Hidden disease discovered in brains of most elderly adults in study

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FACT CHECKED

HELSINKI, Finland — A little-known brain condition may be far more common in older adults than previously thought, potentially rivaling Alzheimer's disease as a major cause of dementia. The research, conducted on a unique population of individuals aged 85 and older in Finland, found that nearly two-thirds of participants showed signs of a disease called *limbic-predominant age-related TDP-43 encephalopathy* (LATE).

LATE is a relatively newly recognized condition, first defined by scientists in 2019. It's characterized by the abnormal buildup of a protein called TDP-43 in areas of the brain crucial for memory and thinking. This protein accumulation can lead to brain cell death and cognitive decline, much like the more well-known plaques and tangles seen in Alzheimer's disease.

"The results suggest that LATE is, alongside Alzheimer's, one of the strongest determinants of dementia in the oldest old," says Associate Professor Liisa Myllykangas from the University of Helsinki in a media release.

The study, published in the journal *Brain*, provides some of the strongest evidence yet that LATE may be a major contributor to dementia in the oldest members of society. The researchers examined the brains of 295 deceased individuals who had been part of the Vantaa 85+ study, a long-term research project that followed all residents of Vantaa, Finland who were 85 or older in 1991.

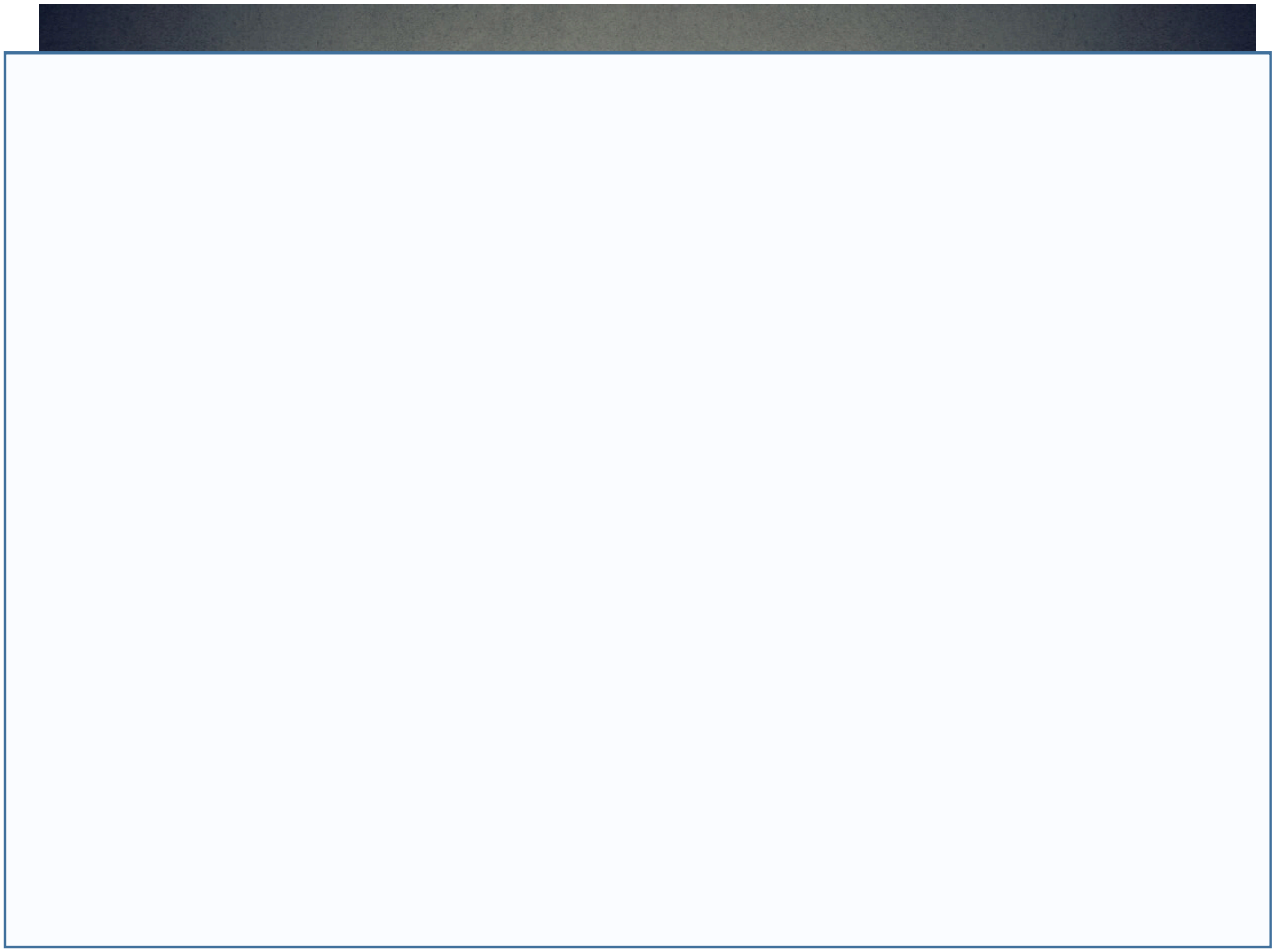
What makes this study particularly valuable is its population-based approach. Rather than focusing on individuals who sought medical care for memory problems, the Vantaa 85+ study included a cross-section of all elderly individuals in a specific geographic area. This gives researchers a more accurate picture of how common various brain conditions are in the general population of the very old.

The results were striking. The team found evidence of LATE in **64.1%** of the brains researchers examined. Even more surprisingly, LATE appeared to be independently

associated with dementia, even when accounting for other brain changes like those seen in Alzheimer's disease.

To put this in perspective, imagine a small town where nearly two out of every three residents over 85 are walking around with a potentially dementia-causing protein building up in their brains. It's a sobering thought, especially considering how little we currently know about treating or preventing LATE.

"LATE likely affects tens of thousands of people in Finland," notes Myllykangas. "This disorder is a significant concern for the public health system."



The study also shed light on how LATE interacts with other brain conditions common in old age. Many individuals showed signs of both LATE and Alzheimer's disease, and

these participants tended to have more severe cognitive decline than those with either condition alone. It's as if these two diseases team up to deliver a one-two punch to the aging brain.

Interestingly, the researchers found that LATE was strongly associated with a condition called hippocampal sclerosis, where the hippocampus – a seahorse-shaped structure crucial for memory – becomes shrunken and scarred. Almost all individuals with hippocampal sclerosis also showed signs of LATE, suggesting a close relationship between these two conditions.

The study also explored potential risk factors for LATE. While some previous research has suggested links to high blood pressure or diabetes, this study didn't find strong connections to these or other common health conditions. However, the team did identify two genetic variants that seem to increase the risk of developing LATE, opening up new avenues for future research.

Perhaps most importantly, this study highlights how complex dementia can be, especially in the very old. Most participants with dementia had multiple brain conditions contributing to their cognitive decline rather than a single, clear cause. This "mixed pathology" may help explain why treatments that target only one aspect of brain aging, like those focused solely on Alzheimer's disease, have had limited success so far.

The findings from this study could have a significant impact on how doctors approach dementia diagnosis and treatment in the future. If LATE is indeed as common as this research suggests, it may be necessary to develop new diagnostic tools to identify it in living patients and explore targeted therapies that can prevent or slow the buildup of TDP-43 protein in the brain.

Moreover, the high prevalence of LATE in this population underscores the need for a more holistic approach to brain health in old age. Rather than focusing on a single disease like Alzheimer's, future strategies may need to address multiple aspects of brain aging simultaneously to effectively combat cognitive decline.

Paper Summary

Methodology

The study examined brain tissue from 304 deceased individuals who were part of the Vantaa 85+ study in Finland. Researchers used specialized staining techniques to detect the presence of abnormal TDP-43 protein in different brain regions. They then categorized the severity of LATE into stages based on how widespread the protein buildup was.

The team also assessed other brain changes associated with conditions like Alzheimer's disease and Lewy body dementia. These neuropathological findings were then compared with clinical information collected during the participants' lives, including cognitive assessments and medical history.

Key Results

The study found that 64.1% of participants showed some level of LATE pathology in their brains. The most common was stage 2 (28.5% of all participants), followed by stage 3 (12.9%). LATE was significantly associated with dementia diagnosis and lower scores on cognitive tests, even after accounting for other brain pathologies.

The presence of LATE was also strongly linked to hippocampal sclerosis, with 93.4% of those with hippocampal sclerosis also showing LATE pathology. The study identified two genetic variants (in the GRN and TMEM106B genes) associated with increased LATE risk.

Study Limitations

While this study provides valuable insights, it has some limitations. The population studied was ethnically homogeneous and from a specific region in Finland, so the findings may not be fully generalizable to other populations. The study relied on post-mortem brain examination, which means it can't directly show how LATE progresses over time in living individuals. Additionally, the cognitive assessments

used were conducted in the 1990s and may not reflect the most current diagnostic criteria for dementia.

Discussion & Takeaways

This study highlights LATE as a major contributor to dementia in the very old, potentially rivaling Alzheimer's disease in importance. It underscores the complexity of dementia in advanced age, with most individuals showing multiple brain pathologies.

The findings suggest that future approaches to dementia prevention and treatment may need to address multiple aspects of brain aging simultaneously. The study also raises questions about the need for new diagnostic tools to identify LATE in living patients and the potential for developing targeted therapies to prevent or slow TDP-43 protein accumulation.

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