A study using a new PET imaging agent finds that measures of tau protein in the brain more closely track cognitive decline due to Alzheimer's compared with long-studied measures of amyloid beta. The image on the left shows the average amount of tau buildup in brains of cognitively normal people. The image on the right shows the average amount in the brains of people with mild Alzheimer's symptoms.

Scientists have shown that measures of the tau protein inside nerve cells better predict symptoms of dementia than the protein amyloid beta, where research has largely focused.

The study by Washington University School of Medicine was published Wednesday in the journal *Science Translational Medicine*, a journal addressing international health issues.
While Alzheimer's research has focused on the accumulation of amyloid beta, scientists recently began to pay closer attention to tau. The tau protein has long been associated with disease, but it has not been studied as thoroughly because researchers had no way to effectively view and measure tau.

Using a new imaging agent that binds to the tau protein and makes it visible in positron emission tomography (PET) scans, Washington University scientists found that measures of tau are better markers of cognitive decline associated with Alzheimer's than measures of amyloid beta.

A buildup of plaque and dysfunctional proteins in the brain are hallmarks of Alzheimer's disease, the sixth leading cause of death in the U.S. The accumulation of amyloid beta, a sticky protein fragment in the brain, leads to the destruction of nerve cells.

“Our work and that of others has shown that elevated levels of amyloid beta are the earliest markers of developing Alzheimer's disease,” said neurologist and senior study author Dr. Beau Ances. “But in the earliest stages of Alzheimer's disease, even with amyloid buildup, many patients are cognitively normal, meaning their memory and thought processes are intact. What we suspect is that amyloid changes first and then tau, and it's the combination of both that tips the patient from being asymptomatic to showing mild cognitive impairment.”

The study was small — 36 cognitively normal patients were compared to 10 with mild Alzheimer's — but showed the new imaging agent is an important tool for understanding the progression of the disease and pinpointing which parts of the brain are gathering abnormal proteins. “Our new study suggests you can tolerate a certain amount of tau clumped in the hippocampus,” Ances said, “but once it starts spreading to other areas, especially the lateral and parietal lobes, that seems to be the tipping point.”

Researchers now have the tools necessary to test the effectiveness of therapies against the buildup of both amyloid beta and tau, he said. “We want to develop ways to make earlier diagnosis and then design trials to test drugs against amyloid buildup and against tau buildup,” Ances said. “While we currently can't prevent or cure Alzheimer's disease, delaying the onset of symptoms by 10 to 15 years would make a huge difference to our patients, to their families and caregivers, and to the global economy.”

About 5.2 million Americans have Alzheimer's, and that number is expected to nearly triple by 2050 without the development of medical breakthroughs to prevent or cure the disease. This year, Alzheimer's and other dementias will cost the nation $236 billion.