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Novel radiotracer shines new light on the brains of Alzheimer's disease patients

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A trial of a novel radioactive compound readily and safely distinguished the brains of Alzheimer's disease patients from healthy volunteers on brain scans and opens the doors to making such imaging available beyond facilities that can manufacture their own radioactive compounds. The results, reported by a Johns Hopkins team in the June *Journal of Nuclear Medicine,* could lead to better ways to distinguish Alzheimer's from other types of dementia, track disease progression and develop new therapeutics to fight the memory-ravaging disease.

Previously, the only way to peer into the brains of Alzheimer's patients was through autopsy or the use of another radioactive compound used in scans, or radiotracer, known as Pittsburgh compound or PIB. PIB is drawn to a protein known as beta-amyloid, which accumulates abnormally in the brains of Alzheimer's patients. However, PIB has a half-life of only 20 minutes, meaning that half of the substance degenerates every 20 minutes after it is made. Consequently, PIB's use is possible only at a few hospitals or academic medical centers with facilities to manufacture it since this compound degenerates so rapidly.

To solve this conundrum, Dean F. Wong, M.D., Ph.D., a professor of radiology and psychiatry at the Johns Hopkins University School of Medicine, and his colleagues looked to a new radiotracer known as 18F-AV-45 (also known as florbetapir F18). This compound, based on the radioactive isotope fluorine-18, is drawn to beta-amyloid like PIB. However, unlike PIB, florbetapir has a half-life of about 110 minutes, greatly increasing its ability to be transported significant distances away

from manufacturing facilities.

Testing the new compound for the first time in humans, Wong and his colleagues recruited 26 volunteers — 11 previously diagnosed with Alzheimer's disease, and 15 healthy subjects of similar age who performed normally on cognitive tests. Each of these volunteers received an injection of florbetapir, then received a PET scan of their brains. The brain scans, acquired over a 90-minute period, allowed the researchers to see the uptake of florbetapir in the brain over time.

Florbetapir had significantly heavier accumulation in the Alzheimer's patients' brains compared to the healthy volunteers, collecting in brain regions expected to be high in beta-amyloid deposits based on previous research. The results in AD patients were readily distinguishable from those of healthy subjects by 30 minutes after injection, and the differences continued for up to at least 90 minutes after injection of florbetapir. None of the AD patients or healthy volunteers suffered any ill effects from florbetapir and showed normal vital signs, electrocardiograms and blood-work after the scan.

"We could easily tell apart the two groups of patients. Those without Alzheimer's disease retained much less of the compound, and those with Alzheimer's disease retained much more of it," Wong says. "This is the first time we've been able to get results like this with a compound that can travel beyond the confines of a major academic medical center to the majority of the U.S. population."

Wong adds that florbetapir's portability could lead to numerous applications for this compound. For example, though Alzheimer's disease can usually be diagnosed from neurocognitive tests, imaging with florbetapir could help settle tricky cases in which patients might have other forms of dementia instead. The compound may also be useful in future studies designed to help solve current medical mysteries, such as

which patients are most likely to progress from mild cognitive impairment to full-blown Alzheimer's disease.

Florbetapir may also be useful in trials of new experimental Alzheimer's therapeutics to measure their success, a purpose for which this compound is already being used on a limited basis, Wong says.

More information: www.hopkinsradiology.org/Nuclear%20Medicine/Index.html

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