Artificial intelligence outperforms clinical tests at predicting progress of Alzheimer's disease

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Cambridge scientists have developed an artificially-intelligent tool capable of predicting in four cases out of five whether people with early signs of dementia will remain stable or develop Alzheimer's disease.

The team say this new approach could reduce the need for invasive and costly diagnostic tests while improving treatment outcomes early when interventions such as lifestyle changes or new medicines may have a chance to work best.

Dementia poses a significant global health care challenge, affecting over

55 million people worldwide at an estimated annual cost of $820 billion. The number of cases is expected to almost treble over the next 50 years.

The main cause of dementia is Alzheimer's disease, which accounts for 60–80% of cases. Early detection is crucial as this is when treatments are likely to be most effective, yet early dementia diagnosis and prognosis may not be accurate without the use of invasive or expensive tests such as positron emission tomography (PET) scans or lumbar puncture, which are not available in all memory clinics.

As a result, up to a third of patients may be misdiagnosed and others diagnosed too late for treatment to be effective.

A team led by scientists from the Department of Psychology at the University of Cambridge has developed a machine learning model able to predict whether and how fast an individual with mild memory and thinking problems will progress to developing Alzheimer's disease. In research published in *eClinicalMedicine*, they show that it is more accurate than current clinical diagnostic tools.

To build their model, the researchers used routinely-collected, non-invasive, and low-cost patient data—cognitive tests and structural MRI scans showing gray matter atrophy—from over 400 individuals who were part of a research cohort in the U.S..

They then tested the model using real-world patient data from a further 600 participants from the US cohort and—importantly—longitudinal data from 900 people from memory clinics in the UK and Singapore.

The algorithm was able to distinguish between people with stable mild cognitive impairment and those who progressed to Alzheimer's disease within a three-year period. It was able to correctly identify individuals who went on to develop Alzheimer's in 82% of cases and correctly

identify those who didn't in 81% of cases from cognitive tests and an MRI scan alone.

The algorithm was around three times more accurate at predicting the progression to Alzheimer's than the current standard of care; that is, standard clinical markers (such as gray matter atrophy or cognitive scores) or clinical diagnosis. This shows that the model could significantly reduce misdiagnosis.

The model also allowed the researchers to stratify people with Alzheimer's disease using data from each person's first visit at the memory clinic into three groups: those whose symptoms would remain stable (around 50% of participants), those who would progress to Alzheimer's slowly (around 35%) and those who would progress more rapidly (the remaining 15%).

These predictions were validated when looking at follow-up data over six years. This is important as it could help identify those people at an early enough stage that they may benefit from new treatments, while also identifying those people who need close monitoring as their condition is likely to deteriorate rapidly.

Importantly, those 50% of people who have symptoms such as memory loss but remain stable, would be better directed to a different clinical pathway as their symptoms may be due to other causes rather than dementia, such as anxiety or depression.

Senior author Professor Zoe Kourtzi from the Department of Psychology at the University of Cambridge said, "We've created a tool which, despite using only data from cognitive tests and MRI scans, is much more sensitive than current approaches at predicting whether someone will progress from mild symptoms to Alzheimer's—and if so, whether this progress will be fast or slow.

"This has the potential to significantly improve patient well-being, showing us which people need closest care, while removing the anxiety for those patients we predict will remain stable. At a time of intense pressure on health care resources, this will also help remove the need for unnecessary invasive and costly diagnostic tests."

While the researchers tested the algorithm on data from a research cohort, it was validated using independent data that included almost 900 individuals who attended memory clinics in the UK and Singapore.

In the UK, patients were recruited through the Quantitative MRI in NHS Memory Clinics Study (QMIN-MC) led by study co-author Dr. Timothy Rittman at Cambridge University Hospitals NHS Trust and Cambridgeshire and Peterborough NHS Foundation Trusts (CPFT).

The researchers say this shows it should be applicable in a real-world patient, clinical setting.

Dr. Ben Underwood, Honorary Consultant Psychiatrist at CPFT and assistant professor at the Department of Psychiatry, University of Cambridge, said, "Memory problems are common as we get older. In clinic I see how uncertainty about whether these might be the first signs of dementia can cause a lot of worry for people and their families, as well as being frustrating for doctors who would much prefer to give definitive answers.

"The fact that we might be able to reduce this uncertainty with information we already have is exciting and is likely to become even more important as new treatments emerge."

Professor Kourtzi said, "AI models are only as good as the data they are trained on. To make sure ours has the potential to be adopted in a health care setting, we trained and tested it on routinely-collected data not just

from research cohorts, but from patients in actual memory clinics. This shows it will be generalizable to a real-world setting."

The team now hope to extend their model to other forms of dementia, such as vascular dementia and frontotemporal dementia, and using different types of data, such as markers from blood tests.

Professor Kourtzi added, "If we're going to tackle the growing health challenge presented by dementia, we will need better tools for identifying and intervening at the earliest possible stage.

"Our vision is to scale up our AI tool to help clinicians assign the right person at the right time to the right diagnostic and treatment pathway. Our tool can help match the right patients to clinical trials, accelerating new drug discovery for disease modifying treatments."

More information: Robust and interpretable AI-guided marker for early dementia prediction in real-world clinical settings, *eClinicalMedicine* (2024). DOI: 10.1016/j.eclinm.2024.102725

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