothesized that it was a way to release damage-causing chemicals that build up in our brains under duress.

Thirty years later, he still gets calls from journalists about the book. But crying is not what he wants to talk about.

"The important stuff I'm doing? This is the important stuff," he said. "The fact that we actually invented a way to improve memory in people, it's telling us: 'This is valuable. This is something that could help people.'"

Want to participate in the intranasal insulin clinical trial? Call 651-254-7936.

Want more information on the Brain Autopsy Program? Call 651-254-2743.

If successful, the benefits of intranasal delivery could be wide-reaching. And it could even save football, Frey said.

One factor to Alzheimer's is the appearance of free-floating iron in the brain; the molecules slam into healthy cells and damage them.

Frey sent an iron-binding drug into the brain through the noses of mice that had had strokes and found that brain damage was reduced by 55 percent. Even more remarkable, he found that giving the drug to animals while they were still healthy reduced stroke damage later.

It's conceivable, he said, that people who are at risk of brain damage — whether from Alzheimer's, stroke, Parkinson's, even from head injury — could take this drug in advance and be protected. Could football players be safeguarded from chronic traumatic encephalopathy before they get a concussion?

"That's the direction we're going, if we can get the funding," Frey said.

In the future, Frey sees potential in treating psychiatric disorders and obesity through intranasal drug delivery. In addition to sending drugs to the brain, the method could also send adult therapeutic stem cells to the areas that need fixing, treating spinal cord injury and multiple sclerosis, too. Later this year, he will begin a study treating veterans with post-traumatic stress disorder with intranasal insulin.

"Think of the huge potential of this," he said, "to change everything, really."

And, thanks to Frey's work, researchers in Europe have found that intranasal insulin can sharpen memory in healthy adults, as well. Perhaps one day, we could all carry a spray that we use twice a day to help us live, think and work better.

"Believe me," said Frey, "if it was approved, I would probably do it."

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A family's search for answers

Pat Fiske's brother, Kevin, was in the best shape of his life in 2010 when he was found to have Alzheimer's disease at age 59. Kevin was a year-round athlete, a nationally ranked cyclist and an internationally ranked cross-country skier, a "bigger than life guy," his brother said.

Just three years later, Kevin died.

Pat, who had cared for Kevin in his Stillwater home, wanted to know just what had taken his brother, his "hero," so early. So, he sent Kevin's brain to William H. Frey II's team at the HealthPartners Center for Memory and Aging.

Since 1978, the Brain Autopsy Program at what is today Regions Hospital has studied more than 2,500 cases. For researchers, having organs with dementing illnesses made it possible to discover a possible treatment for Alzheimer's. For families, a brain autopsy can identify which illness a person had when he or she died, providing closure.



"If you have a family history like I do, then you become interested in wanting to know what disease that your father and his brother have," Frey said. "The only way to know for certain is to have an autopsy and neuropathology examination of the brain."

Fiske, who is now on the Regions Hospital Foundation board of directors, wondered whether his brother had gotten Alzheimer's so young because of an injury from playing sports. He also wondered whether he should be worried about getting the disease.

As soon as Kevin died, his brain was transferred to the neuropathology lab. Some weeks later, Frey called Pat with a full report.

"In spite of having pushed himself and being used to having injuries, Kevin just had Alzheimer's disease and he got it early," Pat learned.

He sent the results to his children. "Whatever information could be attained through an autopsy could be very important information later on to a doctor who was diagnosing my children or grandchildren or great-grandchildren."

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