Ambitious NIH drive to solve brain mysteries faces uncertain future

BRAIN Initiative's budget has fallen from \$680 million to \$320 million in last two years

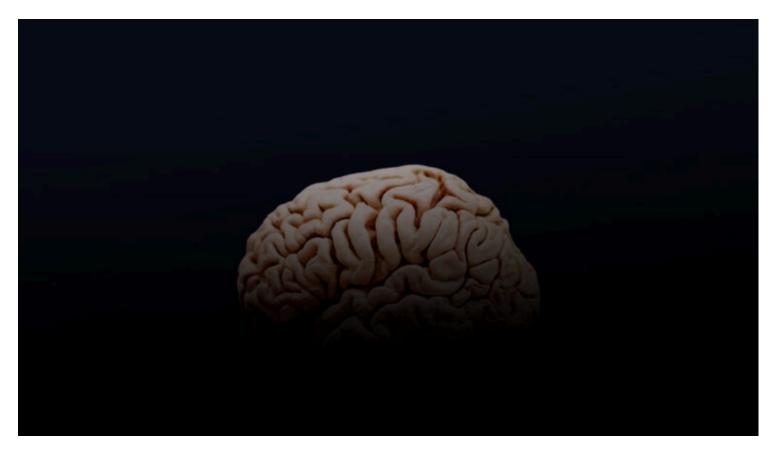


Photo illustration: STAT; Photo: Adobe



By Jonathan Wosen and O. Rose Broderick April 1, 2025

In 2021, scientists at the University of California, San Francisco, decoded <u>brain signals</u> from a man who hadn't spoken in more than 15 years to generate words that flashed on a

screen.

This March, Medtronic, a medical device company, won <u>regulatory approval</u> for a first-ofits-kind therapy that delivers precise, adjustable pulses of electricity to the brains of people with Parkinson's disease.

These and other advances have been fueled by a multibillion-dollar bid by the National Institutes of Health to better understand the human brain. But that dozen-year effort now faces an uncertain future after consecutive years of big funding cuts.

The program, known as Brain Research Through Advancing Innovative Neurotechnologies, or the BRAIN Initiative, has been likened to a Human Genome Project for the brain, with the goal of unravelling the mysteries of the body's most important and complex organ. That work must now proceed with reduced support after Congress passed a 2025 budget that set aside about \$320 million for the initiative, a 20% decrease compared to 2024 levels — which were in turn 40% less than the \$680 million budgeted in 2023.

This plunge raises questions about the long-term viability of an initiative that was widely praised when it launched in 2013, with then-President Obama heralding its potential to improve lives during a <u>White House address</u>. Since then, NIH has awarded more than \$3 billion to BRAIN-funded researchers who've developed a deeper understanding of the cell types of the brain and how these cells are connected, devised new techniques for imaging the brain and eavesdropping on its electrical communiqués, and collected clues that could help us understand what makes humans different from <u>other species</u>.

During remarks at the March "Stand Up for Science" rally in Washington, former NIH director Francis Collins called the initiative groundbreaking and warned it was at "<u>severe</u> <u>risk</u>" because of budget and workforce cuts.

Some experts told STAT that comparing BRAIN to the Human Genome Project oversold what it could achieve, adding that the initiative has yet to fully live up to lofty expectations. They stressed, however, that the effort has laid the groundwork for advances that could allow researchers to better treat devastating neurological conditions. President Trump said last year that, <u>under his leadership</u>, a cure for Alzheimer's would finally be within reach — current therapies only slow the disease's progression. But neuroscientists said that cuts to BRAIN funding could hinder advances in researchers' understanding of the condition when the U.S. is on track to see a <u>doubling</u> of new dementia cases each year by 2060.

"How can it be controversial that we would want to put in just a little bit of investment into this area and have huge impacts, where we could help people with Alzheimer's, Parkinson's, PTSD, depression, and anxiety?" said Nanthia Suthana, a neurosurgeon and soon-to-be faculty member at Duke University. "I call it the golden decade of human neuroscience to be able to do all those things. I worry that that's under threat."

During a conversation with STAT about BRAIN's accomplishments and the program's future, initiative director John Ngai acknowledged that funding has been "challenging, for sure."

"There's still a lot of great science we can fund and are [funding]. It's just that some of the good stuff is going to be left on the table for now," he added. "It certainly sharpens the focus."

A group of outside experts convened by NIH laid out a vision for the initiative in a 2014 <u>report</u> that called for \$4.5 billion in federal funding over a 12-year period. "We stand on the verge of a great journey into the unknown — the interior terrain of thinking, feeling, perceiving, learning, deciding, and acting to achieve our goals," the advisory committee wrote.

The challenge, then, was translating that idealism into a concrete research plan for studying an organ made of about 100 billion neurons, each of which connects with up to 10,000 other cells, plus another 100 billion <u>cells</u> that support and regulate neurons.

NIH focused on three broad areas: identifying the brain's many cell types, understanding how these cells are connected to one another, and developing tools that allow researchers to precisely target specific brain regions.

Amy Bernard, head of strategy and programs for the Science Program of The Kavli Foundation, which supported the initiative's early efforts, describes it as learning the alphabet and vocabulary used by the brain: "[We were] getting that fundamental language of the brain, its structure, and its parts, and doing so in a way where that information is usable by many people."

In October 2023, BRAIN-funded researchers <u>published</u> a draft atlas that identified many of the components of this alphabet: more than 3,000 cell types, roughly 10 times what scientists have detected in previous reports. That resource has since allowed other researchers to compare the brains of Alzheimer's patients to this reference map and <u>identify cell types</u> that die off before patients show symptoms — and before beta-amyloid or tau proteins build up in the brain — suggesting that protecting these cells might lead to new therapies.

BRAIN researchers have also developed a complete map of the more than 50 million connections between the 130,000 cells of the <u>fruit fly brain</u> and built a cellular map of the <u>mouse brain</u>, advances that scientists say will allow them to use animal models to better understand neurological disease and how the brain processes information.

Between 2014 and 2024, nearly 1,800 principal investigators across more than 260 institutions were supported by BRAIN funding. In total, its grants have led to more than 5,000 scientific publications.

"There was some initial concern that this [initiative] is going to be one of those fancy, shiny things that was not going to really help anybody and yet take resources away from really creative hypothesis-driven researchers," said Ngai. "I think it's fair to say none of those things have happened."

Catharine Young, a science policy expert who served in the Office of Science and Technology Policy during Joe Biden's presidency, praised the initiative's progress in building foundational knowledge — even as she acknowledged that those insights have yet to translate into major clinical breakthroughs.

"I don't think we are as far as we hoped we would be," said Young, who is a trained neuroscientist. "I think this is a very valid concern, both within the science community, but also with the public, kind of given the amount of money that has been put into these initiatives." While large-scale, collaborative research projects are commonplace in astronomy and physics, they're less the norm in the life sciences. One of the most notable exceptions was the Human Genome Project, a 13-year, \$2.7-billion effort to read our genetic code. BRAIN has since its inception been compared to this effort by government officials and many of the initiative's proponents.

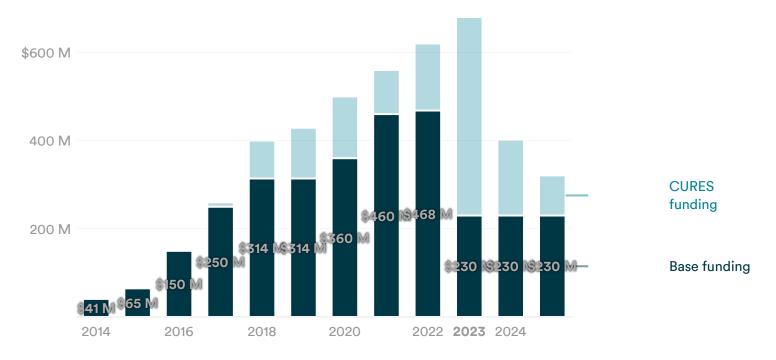
But an NIH researcher who works closely with BRAIN-funded scientists framed this comparison as a "marketing ploy" that threatened to oversell what the program could realistically achieve. The researcher, who requested anonymity to speak freely, noted that the main challenge of the genome project was developing technology to read the billions of nucleotides, the A's, T's, G's, and C's, that make up our DNA. By comparison, they said, researchers still have a crude understanding of what the brain *is* and how it works.

"This is bigger than any computer we can conceive of," the researcher told STAT. "It's just staggering to think the hubris that we have as scientists to say, 'Oh, we're going to do the Human Genome Project for the brain and we'll understand it in like 10 years." But the scientist was also adamant that it would be "incredibly myopic" to cut funding.

And yet that's what has happened these past two years. Funding for BRAIN comes from two sources: line items in the budgets of the 10 NIH institutes and centers affiliated with the effort, and funds authorized by the <u>21st Century Cures Act</u>. Last year, a predetermined dip in Cures Act support for BRAIN caused the program's funding to fall to around \$400 million compared with \$680 million in 2023.

BRAIN Initiative funding on the downswing

Budget per fiscal year



Base funding refers to line items in budgets of NIH centers. CURES funding refers to funding from the 21st Century Cures Act. Chart: J. Emory Parker/STAT • Source: National Institutes of Health

BRAIN's 2025 budget fell to \$321 million because of another expected decrease in Cures Act funding. That's a situation NIH leaders and neuroscience advocates had sought to avoid. Last year, the agency's then-director, Monica Bertagnolli, requested \$589 million in non-Cures Act funding to keep total BRAIN funding equal to 2023 levels. In a separate letter, more than 100 scientific organizations asked Congress to set aside \$740 million for BRAIN this year — more than twice the amount Trump signed into law.

The new administration's disruptions to grant reviews have also stalled <u>\$65 million</u> in funding for Alzheimer's research. And the NIH is seeking to dramatically slash <u>research</u> <u>overhead</u> payments. Those plans have for now been held up by a preliminary <u>injunction</u> pending a decision from a federal judge on the policy's legality.

Last year's BRAIN cut led NIH to cancel several <u>funding opportunities</u>, including developing new ways to record and <u>electrically stimulate</u> the human brain. It's unclear how more recent cuts, including to early-career fellowships and internships, will further impact research, and it may take a number of years to see the fallout, said Bernard. She knows graduate students and postdoctoral fellows losing training and opportunities that should be catapulting research careers. Some are even leaving science, altogether.

"It's maybe not going to be felt next year or the year after. It's going to be felt in several years, when there's literally no training of the scientists needed to make the discoveries

and advances that we need for the future. It's kind of an 'eating our young' sort of approach. It's undermining our ability to sustain the future of knowledge," said Bernard.

On a recently updated version of its BRAIN funding <u>page</u>, NIH says that it will "make decisions to best maintain the momentum we've built over the past decade, while considering overall portfolio balance of innovative neuroscience research and neurotechnology development."

The agency also notes that Cures Act funding will run out by 2026, at which point the amount of research the initiative can support will depend entirely on congressional allocations to the 10 BRAIN-affiliated institutes and centers.

"We just have our foot firmly planted on the gas and are just trying to do the best science we can support for as long as we can," Ngai said. "I'm hopeful for the future, and hopefully others will see it that way, too."