

Study indicates high prevalence of recently defined non-Alzheimer's dementia

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Researchers from the University of Kentucky's Sanders-Brown Center on Aging say a paper recently published in *Acta Neuropathologica* is the most definitive assessment yet of the prevalence of a form of dementia

classified in 2019 and now known as LATE. The results show that the prevalence of brain changes from LATE may be roughly 40% in older adults and as high as 50% in people with Alzheimer's disease.

"This is a fundamental question about any disease or condition, 'How commonly is it seen in peoples' brains?' and it is deceptively challenging to answer that question," said Pete Nelson, M.D., Ph.D., neuropathologist and the R.C. Durr Foundation Chair in Alzheimer's Disease at UK.

In 2019 Nelson and large group of international experts, working together, [named](#) this new form of dementia named limbic-predominant age-related TDP-43 encephalopathy (LATE).

The data for this new research came from 13 existing community and population-based study cohorts. The study included autopsy, genetic and [clinical data](#) from more than 6,000 brains. Five different countries across three continents are represented in the samples and data. The results indicated that more than a third of the brains had LATE pathology.

Symptoms of LATE mimic Alzheimer's disease by causing [memory loss](#) and problems with thinking and reasoning in old age. But researchers found the LATE-affected [brain](#) looks different from the Alzheimer's brain, and the therapies that may work for one probably would not work for the other.

Ten NIH-funded Alzheimer's Disease Research Centers, including University of Kentucky, were represented and worked together as a large coherent team. In addition to these U.S. centers, two cohorts from the United Kingdom, and one cohort each from Brazil, Austria, and Finland took part in this study.

"Not only is the size of this combined analysis important but also the fact that those who took part in the studies leading to brain donation were derived from longitudinal studies in researched populations. Due to this we can say more about the contribution of LATE to dementia in older populations. This is quite different from most research which is effectively from individuals without that anchoring," said Carol Brayne, M.D., British academic and Professor of Public Health Medicine at the University of Cambridge. "Given older ages are when dementia is most common, the LATE findings are particularly important. Although there are many differences between the studies that are combined here—from design to methodologies—they all reveal the importance of LATE and suggest our findings will be relevant beyond any individual country or region of the world."

In addition to the University of Kentucky, other U.S. Alzheimer's Disease Research Centers involved in this work include Northwestern University Medical Center, Rush University Medical Center, Mayo Clinic (both MN and FL campuses), Duke University, University of California (Davis), University of California (Irvine), University of California (San Francisco), University of Washington, and Stanford University.

"The inclusion of so many high-quality cohorts from around the world is unprecedented. Every single research center has its own set of biases and blind spots when it comes to recruiting research volunteers," said Nelson. "To achieve progress, we need collaboration between institutions and across borders. The NIH/NIA-funded Alzheimer's Disease Research Centers leveraged their multidisciplinary resources and our esteemed international collaborators brought extraordinary expertise of their own."

While there have been prior reports about LATE from individual research centers and from various groups, there has not been a prior study bringing together findings from many community-based autopsy

cohorts.

Nelson says that ultimately this study helps indicate that LATE is an extremely common contributor to the devastating clinical syndrome that is often referred to as Alzheimer's disease or dementia. While looking at the findings, Nelson and the other researchers indicated that LATE was even more common in brains with severe Alzheimer's disease neuropathologic change (ADNC)—over half of severe ADNC cases also had LATE.

With the first clinical trial in the world for LATE currently underway at the University of Kentucky, and attention turning towards preventing LATE and Alzheimer's, Nelson says basic information gained through studies like this one is crucial. "It helps us frame key questions like, 'Who should be recruited into a research study? What should we be looking for?' It can also help guide us on how to better study LATE and Alzheimer's disease when those two brain diseases are so often present in the same person."

While progress is being made, there still are many knowledge gaps.

"We need more information in more diverse cohorts. People with African or Asian heritage were relatively under-sampled in this study. So far, it does not appear that people with different ethnic backgrounds have differing risk for LATE but further work is required in this important area," said Nelson.

More information: Peter T. Nelson et al, Frequency of LATE neuropathologic change across the spectrum of Alzheimer's disease neuropathology: combined data from 13 community-based or population-based autopsy cohorts, *Acta Neuropathologica* (2022). [DOI: 10.1007/s00401-022-02444-1](https://doi.org/10.1007/s00401-022-02444-1)

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