

# TECH INSIDER

## This breakthrough could help scientists see exactly how depression, Alzheimer's, and autism transform our brains



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There are approximately 86 billion neurons in a human brain, one of the most intricate known structures in the universe. These brain cells all communicate constantly with each other using perhaps 100 trillion synapses, the messaging points between brain cells where signals can pass from one neuron to thousands of others.

But sometimes in the case of mental disorders, something goes wrong. People lose too many of those synapses, disrupting critical networks of communication in the brain.

Mostly we've only been able to see that die-off by examining a physical section of the brain that's been removed — an invasive procedure that's only done at autopsies or in extreme cases. Being able to measure synapses in a living person could allow us to spot the start of neurological problems and perhaps intervene.

Until recently, however, that was simply not possible, leaving scientists virtually unable to access information that could be crucial to helping patients with diseases as disparate as epilepsy, depression, Alzheimer's, and autism. But now a team of scientists say they've found a way.

In a study published July 20 in the journal *Science Translational Medicine*, researchers from Yale University report that they have developed a process that allows them to measure synapses in living brains in a non-invasive way (no cutting or removing parts of the brain required).

They do this by circulating a radioactive tracer through the brain that identifies a protein that is found where there are synapses. The images that result can reveal the presence, absence, and perhaps most importantly, the change over time in the density of these essential elements that enable the networks of communication in our mind.

The research is in its earliest stages. And as the authors describe it, this has not been done before.

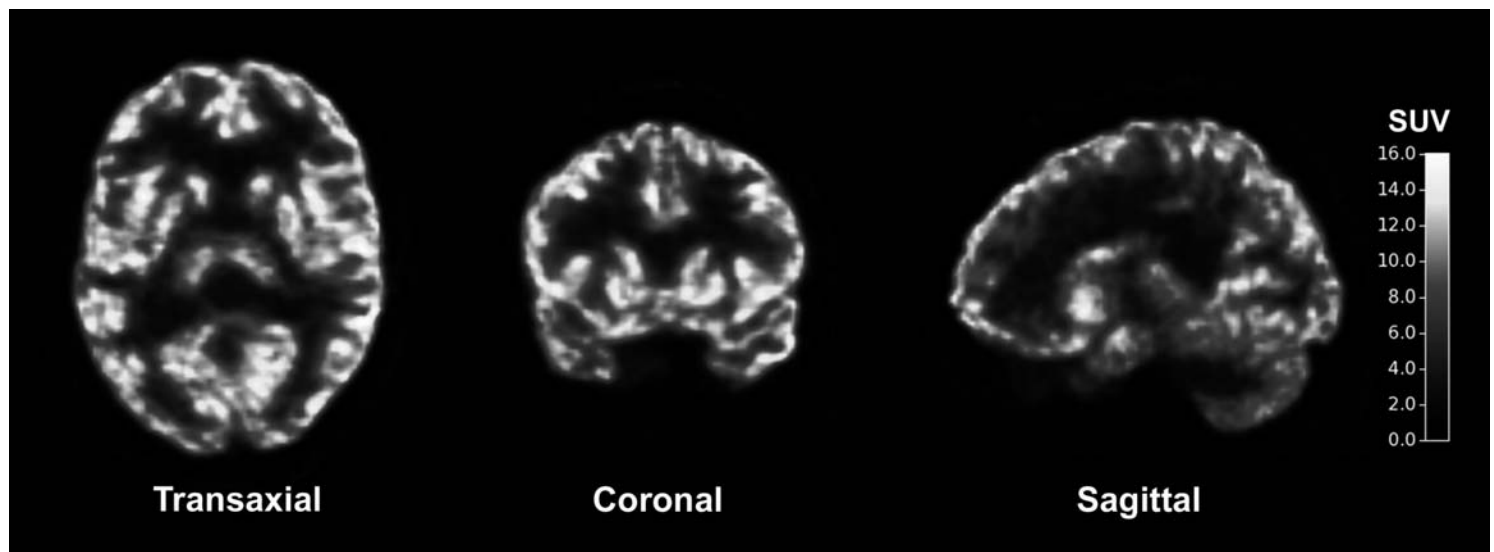


*Matt Cardy/Getty*

“We think this is the first time we can measure changes in synaptic density on a molecular level,” Sjoerd Finnema, a researcher in radiology and biomedical imaging at Yale University and lead author of the study, told Tech Insider.

By revealing changes over time, we might be able to see where sections of synapses are dying off as Alzheimer’s, Parkinson’s, epilepsy, depression, or any other disorder of the brain sets in. And if we can see where these die-offs are happening, we might be able to start intervention sooner. We may even be able to develop drugs that can stop or reverse these changes in the brain (several drugs that may be able to do this are in development, though none are ready for human use yet).

This new understanding of the brain could help us develop treatments for the numerous mental disorders that we often have little or no way to treat now. Still, this initial version of the imaging approach will need to be further tested and refined before it can be used to treat patients, and questions remain about what exactly we will learn using this process.



Scans of a healthy patient that reveal the presence of a protein that is found where there are synapses.

*Finnema et al., Science Translational Medicine 2016*

## How it works

The Yale team used a technology called Positron Emission Tomography (PET) that’s widely used to measure biochemical changes in body tissues. We already use PET scans of brain tissue to measure the presence of the amyloid plaques that form in Alzheimer’s disease, Richard Carson, senior author of the study and the director of the Yale PET lab, told Tech Insider.

Carson said that the team behind the study realized that an epilepsy drug called Keppra (made by UCB Pharma, which provided some of the funding for the study) targeted one specific protein that could help identify synapses throughout the brain. This particular protein, SV2A, may actually even be a better measure for synaptic density than the gold standard currently used to measure synapses in autopsies, according to Finnema.

They first tested the new agent in a baboon brain, comparing the results they got using the new technique to the current gold standard.

Then, they conducted scans with the new agent in 10 healthy human subjects and three epilepsy patients. The scans showed the density of synapses as they should exist in healthy patients and showed synapse loss in epilepsy patients. That’s consistent with prior research on epilepsy’s effects on the brain.

The team behind the study says that this work shows a proof of concept for a process that can analyze synapse density in living people’s brains, a remarkable advance. Carson said that being able to specifically identify

problem regions of the brain (affected by synapse loss) could be incredibly important for patients with any sort of mental disorder.

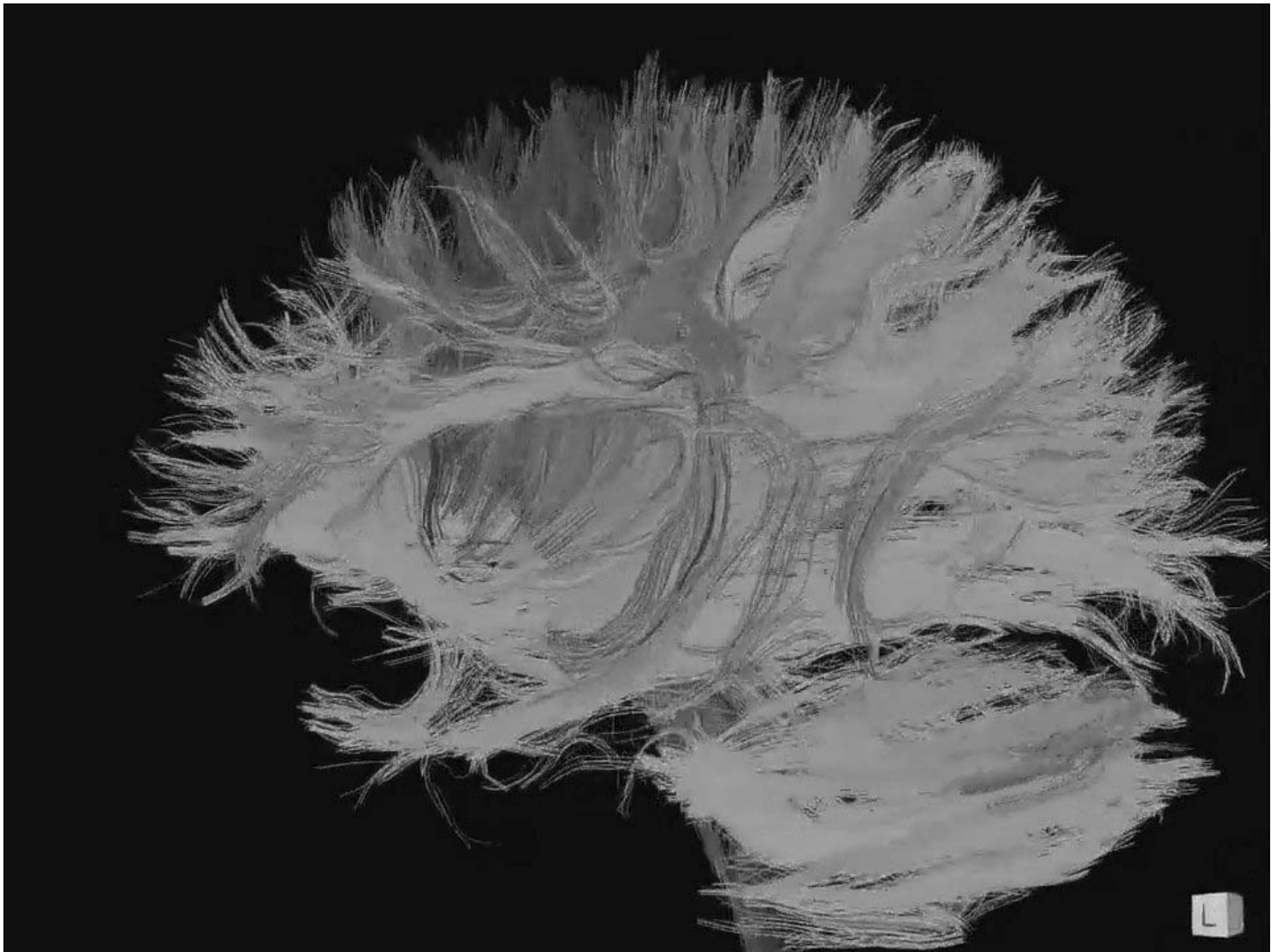
Other researchers not involved with the study are intrigued by these results.

"This is really interesting," said Alison Barth, a researcher and professor at Carnegie Mellon University who studies the brain. Barth says that previously, we haven't been able to see how synapses are changing in people's brains over time, and that this looks like it could allow us to do a study where we track those changes.

"Developing a PET sensor to detect the proteins that compose synapses is an innovative and promising idea," Forrest Collman, a researcher in the Human Cell Types group of the Allen Institute for Brain Science, told Tech Insider via email. Being able to do this is "hugely important," he said.

Collman explained that neuroscience researchers think synapses form "the physical basis of our mental life."

"When examining brains of those with mental disorders, synapse loss tends to be the most predictive measure of how much cognitive decline a person has experienced," he said, adding that that early detection of these changes could help us slow diseases before too much is lost.



The complexity of this structure is amazing.

*jgmarcelino/Wikimedia Commons*

## What's next

There are still a number of questions that need to be answered before these PET scans could be used to track patients' brains regularly.

"As a proof of principle, [the study] is reasonable," said Barth. "For diagnostic purposes, you need to get a good idea of the spread of your measurements in normal individuals." She explains that since each person's brain can vary by a good amount, you need to conduct these measurements in a large number of people to see how well this particular agent works and to see if it does reveal changes over time.

One potential challenge is dealing with other factors that may cause the levels of the synapse-identifying protein to rise or fall over time, Collman explained. He also pointed out that these results would be best confirmed by comparing these scans to autopsy results, something that can't happen until the scans are conducted in a much larger population.

For now, Collman said, this approach would be most helpful for measuring changes in an individual. A single screening of a brain wouldn't provide as much information for now, due to individual variation.

Barth and Collman both also wondered whether it might be possible to refine the scan so that it could identify not only the presence of synapses but also different types of synapses, of which there may be thousands. Different diseases may affect different components of the brain, and the more specific we can get, the more accurate our understanding of these diseases will be.

The team behind the study said that the next step is to get a large number of PET centers working with this scan to determine how sensitive it is and how it can be best refined. This will help make sure this approach is tested with a large number of people, and it will give them the ability to refine the radioactive liquid used for the scan. As that is improved by experiments at different centers (as is normal for PET scans, Carson explained), they'll be able to get more and more information.

Still, the potential of tracking synaptic change in live patients with mental disorders of any kind is enormous.

Carson said that for the first time, it seems they've actually been able to measure density in living brains "as if we had gone in and popped out a piece of tissue."

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