# The Mental Note

FROM THE HARVARD AGING BRAIN STUDY STAFF

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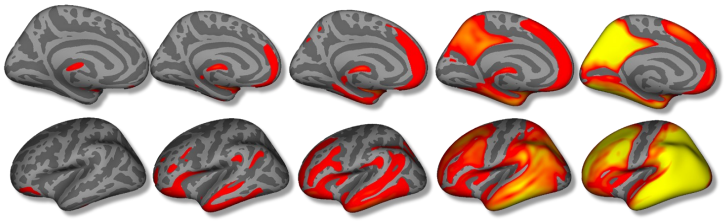
## The advent of PET scanning over the last century

Alois Alzheimer first characterized Alzheimer's Disease (AD) in 1906. Dr. Alzheimer's 55-year old patient passed away after experiencing paranoia, confusion, and severe memory loss. When Dr. Alzheimer performed an autopsy, he identified two abnormalities: tangled clumps of nerve fibers and patches of disintegrated nerve-cell branches in the brain. We now know these distinctive characteristics as amyloid plaques and tau tangles.

For decades, doctors could only diagnose their patients with AD by performing autopsies. More recently, researchers have studied the brain tissue of people at different stages of AD in order to understand how amyloid and tau accumulation contribute to AD symptoms, such as memory loss. Despite decades of research, we still have many questions about how these proteins affect memory decline. For example, autopsy studies reveal that approximately one-third of individuals with pathologic levels of amyloid and tau do not display memory problems before death.

In 2004, AD researchers started using Positron Emission Tomography (PET) to study brain changes in living individuals. PET imaging has improved our understanding of how the brain changes during healthy aging and Alzheimer's disease. Three types of PET scans are commonly used in AD research: Amyloid, Tau and FDG. Each tracer binds to specific proteins in the living brain, and enables researchers to visualize and measure the location and quantity of each protein, thus advancing scientific research. More information on the specific tracers can be found on the back of this page. Currently, amyloid and tau PET scans are used for research purposes only. FDG is used for various clinical purposes to study brain function and metabolism.

Research suggests that amyloid plaques start accumulating in the brain as many as 20 to 30 years before AD symptoms arise. PET imaging is helping researchers understand what is happening in the brain during this preclinical stage, before a person develops AD symptoms. In the future, doctors may have the potential to detect signs of AD risk very early and intervene, or possibly, prevent the disease entirely.



From the laboratory of Dr. Keith Johnson: these PET images show levels of tau tangles in different parts of the brain. These figures are created by combining data from many participants' scans across various research studies. Grey = healthy brain with no tau. Red = low levels of tau. Yellow = higher levels of tau.

## Featured Staff: Keith A. Johnson

Keith Johnson is a Professor of Radiology and Neurology at the Harvard Medical School. He is also a Radiologist and the Director of the Molecular Neuroimaging in the Division of Nuclear Medicine and Molecular Imaging (Department of Radiology) at the Massachusetts General Hospital (MGH). Dr. Johnson also serves as an associate physician and staff neurologist in the Center for Brain Mind Medicine at the Brigham and Women's Hospital as well as a Clinical Associate in Neurology at the MGH.

Dr. Johnson is the co-director of the Neuroimaging Program of the Massachusetts Alzheimer's Disease Research Center and the co-principal investigator of the **H**arvard **A**ging **B**rain **S**tudy. His major research interests include early diagnosis and treatment monitoring of neurodegenerative diseases, including Alzheimer's Disease, Parkinson's disease and dementia with Lewy bodies.

## AMYLOID

**Amyloid-PET** scans use radioactive tracers such as Pittsburgh Compound B and Florbetapir-F18, which bind to amyloid plaques throughout a living individual's brain to detect the amount and distribution of the protein amyloid-beta. Advances in amyloid-PET scans have enabled scientists to better understand the relationship between amyloid-beta and the aging brain and how this protein might be involved in Alzheimer's disease-related cognitive and behavioral changes.

## TAU

In the last decade, there have been significant efforts to develop selective tau tracers that are sensitive to neurofibrillary tangles, another brain change associated with AD. Since tau accumulates inside brain cells, scientists took longer to develop a way to measure this protein. In HABS **Tau-PET** scans, we use a tracer called T807 (AV1451) to measure the amount of tau accumulation in a living brain. Unlike amyloid, which tends to accumulate in the very earliest stages of AD, even before there are any noticeable cognitive changes, tau is more closely related to symptom onset and diagnosis.

## FDG

The brain consumes glucose, a process known as glucose metabolism, to produce energy. **FDG** stands for fluorodeoxyglucose, which is used to assess brain glucose metabolism. Recent research has linked brain glucose metabolism to AD, in that it appears to differ by ApoE genotype. The *ApoE4* gene, which is the most common risk factor for AD, is associated with reduced glucose uptake by cells as well as impaired metabolism. The *ApoE2* gene, which is protective against AD, is associated with increased glucose uptake and increased metabolism. Impaired glucose metabolism is a component of Alzheimer's disease, and clinicians will sometimes use this scan outside of the research environment to aid an AD diagnosis.

## Interested in Learning What We Have Accomplished With PET Data?


Sign Up for the first
Food for Thought lecture

Friday January 25th, 2019 at
11:00 am

*presented by:*
*Heidi Jacobs, Ph.D.*

Dr. Jacobs' current main interests are focused on understanding the disease mechanisms of Alzheimer's disease by investigating the interaction of biomarkers and other brain changes, such as structural and functional connectivity, and how these mechanisms relate to cognitive changes.

THE HARVARD AGING BRAIN STUDY, MASSACHUSETTS GENERAL HOSPITAL
149 13TH STREET CHARLESTOWN MA 02129
**Contact us!** HABS@MGH.HARVARD.EDU ● 617-643-5200

CONTRIBUTING WRITERS: EMILY KILPATRICK, BS,; MARTHA C. MUÑIZ, MA; KELSEY BIDDLE, BA; YAKEEL T. QUIROZ, PHD;
HABS CLINICAL CORE LEADER: DORENE M. RENTZ, PSY D;
HABS PRINCIPAL INVESTIGATORS: REISA A. SPERLING, MD; KEITH JOHNSON, MD