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NTU Singapore Researchers Identify Early Alzheimer's Warning Sign in Brain Imaging

Scientists at Nanyang Technological University, Singapore (NTU Singapore) have uncovered a significant finding regarding the brain's waste removal system, particularly in relation to Alzheimer's disease. Their research indicates that blockages within this system, identified as "enlarged perivascular spaces," often occur in individuals showing early symptoms of Alzheimer's, well before more pronounced dementia symptoms are apparent.

This discovery suggests that these blockages could act as an early warning sign of Alzheimer's, the most prevalent form of dementia. Associate Professor Nagaendran Kandiah from NTU's Lee Kong Chian School of Medicine (LKCMedicine), who spearheaded the study, mentioned that these anomalies can be detected through standard magnetic resonance imaging (MRI) scans. Thus, identifying them could enhance early detection efforts, eliminating the need for additional and potentially costly testing.

In highlighting the urgency of early detection, Justin Ong, a fifth-year medical student and the primary author of the study, noted that recognizing Alzheimer's at an earlier stage allows for timely medical interventions. Such early action may help slow the progression of symptoms like memory loss, decreased cognitive speed, and mood variations. This research emerged from LKCMedicine's Scholarly Project module as a component of their Bachelor of Medicine and Bachelor of Surgery program.

The relevance of this study is amplified by its focus on Asian populations, which have historically been underrepresented in Alzheimer's research. Most prior studies primarily engaged Caucasian participants, potentially narrowing the applicability of their findings. The NTU team examined nearly 1,000 individuals in Singapore, encompassing diverse ethnic backgrounds that mirror the local population. Among these participants were both cognitively healthy individuals and those exhibiting mild cognitive impairments.

Research has underscored that dementia does not uniformly affect all ethnic groups, making region-specific investigations essential. For instance, studies have shown that the prevalence of the apolipoprotein E4 gene, a significant risk factor for Alzheimer's, is found in approximately 50-60 percent of Caucasian dementia patients, whereas it drops to less than 20 percent among dementia patients in Singapore, according to Assoc Prof Kandiah, who directs the Dementia Research Centre in LKCMedicine.

The study delves into the brain's waste removal processes, which depend on perivascular spaces surrounding blood vessels to eliminate toxic substances, including beta amyloid and tau proteins. When these pathways become less effective, they tend to enlarge and become visible on MRI scans. This research aimed to explore the links between these changes and established indicators of Alzheimer's disease.

The study comprised nearly 350 participants with normal cognitive abilities, alongside others exhibiting early signs of cognitive decline, particularly those with mild cognitive impairment (MCI), a condition often preceding more severe dementia. Findings indicated that individuals with MCI were significantly more likely to have enlarged perivascular spaces compared to their cognitively healthy counterparts.

Beyond MRI assessments, the researchers also measured several Alzheimer's-related biochemicals in the blood of the participants, including elevated levels of beta amyloid and tau proteins, known as warning signs for Alzheimer's disease. Notably, enlarged perivascular spaces correlated with four of these seven biochemical measurements, implying that individuals with these drainage obstructions are at increased risk of developing Alzheimer's.

Interestingly, among those with MCI, the association between enlarged perivascular spaces and Alzheimer's-related biochemicals was found to be stronger than that with white matter damage, a conventional indicator of the disease. This suggests that early signs of Alzheimer's disease may be more reliably indicated by clogged drainage pathways in the brain.

The implications of these findings could significantly impact diagnosis and treatment. Assoc Prof Kandiah noted that while current clinical practices often prioritize white

matter damage observable on MRI scans, these new results present enlarged perivascular spaces as a promising tool for the early detection of Alzheimer's.

Experts not involved in the study, such as Dr. Rachel Cheong Chin Yee, highlighted the importance of these findings in recognizing the early risk of Alzheimer's, suggesting that MRI scans indicating enlarged perivascular spaces could aid in identifying individuals at higher risk, even before symptoms manifest.

Dr. Chong Yao Feng, also an independent consultant, added that this study blurs the lines between cerebrovascular diseases and Alzheimer's, suggesting that the two conditions may interact more than previously acknowledged. Consequently, clinicians evaluating MRI scans should be cautious in attributing cognitive symptoms solely to vascular issues when signs like enlarged perivascular spaces are present.

Looking ahead, the NTU research team intends to monitor the participants over time to ascertain how many eventually develop Alzheimer's dementia. This longitudinal aspect will help validate whether enlarged perivascular spaces can reliably signify the risk of progressing to dementia. If subsequent studies in different populations affirm these initial findings, the routine identification of these blockages through MRI could become a key strategy for detecting Alzheimer's risk at much earlier stages than currently practiced.

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