7T brain scans reveal potential early indicator of Alzheimer's

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Researchers from the Center for BrainHealth at The University of Texas at Dallas are investigating a potential new early indicator of the decline toward Alzheimer's disease: measuring the energy metabolism of the living human brain using cutting-edge imaging techniques.

The scientists devised a unique way to illustrate energy consumption and reserves in the brain with phosphorus magnetic resonance spectroscopy using an ultra-high-field 7 Tesla MRI scanner. Their results suggest that neurological energy metabolism might be compromised in mild cognitive impairment (MCI), the stage of decline between healthy aging and more serious disease states like dementia and Alzheimer's.

Dr. Namrata Das, Ph.D.'20, a program specialist and research neuroscientist in the School of Behavioral and Brain Sciences, is lead author of the study published online April 6 in *Frontiers in Neuroscience*.

"Much of what we know about cognitive decline at the molecular level comes from post-mortem brain examinations or animal models," said Das, who also holds a medical doctorate and master of public health degree. "What we set out to do was monitor in real time the biological mechanisms that cause this decline in humans to better understand the multiple factors involved."

Senior author Sandra Bond Chapman, Ph.D., chief director of the Center for BrainHealth at UT Dallas, said the results demonstrate "new pathways to advance discovery."

"This research provides a promising new way to elucidate the brain's health—or early disturbance of its health—due to changes in metabolism. The new approach is the utilization of 7 Tesla magnetic resonance imaging, a noninvasive, safe technology," said Chapman, the Dee Wyly Distinguished University Chair in BrainHealth. "It has exciting implications for early detection of Alzheimer's disease and the potential to measure disease response to treatments."

Although Alzheimer's disease was first defined more than a century ago, treatment remains elusive. According to Das, this is because "multiple mechanisms become abnormal, causing a cascade of events, and we don't know which comes first.

"Most current research is focused on accumulation of beta-amyloid and tau protein in the brain. Here, we're trying to learn if there are other early markers that can be tracked live via imaging. We hope that our findings, when integrated with measurements of tau and beta-amyloid, will give more profound information."

The researchers theorize that the energy level disturbance occurs early in Alzheimer's disease, based on prior post-mortem work that indicated the metabolism deficit is lower in earlier stages of Alzheimer's than it is in severe cases.

"That research set the path we are on to answer

these questions with imaging technology," Das said.

The current study was conducted at the Advanced Imaging Research Center (AIRC), a collaborative facility shared by UT Dallas and other North Texas institutions and located on the UT Southwestern Medical Center campus. The facility houses several MRI scanners that operate at magnetic fields up to 7 Tesla (7T) for human studies. MRIs using such strong magnets—the magnet in a 7T machine is more than twice as powerful as 3T clinical MRIs—can illuminate metabolic processes and provide unprecedented detail in the resulting images.

In the study, 41 participants—15 cognitively normal, 15 with MCI and 11 with early Alzheimer's—underwent assessment of executive function, memory, attention, visuospatial skills and language. The 7T MRI scans focused on measuring ratios between the energy molecules adenosine triphosphate (ATP) and phosphocreatine (PCr), and inorganic intracellular phosphate.

"Most of the energy in a cell is coming from the mitochondria," Das said. "It is theorized that mitochondrial dysfunction occurs early in Alzheimer's disease and that ATP and PCr are not synthesized properly. With 3T MRI, we could not see these molecular levels accurately. The 7T gets us there."

The researchers' scans of the participants' temporal lobes indicated that the ratio of PCr to ATP—which Das referred to as the energy reserve index—correlated with the participants' cognition levels.

"The energy reserve was lower in patients with mild cognitive impairment and lower still in those with Alzheimer's," she said. "We believe this is the first paper to confirm that energy reserve decreases in MCI, in many cases, years before Alzheimer's disease sets in."

While 7T MRI machines are not yet widely available for routine clinical evaluation of patients, Das said that the techniques used in the research study could be adapted to more commonly available 3T machines.

"The technology is evolving in such a way that we may soon be able to modify what we see on 7T scans to be detected with 3T, and 3T is available everywhere," she said. "We can tweak some of the MRI parameters we use to acquire these images with 3T, as has been done with proton spectroscopy. We hope this can be accomplished within the next few years."

In the future, the research team intends to combine this energy-level biomarker with positron emission tomography scans that measure beta-amyloid and tau protein, the most widely known markers of Alzheimer's disease. Meanwhile, Das will continue her research on using MRI to find novel neuroimaging markers at Harvard Medical School's McLean Imaging Center beginning July 1.

"We hope to determine if the abnormal brain energy metabolism has a relationship with the accumulation of beta-amyloid and tau," Das said. "Researchers have hypothesized for years that such metabolism shortfalls might precede such accumulations, but only now, with 7T, do we have the modality to find out."

More information: Namrata Das et al, Phosphate Brain Energy Metabolism and Cognition in Alzheimer's Disease: A Spectroscopy Study Using Whole-Brain Volume-Coil 31Phosphorus Magnetic Resonance Spectroscopy at 7Tesla, *Frontiers in Neuroscience* (2021). DOI: 10.3389/fnins.2021.641739

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