Brain's 'autopilot' provides insight into early development of Alzheimer's disease

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Watching the brain's "autopilot" network in real time may help determine the onset of cognitive decline and potentially aid in making an early diagnosis of Alzheimer's disease, according to researchers at Duke University Medical Center.

While traditional MRI and imaging studies conducted in Alzheimer's disease have focused on the anatomy and function of individual regions of the brain, the Duke team conducted the first study to test how the integrity of an entire brain network relates to future cognitive decline. This "autopilot" network, known more formally as the default mode network, has been linked with the presence of the hallmark amyloid plaques believed to underpin Alzheimer's disease.

The study found altered patterns of brain activity in the default mode network among people with mild memory problems who later progress to Alzheimer's disease compared to those whose memory remains intact over a two- to three-year period.

The default mode network is increasingly becoming a target for better understanding Alzheimer's disease. It is a unique network because it becomes more active when the brain turns inward, rather than when it is outwardly engaged in cognitive tasks.

"It's like a reservoir that holds cognitive reserves," said Jeffrey R. Petrella, MD, the study's lead author and associate professor of radiology at Duke. "The default mode network shuts down its resources to

reallocate them to other networks that are actively participating in a task, such as reading, speaking or remembering."

"While the default mode network has been implicated in memory development and Alzheimer's disease, until now no one had tested its role in predicting future cognitive changes in those with mild memory complaints," Petrella said. "Our study found a significant relationship between patterns of activity in the default mode network and future onset of Alzheimer's disease, which were seen above and beyond the typical measures used in routine clinical practice."

For the study, Petrella and colleagues set out to identify changes in network connectivity during a memory task and to correlate these changes with the degree of memory impairment present in patients with Alzheimer's disease or mild cognitive impairment over time. The researchers studied 12 patients with mild Alzheimer's disease, 31 patients with mild cognitive impairment and 25 healthy controls.

Researchers found different levels of connectivity in the default mode network among patients with varying degrees of cognitive impairment. Such patterns were strongly associated with future changes in memory performance and functional ability in people with mild cognitive impairment (MCI), a group known to be at high risk for Alzheimer's.

There is speculation that overactivity in the default mode network in early and midlife may predispose a person to amyloid development later in life.

"When it comes to amyloid accumulation and network disruption in the brain, we have a chicken and egg phenomenon – we don't know which came first," said study co-author P. Murali Doraiswamy, MBBS, FRCP, professor of psychiatry and medicine at Duke. "But our study, along with prior findings in the field, suggests that people who have both pathologic

lesions and network disruptions are most vulnerable to development of Alzheimer's in the future."

"These findings may help explain why mental engagement may protect against Alzheimer's disease," Petrella said. "When someone is actively engaged in a task, the default mode network becomes less active."

The researchers said that fMRI may eventually help to identify patients at risk for developing Alzheimer's disease and play a key role in early diagnosis when combined with clinical, genetic and other imaging markers.

Given the small size and limited follow-up time, a larger study is needed to confirm the findings. The next step is to conduct a larger, multicenter study to see if fMRI can be combined with other tests to scan for future disease.

  More information: The study is published in *Neurology*, the medical journal of the American Academy of Neurology.

Provided by Duke University Medical Center