

Fading Minds: Why There's Still No Cure for Alzheimer's
APM Reports Transcript

Billboard

Desiree Cooper: From American Public Media, this is an APM Reports documentary. I'm Desiree Cooper.

Forty years ago, a new federal health agency told millions of older Americans that they suffered from a disease -- Alzheimer's disease. Congress asked scientists what they needed to cure it.

Leonard Berg: There are 3 answers. Dollars dollars and dollars.

Eric Siemers: I don't think anybody thought it would take this long and be this hard.

Newscaster 1: Some more bad news in the Alzheimer's space, this time coming from Merck. They're saying they're stopping a late stage study in mild to moderate...

Zaven Khachaturian: Every major pharmaceutical company put money into the idea, and they all failed.

Research pursued one way to stop Alzheimer's. Now scientists are exploring what was overlooked.

Laura Baker: If there was a way for some company to make money on exercise as a therapeutic it would be it would have been tested a long time ago.

Coming up, *Fading Minds: Why There's Still No Cure for Alzheimer's*. First, this news.

Part 1

Desiree Cooper: From American Public Media, this is an APM Reports documentary.

(Sound of Cooper helping her mom move)

Cooper: I know my hands are cold.

Mom: Ay.

Cooper: I know I know my hands are cold. Come on. Can you get up? There you go...

That's the sound of me trying to move my 85-year-old mother from a chair in her living room. Mom has suffered from Alzheimer's disease for 15 years.

Cooper: Yep, ok come on.

The memory of her is being replaced by the reality of her now. And, so it's hard for me to go back and remember the vibrant person that raised me.

Cooper: You're going to come. I've got your hands so you can focus.

My name is Desiree Cooper and I'm a journalist and writer. It's not just my mom. My dad has been diagnosed with Alzheimer's too.

Cooper: How old did you turn on your birthday?

Dad: I turned ...I turned 69. I believe somewhere in there.

Cooper: Try a little older.

Dad: 69 and 79.

Cooper: 85.

Sometimes, I like to take my parents on Sunday drives.

Cooper: Do you want to go to the Virginia Diner today?

Dad: I don't care.

Cooper: Alright, I don't know how to get to the Virginia Diner.

Dad: You gotta get to Waverly.

Cooper: I gotta go to Waverly. Ok. Do you know how to get to Waverly?

Dad: Sometimes.

(Cooper laughter)

Cooper: Is this going to be one of the times that you know where to go?

Dad: Yeah.

(Mom's laughter)

My mom still laughs along at conversations, but she doesn't talk much anymore. She sits in the back seat, staring out of the window.

Dad: And you're with her with all of what, two hours a week?

Cooper: Uh, no, I live with you.

Dad: Huh?

Cooper: I live with you. I'm with you 24-7. Every day.

Dad: Huh?

Cooper: Hmm? I've been living with you for almost three years now.

Dad: Oh no.

Cooper: You don't believe me?

Dad: No.

Cooper: What about that room in the back?

Dad: What about it?

Cooper: Have you noticed? That it's, like where I live. Where I sleep every night.

Dad: No. I didn't notice that.

Cooper: Oh. Three years.

Dad: So you just snuck in, huh?

Cooper: I don't know if you can call it sneaking in when you see me all day, every day for three years.

Dad: I don't believe that.

Cooper: I fix all of your meals. I put mom to bed every night.

Dad: How can you do that and I not know it?

Cooper: I don't know.

Dad: I'm not complaining, I'm just surprised.

Cooper: I know...

That conversation was such a gut-punch. I've given up a lot to care for my parents. I moved from Detroit to Virginia to live with them. I went from being a professional journalist and radio host to an isolated caregiver in a town where I have no roots. And they didn't understand why I was suddenly usurping their autonomy-- taking over the bills, the lawn, the kitchen, the car keys. It's really been hard for all of us.

There are no medications to reverse my parents' decline. At best, the few existing drugs for Alzheimer's prolong the stage that they're in for a few months. It seemed pointless, especially given the side effects.

I've been hearing on the news for years that scientists thought they'd come up with something better. Some promising new lead.

Newscaster 2: New research has just been published about a drug which could slow the pace of brain decline in people who have Alzheimer's...

Newscaster 3: ...The final step before FDA approval. If it works, it could add years to patients' lives and mean they'll be able to live at home longer...

So why hasn't anything worked? Why are so many families in the same situation that we're in? Why isn't there a treatment for Alzheimer's?

My former radio colleagues at American Public Media have been working to find an answer to that question. The documentary team there, APM Reports, produced this story, *Fading Minds: Why there's still no cure for Alzheimer's*. Here's reporter Maja Beckstrom.

Maja Beckstrom: I've spent the past year looking for an answer to that question- why don't we have a cure for Alzheimer's? The obvious answer is that developing an Alzheimer's drug has been harder than scientists expected. And that's true. But another answer is that researchers got focused on one approach - one idea about what causes dementia - that dominated the field for decades and hasn't paid off. I want to tell you how that happened. And then I want to tell you

about how the failure to develop a drug is finally opening the door to other ideas about how to slow dementia- ideas that could be as effective as any new drug.

(Music)

For me, this story starts in my grandmother's kitchen on a farm in southern Minnesota. We were making chicken soup, and I asked her for a ladle. She pulled out a slotted spoon. I thought she was joking, and I laughed. And she looked down at the spoon. She was so embarrassed and puzzled... and I realized that something was wrong. Grandma's mind wasn't working.

When I was growing up, no one would have said their grandmother had Alzheimer's. "Senile" was the word we used. And nobody thought it might be possible to stop senility. It was just part of getting old.

But in the 1970s, a psychiatrist and gerontologist named Robert Butler started to challenge that assumption.

Butler: Because one of the glories of human existence is the potential now to grow old and to enjoy the richness and the rich possibilities of an extended and happy later years. Thank you for your attention.

(applause)

Butler won the Pulitzer Prize in 1976 for his book Why Survive? Being Old in America. He coined the term "ageism." That same year, Butler got a chance to turn his ideas into federal policy. He was named director of a new agency within the National Institutes of Health called The National Institute on Aging.

Zaven Khachaturian: He was a great spokesperson. He was a cheerleader for ageing partly because of his life experiences.

Butler died in 2010. This is Zaven Khachaturian, who worked with him at the NIA.

Khachaturian: He was brought up by his grandparents on a chicken farm in New Jersey and he developed a great love for his grandparents and that love for older individuals... had an indelible thing on his psyche.

Khachaturian and Butler wanted to get scientists interested in studying the reasons some people develop thinking and memory problems as they age while others do not. Aging research was a backwater. But Butler had an idea for bringing new attention to the field. He was intrigued by new research some scientists were doing on an old, obscure disease.

(Music)

Alzheimer's disease was first described in 1906 by a German psychiatrist named Alois Alzheimer. He wrote a case study of a woman who developed senility young, at age 51. She died in a mental hospital. When Dr. Alzheimer looked at slices of her brain under a microscope, he saw mysterious blobs of protein plaque. Inside the destroyed neurons, he spotted tangles of tough thready stuff.

These "plaques and tangles" became the hallmarks of the disease named after him.

For the next 70 years, Alzheimer's disease was only diagnosed in people under age 65. But in the 1970s a handful of researchers started to question that age limit. When they autopsied older people with senility, they often -- but not always -- found the same plaques and tangles that Dr. Alzheimer described. They said that perhaps half of senility was really Alzheimer's disease.

That suggested millions of people didn't have an inevitable condition caused by aging. They had a disease.

And Butler picked up this argument.

Butler: It's an extraordinarily common disease.

Butler believed if scientists really dug into Alzheimer's, they'd crack it. He reflected the optimism of mid-20th century America. Modern medicine was on a winning streak.

Butler: I would argue that Alzheimer's disease is the polio of geriatrics, and that the nursing home is the iron lung of geriatrics. And just as we no longer hear the thump thump of the iron lung in the spring and parents are no longer scared about their kids going into swimming pools because we no longer have polio, so too I think the day will come when we will no longer have Alzheimer's disease.

Butler's decision to call senile dementia Alzheimer's was as much political as scientific. He knew that he could attract credibility, public support and money to the NIA by embracing a terrifying disease.

Khachaturian: In order to bring funding to the NIA, the claim -- the headline -- was Alzheimer's

Zaven Khachaturian-

Khachaturian: And we defined it very broadly... It was just the linguistic kind of thing rather than a clear-cut medical diagnostic sorting out.

This expanded definition of Alzheimer's would eventually have huge consequences for what researchers would study. It created tunnel vision that focused on similarities between middle-aged and elderly patients and encouraged researchers to overlook the wider and more complicated picture of dementia in old age. But Butler's rebranding of Alzheimer's was an effective strategy for getting people to stop accepting senility as inevitable.

Khachaturian: We began to tell a story and there was a lot of stories we fed to media like newspaper articles ... also inculcating the idea that aging per se does not cause that

disease, that it's a separate brain disease and that took a number of years to change the narrative.

Newscaster 4: Until a few years ago, few Americans had ever heard of Alzheimer's disease. Most people just called it by its old name, senility. But scientists now know...

Newscaster 5: Well, most of us have never heard of it but it kills 100,000 Americans every year. It's called Alzheimer's Disease...

Newscaster 6: ... one out of every 10 people over age 65 may be suffering from Alzheimer's disease. Researchers say if that's true...

(Music)

As Alzheimer's disease became a household word, its boundaries grew fuzzier. Scientists initially were careful to say not all seniors with memory loss and thinking problems had Alzheimer's disease. But to the public, Alzheimer's became interchangeable with senility.

Groups like the Alzheimer's Association pressured the government to do something. Butler had helped found that organization. He was inspired by the success of citizen groups that lobbied for more cancer and heart disease research. He called it "the health politics of anguish."

Here's researcher Leonard Berg, from the Alzheimer's Association medical advisory board, testifying before a congressional committee in 1992.

Leonard Berg: Mr. Chairman you described Alzheimer's disease as a time bomb. Nothing could be more accurate...

Members of Congress wanted to know how to defuse this time bomb. They worried Alzheimer's would bankrupt Medicare.

Representative Helen Bentley: Obviously Dr. Berg, research is extremely important in all of this. You say in your testimony that finding a way to delay the onset of Alzheimer's disease by 5 to 10 years is clearly within reach. What more needs to be done so that we can achieve that?

Berg: There are three answers. Dollars dollars and dollars.

Berg and other advocates raised unrealistic hopes for a treatment, telling Congress that breakthroughs were around the corner.

Berg: I would say there will be a reasonable expectation in the next five to ten years of some major impact.

This was nearly 30 years ago.

(Music)

Year after year, Congress gave the NIA money to fight Alzheimer's. By 1990, enough to fund 15 Alzheimer's research centers at major universities.

Aging research was no longer a backwater and the labs got busy. Looking over old studies, I was amazed at the many ideas scientists explored searching for what causes Alzheimer's: Missing neurotransmitters. Inflammation. Aluminum. Not enough glucose. Estrogen. Were plaques the cause? Or just debris left behind by something else that was causing the disease?

It was incredibly difficult to sort through the mess of a damaged brain.

One researcher compared it to showing up at a football stadium after the game was over, and then trying to piece together what had happened from the trash on the field and in the bleachers.

But in the 1990s, new research in human genetics seemed to promise a map out of the chaos.

Scientists began looking at families who inherit a rare form of Alzheimer's disease that strikes in middle age. They hoped that finding the gene defect that causes the inherited version would lead to identifying what was causing the brains of people in those families to deteriorate. Armed with that knowledge, they might be able to create a drug to help millions of people evade Alzheimer's in old age.

Marty Reiswig's extended family was at the center of the Alzheimer's gene hunt. His dad's father Ralph was from a big Oklahoma farm family. Grandpa Ralph developed Alzheimer's symptoms at around age 50, along with nine of his siblings. They all died young.

When Marty was a kid, he went to a family reunion held at a school... and medical staff showed up.

Marty Reiswig: Grandma Esther... kind of went in the gymnasium and kind of shut the doors behind her and said 'Okay everybody is gonna give blood now.'

Marty didn't really think much about that that blood draw until years later. When he was in college, he attended another family reunion. They met up in a pizza parlor.

Marty Reiswig: Uncle Roy and Aunt Georgia showed up and they were greeting everybody and giving hugs and things and they went to sit down. And my Uncle Roy reached for the back of his chair to pull it out and he missed. And he reached for it again and he missed, and he missed. And he finally grabbed that chair and scooted it out pulled it out a bit and went to sit down and nearly fell. And, I sort of thought that was odd. But as I looked around the table, I just saw fear and anger and sadness. And that's when it really dawned on me. Oh my gosh this Alzheimer's thing that they say runs in our family is really real.

By then, the researchers studying Marty's family and others like it were making some real progress. In the 1990s, the blood samples led researchers to discover the genetic mutations that cause early onset Alzheimer's.

It was a huge breakthrough. The paper about the first mutation was one of the most cited in 1991.

But knowing what was wrong still hadn't led to a cure. There was still no treatment for Uncle Roy - or anyone else in the family who carried the gene defect.

Marty had brought his girlfriend, Jaclyn to that reunion at the pizza place. That night the two of them took a walk.

Marty Reiswig: And about halfway through the walk I stopped and grabbed both hands and looked her right in the face and I just said "If you want out -- you know we're not engaged or married or anything -- if you want out, I understand" and without skipping a beat she said "I'd rather have 30 good years with you than a lifetime with anybody else."

Jaclyn Reiswig: And I do remember that walk with him and him saying that to me and I didn't care. I was young and in love.

Marty Reiswig: And stupid (laughter)

Jaclyn Reiswig: No, I don't regret anything.

Marty and Jaclyn got married and started a family. Their kids are 11 and 13 now.

(Sounds of family outside)

On a Sunday after church, Marty and the kids are in the backyard at their home in Denver, pulling weeds. Jaclyn's inside frying chicken for lunch.

Jaclyn Reiswig: It'll be done in 35, 40 minutes.

In the family room, sympathy cards line the mantel. Marty's dad died six weeks ago from Alzheimer's. He was 66.

Marty Reiswig: He was kind of humble. Did his thing. He was a mailman and a soccer coach.

Marty and his dad spent a lot of time together during his dad's 16-year descent into Alzheimer's.

Marty Reiswig: Every now and then once dad was symptomatic, I would turn on my iPhone and hit the voice memo recording button and just set it on the dinner table while he was trying to tell stories and stuff.

(Sound of recording)

Marty's Dad: So, we went out and, and had a sleepover in the Sand Hills and that's where I had my first cigar – a Swisher Sweet!

(Laughter)

Marty's Dad: I was just recording the progression of the disease.

(Sound of recording)

Marty's Dad: My worst remembrance.

Marty: Memory?

Marty's Dad: Yeah, can you envision if you see an old, uh, pickup...

(Recording fades)

Marty Reiswig: And just um, just listening back and wishing he could tell that story better.

Marty's children didn't know their grandfather while he was well. Marty's 13-year-old daughter Raya joins the conversation. He asks her what she remembers about her grandpa and if she worries about the Alzheimer's in their family.

Raya Reiswig: I have a few memories from when he wasn't as sick, usually I just remember from when he was already in the nursing home.

Marty Reiswig: I'm kind of curious, how often do you think about it or worry about it for me?

Raya Reiswig: Um, usually when we used to be around Papa, and then like the night of the day we were around Papa.

Marty Reiswig: Mm hm. I don't know about you, I would go and I'd be sad for him, and then I'd leave and start being really sad and scared for me. Is that what you mean?

Raya Reiswig: Uh-huh.

Marty Reiswig: Yeah.

Marty is 40. His dad started developing symptoms around age 50.

For now, Marty has chosen not to find out if he carries the family gene mutation. There's a 50 percent chance he does, and if he does, then his children have a 50 percent chance. Jaclyn says Alzheimer's might steal a whole lot of joy later. So why should they let it start stealing joy now.

(Music)

The genetic discoveries from families like the Reiswigs had huge implications for Alzheimer's research. Different families had different mutations, but they all seemed to speed up the accumulation of a protein chunk called amyloid beta. This is the same protein that piles up in the plaques that Dr. Alzheimer saw back in 1906. This seemed like proof that the plaques caused Alzheimer's. Suddenly pharmaceutical companies thought they had a specific thing they could attack with a drug.

Eric Siemers: That would be what we call the target.

That "target" became the focus of Eric Siemers' career. Siemers oversaw Alzheimer's drug development at Eli Lilly, one of the big pharmaceutical companies that pursued Alzheimer's. He retired in 2017. Siemers was drawn to Eli Lilly in 1998 by a sense of possibility, that Alzheimer's research was onto something.

Siemers: I just had this thought that this is very cool. This is where the solutions are going to come from.

Eli Lilly spent billions chasing amyloid beta. Competitors went after the molecule too -- Johnson and Johnson, Merck, Pfizer, Roche... Biogen.

The first to develop a drug that slowed Alzheimer's stood to make a fortune. Big Pharma rushed to gamble on an unproven idea. Half of the Alzheimer's drugs tested were aimed at amyloid beta.

(Music)

Drug companies tried different approaches over the decades, but they hit dead ends. It was difficult to penetrate the brain. Some drugs caused side-effects like skin cancer or brain swelling. Some even made cognition worse.

Meanwhile, in the mid 2000s, the ground beneath Alzheimer's shifted again. Up until this point, Alzheimer's could only be officially diagnosed by doing an autopsy and finding plaques and tangles. Now, new brain scan technology made it possible to peer into the brains of living people. Siemers says the scans revealed that a quarter of the patients in his Alzheimer's trials had dementia but didn't have the plaques.

Siemers: So, they've got some other diagnosis--they're misdiagnosed and that was new information at the time.

Other studies were confirming this. And, brain scans were revealing plaques in the brains of many people who didn't have dementia.

Skeptical voices took this as more evidence that amyloid beta plaque wasn't the cause of Alzheimer's.

But many researchers thought an amyloid drug could work on people with mild symptoms. Siemers wanted to press ahead with another big amyloid study. This time, in 2013, Eli Lilly paid for expensive brain scans to make sure all the volunteers had amyloid plaque in their brains. And, they all had mild symptoms. Siemers really hoped that with this more carefully screened group... the drug -- called solanezumab -- would work.

Siemers: These studies are ridiculously expensive, but I can tell you from my simple-minded scientist standpoint it wasn't really a hard decision. It was like you have to do another experiment to prove that what you think is there is really there.

Siemers would have to wait three years. He got his answer in 2016.

Siemers: We were sequestered at Lilly ... And so we were all in this basement room that was locked. You have to have a special access to get in there, and so we called it 'the cave.'

Down in the cave, the number crunchers gave Siemers' team the bad news. The drug had not made a difference.

Siemers: There were lots of tears I'll tell you. I still have a hard time talking about it actually.

The drug removed amyloid beta...but that didn't stop Alzheimer's. It was a huge blow to the amyloid theory. Similar scenarios played out at other drug companies.

Newscaster 7: Some more bad news in the Alzheimer's space coming from Merck. They're saying they're stopping a late stage study in mild to moderate Alzheimer's patients...

Newscaster 8: ...And a double blow to Roche this morning. The company is ending a late stage...

Newscaster 9: Now, a pharmaceutical giant has announced it is giving up on treating Alzheimer's. The Pfizer drug company reports...

Khachaturian: Every major pharmaceutical company put money into the amyloid idea and they all failed, because the idea was flawed.

Zaven Khachaturian is disappointed by the lack of progress. He'd rallied scientists around Alzheimer's at the National Institute on Aging. He says the amyloid beta hypothesis generated momentum and discoveries. But it stifled other ideas.

Khachaturian: It became gradually an infallible belief system. So, everybody felt obligated to pay homage to the idea without questioning. And that's not very healthy for science when scientists...accept an idea as infallible. That's when you run into problems.

Groupthink made it hard to entertain other ideas for what might cause Alzheimer's. Critics say the focus on one molecule starved alternative approaches of research money and study volunteers -- maybe approaches that could have led to a treatment.

Still, the field is not giving up on amyloid beta. Champions like Siemers, say abandoning it now would be “a tragedy” for patients. He thinks an amyloid beta drug could still work.

Siemers: I mean Apollo 1 didn't land on the moon. And that one of the things about Alzheimer's research right now is, you know, we don't know which Apollo it's going to be. I mean maybe we're at Apollo 6 or 7 right now something like that. But we'll get one there, but you have to essentially learn from your mistakes where every time you go just a little bit closer.

(Music)

Even if the moonshot lands, it may not help people who already have symptoms. One thing scientists have learned is that Alzheimer's starts years before thinking and memory problems appear. By the time someone has dementia, brain cells are dead, and scientists suspect nothing will bring those neurons back.

(Velcro of blood pressure cuff)

A visiting nurse takes Marty Reiswig's blood pressure in his family room. She's prepping an IV infusion. Marty's sitting in an easy chair.

Marty Reiswig: So this is my dad's chair and he sat in it until he basically became bedridden or had to be in his wheelchair.

Almost three decades ago DNA from families like the Reiswigs convinced researchers to focus on amyloid beta. Now, these same families are a final testing ground of the amyloid hypothesis.

Perhaps the drugs failed because they were tested too late. Some researchers think amyloid beta could be the match that starts a forest fire. Once the fire is roaring, it doesn't do any good to blow out the match. But if you blow out the match early enough, you might prevent the fire.

So the National Institute on Aging is funding studies to test drugs in those older people who have amyloid but don't have dementia symptoms.

And, in younger people like Marty, who might carry a mutation.

Five years ago, when he was 35, Marty began rolling up his sleeve for this monthly infusion. Either the drug solanezumab or a placebo, slowly drips into his vein for the next hour. If Marty has the mutation, the changes in his brain that lead to Alzheimer's would already be underway. He still hopes he can do something to help find a cure. If not for himself, then for his kids.

Marty Reiswig: I think regardless of the outcome, I will have known that I did everything I could.

(Music)

If this study fails to ward off Alzheimer's, the next phase is to go even earlier...testing amyloid-busting drugs on people like the Reiswigs as young as 18.

The grip of the amyloid hypothesis has loosened, but no single alternative theory has emerged to replace it. From 2015 to 2019, federal money for Alzheimer's research nearly quadrupled to \$2.3 billion dollars. Ideas like inflammation, infection, insulin are competing for acceptance. A few companies are testing drugs that reduce the protein in Alzheimer's tangles.

Four decades after Robert Butler made Alzheimer's an urgent national priority, he got so much of what he wanted-- public engagement, billions in funding, prestigious scientists--but they haven't added up to a cure.

(Music)

Desiree Cooper: That was Maja Beckstrom. You're listening to Fading Minds: Why there's still no cure for Alzheimer's. I'm Desiree Cooper.

I had no idea that the amyloid research had hit a dead end, at least for treating people who already have dementia, like my 85-year-old parents. So, where's the hope for me? That's what Maja will talk about next: how some scientists are looking for Alzheimer's solutions that might be hiding in plain sight. They want to figure out if we can stave off dementia through social change and better habits.

There's more on our story, including what it's like to be in drug trial that fails. Go to our website, apmreports.org. There you can also browse our archive of hundreds of audio documentaries.

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More in a moment, from American Public Media.

Part 2

Desiree Cooper: You're listening to Fading Minds: Why There's Still No Cure for Alzheimer's. I'm Desiree Cooper.

Baby Cooper: Banana ma! Banana

That's me at age two, talking with my parents. Our family was living in Japan. It was the early 1960s. My dad was stationed there in the Air Force.

Baby Cooper: I don't wanna!

Dad: Why?

Baby Cooper: I don't wanna!

Dad: Aren't you ready to go night night?

(Music)

When I listen to old recordings or see old photos of my parents, I wonder if there are clues about what led them to get dementia years later. I see my dad in his Air Force uniform. He worked on the flight line. Did his exposure to jet fuel affect his brain?

I see my mother, so proud of her homemaking. She kept house like a black June Cleaver—was it her constant exposure to household products?

Or maybe it goes back farther. Maybe it has to do with their childhood poverty growing up in the Jim Crow South.

Reporter Maja Beckstrom found that some researchers are asking exactly those sorts of questions. What's going on in people's lives that might raise their risk of dementia? What could I be doing now that could help me escape that fate?

Maja spent time with three researchers who are trying to find ways to avoid dementia by changing the way we live our lives.

Maja Beckstrom: One of the researchers whose work intrigued me is a professor at Columbia University.

Jennifer Manly: My name is Jennifer Manly. I'm a neuropsychologist and I study inequalities in brain health and dementia and Alzheimer's disease.

Manly didn't start out interested in dementia. Back in the 1990s, she was studying cultural bias in psychological tests - like intelligence tests. Her curiosity led her to Columbia, where researchers were following thousands of elders in mostly black and Caribbean Hispanic neighborhoods in upper Manhattan. They were giving these elders cognitive tests frequently to

see who developed dementia. And just after Manly arrived at the university, the researchers made a surprising discovery.

Manly: They were finding that African Americans and Hispanics were at higher risk for developing Alzheimer's disease.

In fact, African Americans were twice as likely as white people to be diagnosed with Alzheimer's. This was new information.

Most Alzheimer's researchers were studying patients who came through the doors of the Alzheimer research centers at academic hospitals. These patients were overwhelmingly white, educated and relatively well off. This made it look like whites were more likely to have dementia. Columbia researchers had gone census tract by census tract, interviewing people from Medicare rolls, and uncovered this difference.

At first, Manly was skeptical. She suspected that the black and Hispanic elders scored lower on cognitive tests not because they actually had worse thinking and memory problems ... but because the tests were biased.

Manly: So that was my initial thought about why there were higher rates... I had never worked with older adults before. I didn't really know that much about dementia. But I suspected that cultural background affected cognitive tests regardless of age.

Manly found there was test bias, but even when she adjusted for it, black and Hispanic elders were still more impaired. Their memories also declined faster than whites.

So then Manly wanted to know: why?

She and her colleagues looked at genetics. Did the African ancestry shared by African Americans and many Caribbean Hispanics raise their risk? But it turned out they were not more likely to have the gene variation that plays the biggest role in old-age dementia.

To Manly, that left one explanation. Black and Hispanic Americans already suffer higher rates of heart disease, stroke and diabetes because of life experience. Maybe what was happening in their lives was also causing dementia.

Manly: It's dismaying. It's depressing it's worrisome. It's something that like all health inequalities are frustrating for me because health inequalities are avoidable.

Avoidable. If you can figure out what's causing them.

(Sound of footsteps)

To get answers, researchers from Manly's lab have been going on home visits. We're standing outside the door of an apartment on the 27th floor of a high-rise in Harlem.

Columbia Researcher: Hi. It's Isabelle. I'm from Columbia University with the memory study. I'm here for Ms. Pope.

(Sound of door opening)

Columbia Researcher: ... Hello. Hi. How are you. Can we come in?

Pope: Yeah yeah, fine.

Patricia Pope is 70 years old. It's a sweltering day. She's wearing a purple tank top and seems a little tired. Subway trains rumble below her window.

(Sound of subway)

Pope: It's above ground when it gets right here. This is where it goes underground.

Her table is strewn with 17 medication bottles.

Pope: You know, and they keep giving me this to combat that and you know, and no no don't take that

Pope spends the next two hours sitting on the couch with the researcher, answering an exhaustive list of questions.

Columbia Researcher: How about problems with memory, for example, learning new information or finding your way home?

(Laughter)

Pope: Nearly every day.

Columbia Researcher: ...broccoli. At least half a cup.

Pope: Ah yes, I like broccoli.

Columbia Researcher: ...several months or more when your father had no job?

Pope: He was on disability.

Researcher: ...Heart disease, vascular disease, cancer...

Pope: Ok. Well, I have high blood pressure...

Researcher: Feeling down, depressed or hopeless? Would you say none at all, rare...

Pope: More than half the days.

Pope has had many stressors in her life. She illustrates why it's hard to tease out exactly what plays a role in memory and thinking problems late in life. But when Manly heard interviews like this years ago, a common thread caught her ear.

Manly: What I found out was that the African Americans who lived here in Washington Heights came from the South. From North Carolina South Carolina and Virginia primarily. So, they were telling me about their childhood, and it was largely rural. They went to one-room school rooms, the school wasn't open for the whole year because it shut down to allow children to work in the fields.

Manly knew that other studies had linked education and Alzheimer's dementia. On average the more education someone had, the less likely they were to develop dementia. But something didn't add up.

Manly: I started to realize that years of education meant something totally different depending on where you were from and what race you were. And so I began to suspect that there was that there was something about educational experience that might affect someone's risk for developing cognitive decline later in life.

Manly wondered if school quality was a missing puzzle piece that could explain unequal rates of dementia. She found a treasure trove of historic records for thousands of schools across the U.S.

Manly: In 1935 and 1936 in 1937 every single year we had data that would show me directly the historical, administrative resources that went into these schools in different states and in different counties. And when you take a look at it it's shocking. The resources that went to segregated black schools was dramatically lower, like 80 percent lower than the resources that went into the white schools in the same state or into the schools overall here in the north and in New York.

Economists had already mined this data to show that attending a poorly funded school predicted lower income later in life. Now, Manly linked these schools to cognitive problems in old age. Certain natural experiments had played out. For example, North Carolina put more money into black schools than neighboring South Carolina.

Manly: Now we're finding that the brain health outcomes for blacks who grew up in North Carolina and were exposed to those higher quality schools are much better than blacks that grow up in South Carolina.

Manly's theory is that better elementary schools build stronger brains--for the long haul.

Manly: I do not claim that's the only thing that's explaining the difference. But if you don't take into account educational quality, which is something more complicated than just the years of education that you attain, then you're not going to be able to understand completely how people of color seem to be at higher risk.

(Music)

There's a lot that's unknown about how education translates into brain biology.

Good schooling may confer direct neurological benefits -- literally building a bigger brain with more neural connections. It certainly improves job options, income, professional networks and access to health care. Manly says one reason education is such a powerful variable in predicting later health is that it probably does a whole bunch of things and not just one thing.

She wonders how much dementia could be avoidable if more people got better childhood educations.

Manly: That points to a specific policy that we could change that could improve the lives of millions of people. The other important thing to say about my research is that I'm finding similar effects of educational quality in whites. You know, this is not just limited to explaining racial disparities. This is about, you know, finding things that we can modify about how we treat people and how we treat children and how we afford opportunities for people and what we value for everyone.

(Woman speaking in spanish fade under)

Manly's team is following even younger people now.

They're exploring the roots of not just Alzheimer's disease, but other forms of dementia by taking brain scans and blood and spinal fluid samples to map how different brain changes are affected by social experience.

(Music)

They're finding that problems with blood flow play a bigger role in dementia among African Americans and Hispanics than in white people.

For example, black people show more signs of small blood vessel damage in the brain and are more likely to have high blood pressure in middle age. Both are risks for dementia and both are affected by environment and behavior.

By focusing on people most at risk for dementia, Manly uncovered clues that could be relevant in all our lives.

The idea that people can reduce their chance of getting dementia is fairly new and for a long time it was questioned. But there's some evidence we've done it without even trying...

Kristine Yaffe: At first people didn't really believe it because it was contrary to what we'd expect.

That's Kristine Yaffe. She's an Alzheimer's and dementia researcher at the University of California, San Francisco. Yaffe says epidemiology studies in the last ten years detected a surprising decline.

Yaffe: From the 90s say to the 2000s or 2010s that actually the cases of dementia - the new cases of dementia have actually gone down.

What this means is that someone, say age 75, is less likely to have dementia than a 75-year-old ten or twenty years ago.

This seems counterintuitive, since we keep hearing about the coming tsunami of Alzheimer's. The number of people with dementia is going up and up with the aging population and the bulge

of the baby boomers. But the rate of new cases went down slightly in Rochester, Minnesota... in Stockholm, Sweden ... in Framingham, Massachusetts ... in Ontario, Canada.

So, why? Genetics didn't change. Epidemiologists suspect it had something to do with social and medical improvements: perhaps broader education following World War II and better control of heart disease.

Yaffe says these falling rates focused attention on life experience and behavior. And made researchers wonder, could they reduce dementia even more?

Yaffe: And when people say to me what's the number one thing we could do to prevent dementia, I say improve childhood education.

The number two thing?

Yaffe: Heart health. So, there's a saying what's good for the heart is good for the brain.

What improves health below the neck, improves health above the neck.

Yaffe: So, physical activity.

And the things that are bad for the heart -- raise the risk of dementia:

Yaffe: Things like diabetes, blood pressure, cholesterol, or other lipids, obesity.

And, a topic Yaffe is researching these days...

Yaffe: Sleeping!

If someone isn't sleeping so well, the proteins that are the hallmark for Alzheimer's tend to accumulate more.

Yaffe: And so it's almost a way to flush the system out.

Yaffe says other factors may also raise the risk of dementia - traumatic brain injury, depression, poor diet. Adjusting these risks could lower an individual's risk of dementia. And across a population, could dramatically reduce the number of dementia cases.

Yaffe: We think that about a third of the cases overall are attributable to these modifiable risk factors: cardiovascular disease, physical activity, education etc. So we think that if we could modify them even 10 to 20 percent, you know -- get everybody to smoke 20 percent less or exercise 20 percent more. Not radical shifts, but you know modest but meaningful shifts, we actually could have a big downstream effect on how common dementia is.

Maybe an effect as big as a blockbuster drug.

(Music)

For years, testing lifestyle and behavior interventions has taken a back seat to testing drugs. Now researchers are finally starting to subject them to the randomized controlled studies that are the gold standard of science. The National Institutes of Health, or NIH, is putting more money into clinical trials that test prevention strategies.

Yaffe: In some ways it's been because the drugs haven't worked out, that now finally I think the NIH and others are saying, 'Oh wait a second, maybe we need to go back and look at this again.'

Yaffe says some of this more conclusive evidence is beginning to come in. For example, a recent randomized study tested lowering blood pressure.

Yaffe: This was very powerful because it was one of the first studies to show that you could actually prevent getting mild cognitive impairment in dementia with an aggressive treatment of cardiovascular risk.

Europe is ahead of the United States in testing prevention. A study in Finland, for example, found that two years of exercise, a healthier diet and lowering blood pressure slowed cognitive decline in older people who started with normal thinking and memory.

Researchers are now launching similar studies of the behaviors they think have the most promise -- to gather the strongest evidence possible that changing habits can stave off dementia.

(Sound of treadmill)

At a YMCA in Madison, Wisconsin, a trainer named Gretchen Girard is coaching a woman on a treadmill.

Gretchen Girard: Five minutes left 'til we cool down. That's great.

The runner is 80 years old. She's part of an exercise study for seniors with mild thinking and memory problems. They've been randomly assigned to this vigorous aerobic workout or to a gentle stretching class. They exercise 45-minutes, four days a week. Trainers keep the volunteers motivated, and make sure the aerobic group reaches at least 70 percent of their maximum heart rate.

Girard: All right, we are cooling down now...

(Treadmill sound fade out)

The lead investigator of this national exercise study is Laura Baker. She's a neuropsychologist at Wake Forest School of Medicine in Winston-Salem, North Carolina. For 20 years, Baker's been pushing to test exercise as a way to prevent dementia.

Laura Baker: Here's all these risks that are all impacted by exercise. Why aren't we studying exercise as a prevention strategy for cognitive impairment?

Exercise keeps blood flowing through those tiny blood vessels in the brain. It helps brain cells get energy from glucose and improves the health of neurons. But Baker says exercise hasn't gotten a lot of attention in Alzheimer's research.

Baker: If there was a way for some company to make money on exercise as a therapeutic it would have been tested a long time ago.

There haven't been very many randomized controlled studies of exercise. Baker ran some small ones that found six months of aerobic exercise in older people improved a kind of thinking called executive function. This is what helps you plan and prioritize. For example, can you remember a list of errands without writing them down? The exercisers also had less of the abnormal protein found in Alzheimer's tangles. That was a big deal. Baker says no drug has been able to do this in people with mild cognitive problems.

Other studies have had mixed results. Baker suspects volunteers weren't asked to exercise hard enough or often enough, and studies didn't follow them long enough.

Baker: So, I have to do the maximum dose allowable to demonstrate that it works.

At the end of the study, Baker will compare the aerobic group to the stretching group. She'll look at changes in cognitive test scores, brain scans and levels of Alzheimer's proteins in spinal fluid and blood.

If the aerobic group is better off in this carefully controlled, national study, Baker hopes exercise could be adopted as a frontline treatment to reduce dementia.

Baker: My hope is that it can be a prescription that is covered by Medicare and by other insurance policies and the prescription is your membership and trainer.

But she faces resistance from a medical field used to prescribing pills. Doctors --who work out themselves-- tell her they're skeptical:

Baker: 'This is all great Laura. But it will never work. We're not going to prescribe this. What do we say? Go get some exercise. I know it won't happen.'

But Baker is finding some people will keep exercising once they form the habit. After their year with the trainer, volunteers in her study get another six months free membership at the Y. Some participants do stop coming. But Janet Marsh stuck with it.

(Treadmill sound)

Marsh: The warm-up, I start at two miles an hour

Marsh is 78. She's a retired emergency room head nurse.

She joined the study because she has a lot of health issues that raise her risk of getting dementia. She has sleep apnea and depression and had a concussion from a fall down some basement stairs. She says she's never had that great a memory.

Marsh: There were things that other people would remember that I wouldn't. Like thinking back. 'Now, when did I...? What day was that on?' or-- My husband has an exceptionally good memory. Unfortunately. No fortunately I should say because I can ask him, 'What did I do on Tuesday?' And he'll just me know.

Marsh believes she's gotten a lot out of exercising - her dangerously high cholesterol levels dropped. She's lost 14 pounds. Her depression lifted a bit. And she believes she's thinking better.

Marsh: I do think this memory is getting better, but we'll see when the memory test is done last time.

(Treadmill sounds)

Today, she's got her earbuds in, singing along to her workout playlist

(Marsh singing along to YMCA)

Rallying cries to end Alzheimer's by 2020 or even 2025, have fizzled. Researchers I talked with said Alzheimer's won't be solved with one drug, or eating one thing or changing one habit. The biology of the brain has turned out to be more complicated than researchers thought.

And, the unrealistic predictions from the past, have made me skeptical when anyone says that we're on the brink of understanding Alzheimer's or that drug treatments are around the corner.

What does seem to unify the field, is the agreement that whatever we do, it needs to start decades before we feel our memories slipping.

Desiree Cooper: You've been listening to Fading Minds: Why there's still no cure for Alzheimer's. I'm Desiree Cooper.

Both my parents have Alzheimer's and I'm their full-time caregiver.

Cooper: People often say to me how's it going. I'm like 'This is the best day it's going to be. This is the best day it's going to be.'"

You cannot be a caregiver in this situation without wondering -- am I next? You cannot lose your keys without wondering is it starting? You can't forget the name of someone that you're looking at right at their face without wondering-- oh god, here it is.

And if I do get Alzheimer's, will my family be able to care for me? While we wait for some sort of cure, or if a cure never comes, how will we relieve the burdens of so many families like mine?

(Music)

Credits

Desiree Cooper: Fading Minds was produced by Maja Beckstrom and Sasha Aslanian with help from Heena Srivastava and Nikki Pederson.

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We have more about this story on our website – APM Reports dot org. We'd like to know what you thought about this program. Send us an email at contact@apmreports.org.

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