New brain mapping technique sheds light on Alzheimer’s development

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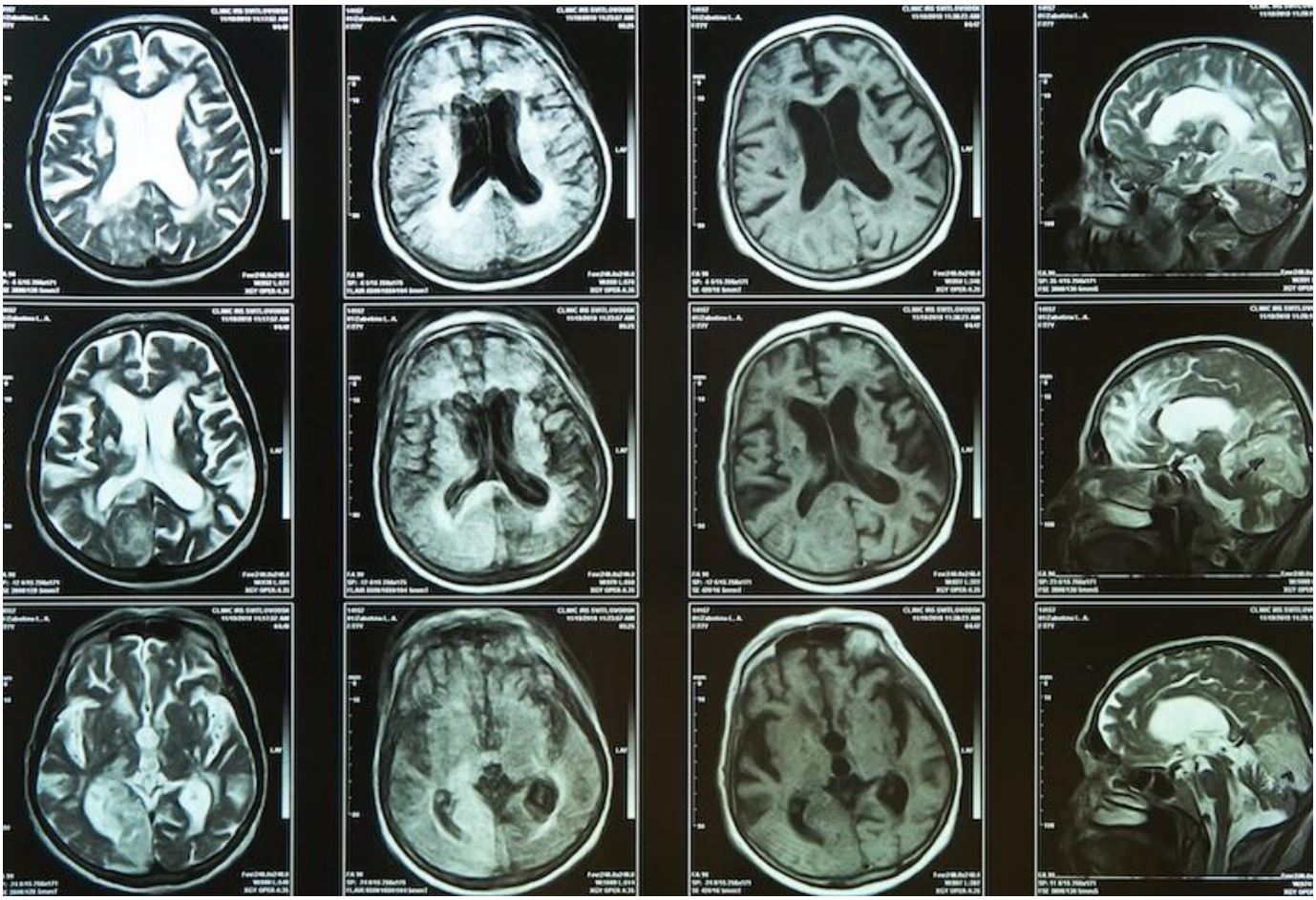

The study sheds light on the genetic mechanisms that cause the loss of brain cells that allow Alzheimer's disease to progress and identifies a key protein as a potential target for treatment. (Photo by Shutterstock)

Researchers at Tulane University have created a first-of-its-kind subcellular map of an area of the brain commonly affected by Alzheimer’s disease, a key step toward unraveling the mysteries of how the degenerative brain disease develops.

The study, published in Nature Communications, illuminated the genetic mechanisms that cause the loss of brain cells that allow the disease to progress and identified a key protein as a potential target for treatment.

More than 55 million people worldwide suffer from dementia, with Alzheimer's accounting for 60-70% of those cases. Despite the prevalence, little is known about its cause, and existing medications can only temporarily ease symptoms, not prevent the disease from progressing.

"The human brain is the most complex organ in the human body and the mechanism of many diseases like Alzheimer's is elusive," said senior author Hui Shen, associate director of the Center for Biomedical Informatics & Genomics at Tulane University School of Medicine. "Using spatial transcriptomics, we were able to create a map of a part of the prefrontal cortex with single-cell resolution to try to understand the underlying factors of Alzheimer's."

The researchers used stereo sequencing to examine a small section of the prefrontal cortex — the region responsible for decision-making and emotional control — in six brains at varying stages of Alzheimer's.

This technology allowed them to "map" the brain tissue at nearly 250 times the resolution of older tools, essentially zooming in to reveal genetic interactions within a single cell and how those shift as the disease progresses.

The study found that genetic modules tasked with protecting neurons weaken or disappear in Alzheimer's patients, allowing harmful proteins linked to the disease to build up and damage cells.

Researchers identified a protein, ZNF460, as crucial to these modules' neuroprotective processes and as a potential target for treatment.

"The most important thing is that we've identified several interesting interactions at the molecular level that work to protect neurons under stress, and these interactions disappeared in Alzheimer's patients," said lead author Yun Gong, instructor at the Center for Biomedical Informatics & Genomics at Tulane University School of

Medicine. “If we can find a way to target ZNF460 in a way that keeps these modules functioning, then we might be able to inhibit the progression of Alzheimer's.”

In another surprising discovery, the study found that the layered structure of the brain disappears as the disease advances, a phenomenon that Gong said “had not been observed before.”

Going forward, Shen and Gong said they hope to further research ZNF460 and ascertain whether its absence alone can be linked to the onset of Alzheimer’s.

“This is just one step toward understanding pathophysiology of Alzheimer disease,” Shen said. “Different areas of the brain may respond differently to the disease development, so we have to keep working to examine other regions and create the most comprehensive image we can.”

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