National Institutes for
Quantum and Radiological Science and Technology

PRESS RELEASE

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Brain imaging for early detection of Alzheimer's disease and other dementias

Researchers at QST in Japan have developed a new imaging agent that allows early detection and differentiation of various types of dementias, including Alzheimer's disease and frontotemporal lobar degeneration disorders

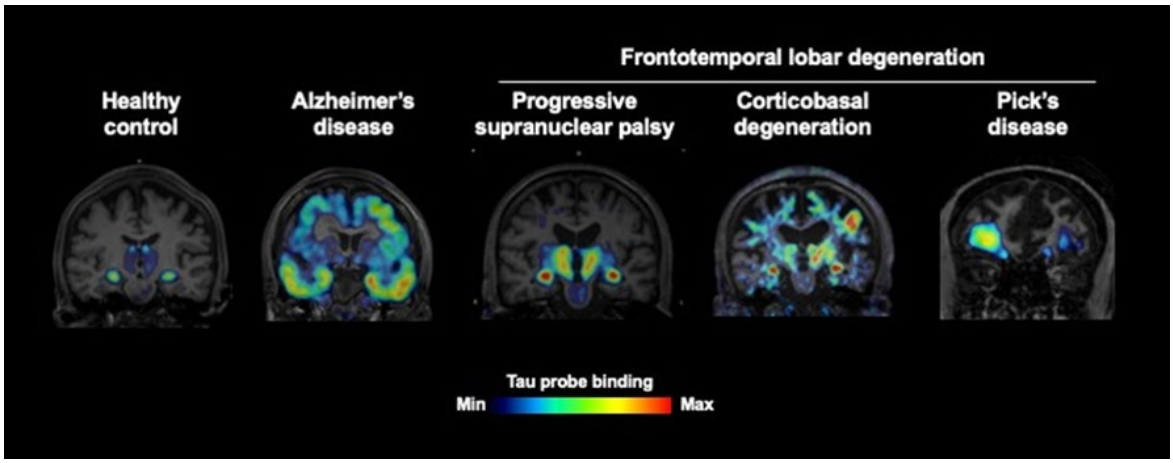
Chiba, Japan — As aging populations rise globally, so too do the numbers of people with dementia. Now more than ever, precise diagnosis and differentiation of Alzheimer's disease and other dementing illnesses is critical. A team of researchers led by Makoto Higuchi at the National Institutes for Quantum and Radiological Science and Technology (QST) in Japan has developed a new imaging probe that can be used for positron emission tomography (PET) of brain pathologies characteristic of these diseases, allowing identification of different types of dementias from an early stage.

Alzheimer's disease and a large subset of frontotemporal lobar degeneration disorders (FTLD) are characterized by the accumulation of abnormal fibrils composed of tau proteins in the brain. Without examining the brain pathology, accurate diagnosis of these dementias is difficult, especially at the earliest stage because they share many overlapping cognitive and behavioral symptoms. Within the brain, each of these dementias is associated with the deposition of tau aggregates with a specific structure in unique locations.

PET imaging of tau pathologies in the brains of living subjects could therefore be both clinically and scientifically of great utility. "Although good PET probes exist for Alzheimer's disease, they do not work well for other types of tau-positive dementias," says Higuchi.

PET scans rely on the ability of a radioligand to bind to the target molecules, in this case, the fibrillary form of tau proteins. Tau assemblies in Alzheimer's disease and FTLD syndromes are structurally distinct from each other, and most currently available PET imaging agents have strong reactivity with tau deposits of AD type but not FTLD type. The QST research group previously generated a PET probe, PBB3, for capturing diverse tau pathologies, but it did not yield high contrast for tau aggregates in the brain due to its propensity to metabolic degradations after systemic injection. In their new study, the researchers at QST modified the PBB3 probe so that it was less susceptible to being metabolized.

The new probe, PM-PBB3, is a longer-lasting and stable probe that produces strong signals in the brain, enabling visualization of pathological tau protein species with high contrast and dynamic range. The probe was tested in patients with Alzheimer's disease and FTLD disorders, including progressive supranuclear palsy, corticobasal degeneration, and Pick's disease, providing the first demonstration of high-contrast imaging of tau accumulations in all these dementing illnesses. According to the distribution of tau depositions detected by PM-PBB3, the researchers could identify and classify the tau-positive dementias even at an early clinical stage of the disease, and the accuracy of this test was proven by performing biopsy and autopsy in several cases who had undergone PET scans.



PET imaging with ^{18}F-PM-PBB3 (^{18}F-APN-1607)

Because tau pathology begins before cognitive symptoms appear, the new probe should facilitate the diagnosis of dementias at preclinical and prodromal stages. "In hospitals equipped with PET scanners, our new radioligand could be practically useful for early diagnosis or accurate typing of various dementias," says the first author Kenji Tagai, also from QST. "Additionally, PET with PM-PBB3 could be used for nonclinical and clinical

tests for candidate anti-tau therapeutics, as this technology is applicable to animal models and humans."

The researchers now hope to use their imaging technique as a reference for the development of a blood-based biomarker for dementias, which would allow efficient and inexpensive early detection at regular health check-ups, followed by more precise and detailed workups using PET.

Paper

"High-Contrast In Vivo Imaging of Tau Pathologies in Alzheimer's and Non-Alzheimer's Disease Tauopathies"

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About QST

The National Institutes for Quantum and Radiological Science and Technology (QST) was established in April 2016 to promote quantum science and technology in a comprehensive and integrated manner. The new organization was formed from the merger of the National Institute of Radiological Sciences (NIRS) with certain operations that were previously undertaken by the Japan Atomic Energy Agency (JAEA).
QST's mission is to raise the level of quantum and radiological sciences and technologies through its commitment to research and development into quantum science and technology, the effect of radiation on humans, radiation emergency medicine, and the medical use of radiation.
To ensure that research and development delivers significant academic, social and economic impacts, and to maximize benefits from global innovation, QST is striving to establish world-leading research and development platforms, explore new fields, and serve as a center for radiation protection and radiation emergency medicine.

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