One barrier to Alzheimer's diagnoses could crumble with discovery of a blood biomarker

June 5 2023, by Hanna Webster

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"My mother has always been my hero," Mario Browne told a crowd of 180 people on Thursday.

Standing by his side was that 79-year-old hero, Joyce Browne, who was diagnosed with early stage Alzheimer's in 2019. The two were among the speakers at the second-annual Pittsburgh Summit on Alzheimer's and Dementia in the African American Community.

"I'm most proud of my mother today because I see her fight when dealing with this disease," said Browne, 61.

Held at the Highland Park Mount Ararat Community Activity Center and sponsored in part by the Alzheimer's Association and AARP, the event brought together local experts and community members to discuss health disparities in Alzheimer's diagnosis and treatment—and look for ways forward.

Most audience members raised their hands when asked if they knew someone with dementia, an umbrella term of which Alzheimer's Disease makes up 60-80% of all cases.

Alzheimer's affects 6.7 million Americans. In its 2023 report, the Alzheimer's Association predicted the state number to increase to 320,000 people by 2025.

And Allegheny County's population continues to age, coming second in an analysis of residents over the age of 65 for the country's 40 largest counties in 2021. Alzheimer's is a costly disease to manage as well; the Alzheimer's Association expects the U.S. to spend $345 billion on it in 2023.

Researchers in Pittsburgh are making real strides toward early detection of Alzheimer's and accessibility of resources and treatment. But none of this matters, said keynote speaker Dr. Margaret Larkins-Pettigrew, chief clinical diversity, equity and inclusion officer at Allegheny Health Network and an OB-GYN, unless health inequities baked into the system

are addressed.

A new Pitt study provides an opportunity to chip away at one primary issue: accessibility.

Published in *Nature Medicine* on Monday, the study found a new biomarker, or "tag," for Alzheimer's by looking at the blood samples of 1,016 participants.

"When you look at all the biological definitions of Alzheimer's, it says it's a condition of amyloid and tau," said senior study author, Dr. Tharik Pascoal, associate professor of psychiatry and neurology at Pitt. "This study provides an update," he said, and addresses a "key piece of the puzzle" in understanding how Alzheimer's progresses.

The study is a collaboration between scientists at Pitt's Psychiatry department, the University of Gothenburg in Sweden, McGill University in Canada and the biotech company Janssen. It was partially funded by the Alzheimer's Association, National Institute on Aging, and National Heart Lung and Blood Institute.

Scientists have long known that people with Alzheimer's develop a build-up of proteins called amyloid-beta, which coat neurons and slow them down. Another protein called tau gets tangled inside neurons, further adding to Alzheimer's pathology.

But in the present study, research might have discovered a main reason why some people with brains full of amyloid plaques never experience profound cognitive impairment, while others do. The answer lies in a kind of brain cell that has been largely underappreciated by scientists for decades: astrocytes.

Astrocytes are helper cells in the brain that respond to injury and

facilitate communication among neurons, vital for metabolism and clearing waste. But because they don't conduct electricity like neurons do, many scientists had cast them aside in the early days of academic research.

The scientists found that the blood samples of some participants revealed an important biomarker: GFAP. This protein is released by astrocytes in response to injury and can be thought of as a signal for how reactive astrocytes are in the brain.

Many of the participants' blood showed signals of amyloid and tau, but only some had the GFAP biomarker for astrocyte reactivity. The scientists watched three cohorts of participants over a span of years and discovered that those with GFAP would go on to show signs of Alzheimer's symptoms, while those with only amyloid or tau would not. And these results were consistent across three cohorts, despite them consisting of different participants over different years.

"This puts astrocytes at the center as key regulators of disease progression, challenging the notion that amyloid is enough to trigger Alzheimer's disease," said Dr. Pascoal in a news release about the study. Not only does this change the way researchers can envision Alzheimer's progression, but it also introduces an important consideration for early detection of the disease. The GFAP biomarker test could be added to blood panels and given during a simple doctor visit, increasing access to early Alzheimer's diagnosis.

Dr. Pascoal said all UPMC physicians are expected to have an opportunity to add this blood test to their gamut.

"This means it can be useful very fast. I think it's coming very soon," he said.

Emily Largent, an assistant professor of medical ethics and health policy at the University of Pennsylvania Perelman School of Medicine, and specializing in Alzheimer's drug regulation, said replicating these findings will be important to confirm how the scientific community can understand and move forward with the results.

"Hopefully, blood-based tests will lower two long-standing barriers to the uptake of Alzheimer's biomarker testing: high cost and high patient burden. Blood-based tests are relatively cheaper and less burdensome to undergo than the alternative imaging tests," she said in an email. Largent was not involved in the research.

"Lowering barriers and increasing access to biomarker testing is increasingly important as drugs that can slow the progression of cognitive impairment are made available to patients living with cognitive impairment caused by Alzheimer's disease."

Larkins-Pettigrew, the keynote speaker at the Thursday summit, heard about the study when it came out on Monday and said that blood tests to detect Alzheimer's could be a noninvasive and cost-effective way to promote early detection.

"As long as biomarkers are used with standards that reflect racial disparities, I think it could be phenomenal," she said.

There are many risk factors for Alzheimer's disease, some imprinted and others changeable. Genetics and family history play a part in who develops the disease because it can be passed down through our DNA. Other immutable factors, such as age, race and sex play a role as well: Women are more likely to develop the disease, as are Black Americans, who are twice as likely as whites to have Alzheimer's.

Larkins-Pettigrew thinks this is due in part to chronic stress from

structural problems, such as food insecurity, poverty, lack of education and lack of access to quality health care. Chronic stress impacts heart health and inflammation, and can accelerate aging.

"Stress is a big deal, and this is 400 years of stress" in the African American population, she said. "It's continuous micro- and macro-aggressions that wear you down overtime, called weathering. That's what's happening to Black people in this country.

"People taking care of you need to understand that stress didn't start yesterday. It started when you took your first breath."

One solution, Larkins-Pettigrew said in an interview, is for health care workers to adopt "cultural humility," which may decrease medical discrimination and increase empathy, directing Black people to quality care and potentially early diagnoses.

Another is to increase accessibility of resources.

One notable local resource for those with Alzheimer's is the Alzheimer's Disease Research Center at Pitt. Melita Terry, the organization's community engagement coordinator, also spoke at the Thursday event and encouraged people to see if they are eligible for clinical trials.

As part of the center's research, which is funded by the NIH at no cost to the patient, those who suspect they have dementia or Alzheimer's can come to the center and receive a complete workup by a team including a physician assistant, neurologist and psychologist. Patients receive a free MRI, and the team can also provide a diagnosis if dementia is present.

Terry first met Joyce Browne at the Kingsley Association in East Liberty in 2019, when Browne had already started experiencing some cognitive impairment. The coincidental meeting ultimately led to Browne's

diagnosis, when Terry encouraged her to visit the center.

Browne, who lives in the East End, now attends the BRiTE (Brain Training and Exercise) Wellness Program, created by occupational therapists at the Pitt School of Health and Rehabilitation Sciences. Members of the program socialize and engage in activities to promote brain health and curb memory loss. Her son is grateful for this, especially as more research comes out about the danger loneliness and social isolation can pose to health.

"Before she got married [five years ago], she was living alone and talked about feeling lonely," said Browne. "That bothers me a little. It makes me feel like she was maybe suffering and not telling us."

Things are better now, because Browne is surrounded by family and friends.

"My mother thrives around people. She loves connection," said Browne. "At BRiTE Wellness, they will play old songs, and people will start remembering. They'll remember things from their 20s and 30s. They'll have memories from when they were a child, and maybe they heard that song on vacation."

Browne said she appreciates the camaraderie from the program and the opportunity to get out of the house. As a Black woman, she said she has not experienced mistreatment in the medical system when seeking Alzheimer's care.

"I don't feel alone anymore," she said. "I feel honored because I have a wonderful family. I've seen people [with dementia] who don't, and I feel bad for them. My hope is for the same sense of community for others."

Heather Hopson, the event's moderator, said her mother was just

diagnosed with dementia.

"Joyce Browne gives people like me hope. She is proof that people with Alzheimer's disease can live a joyful life."