Understanding Memory Loss through Brain Imaging

IND
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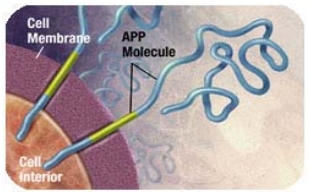
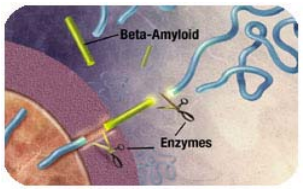
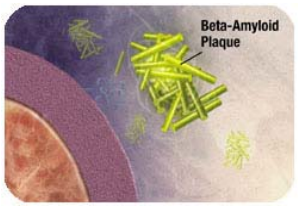
Among the most common questions posed by patients and families of patients with memory loss are: How can we determine the diagnosis? Is there a test to evaluate for Alzheimer's disease? Can we predict if the condition will progress? These questions highlight the need for a tool or marker to help define changes in the brain related to memory loss.

Over the past several years, researchers have been developing a brain imaging technique enabling us to measure changes in the brain that occur in Alzheimer's disease. It is now known that protein deposits in the brain (called beta-amyloid) occur in AD patients and may be at least partly responsible for neurodegeneration of brain cells, which produces memory loss (see Figure 1).

This imaging method targets and chemically tags beta-amyloid, a protein that







Beta-amyloid Plaques

- Amyloid precursor protein (APP) is the precursor to amyloid plaque.
- Enzymes cut the APP into fragments of protein, including beta-amyloid.
- Beta-amyloid fragments come together in clumps to form plaques.

Figure 1

What is IND?

The **Institute for Neurodegenerative Disorders (IND)** was formed in March 2001 as a registered non-profit 501(c)3 research institute that aims to advance research in Parkinson disease, Huntington disease and Alzheimer disease through clinical research and brain imaging. Operating in New Haven, CT, the Institute stands as a premier research facility for clinical trials and brain imaging research into neurologic disorders.

Our Mission

The mission of IND is to develop improved treatments, diagnostic tools and educational programs for neurologic disorders such as Parkinson disease, Huntington disease and Alzheimer disease.

For More Information

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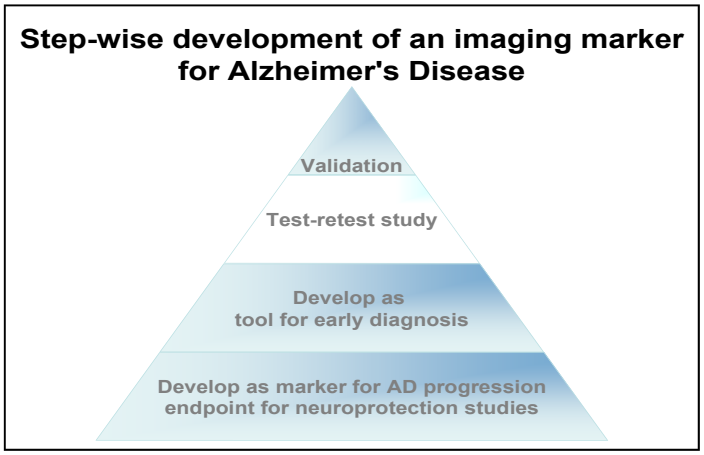

measures. Future studies of possible neuroprotective agents will require an objective marker, such as an imaging marker to evaluate and establish disease protection.

Mild Cognitive Impairment (MCI)

Perhaps the ultimate goal of imaging studies is to enable us to reliably identify and predict those individuals with mild changes in memory or MCI that will develop a worsening of symptoms and ultimately a diagnosis of Alzheimer's disease. While no medication has been clearly shown to prevent the onset of Alzheimer's disease, these imaging studies would prepare us to use one or more neuroprotective agents as they are developed. If imaging proves to be a useful early marker for Alzheimer disease in individuals carrying a diagnosis of mild cognitive impairment the studies will be expanded to include populations considered to be 'at risk' for Alzheimer's disease by virtue of family history.

While it remains too early to make clinical decisions about Alzheimer's disease based on beta-amyloid imaging alone, these imaging studies provide extremely useful information with regard to the diagnosis and natural history of Alzheimer's disease. Neurochemical brain imaging will continue to play an increasingly important role in assessing and defining future treatments for Alzheimer's disease.

is found in the brain of individuals with Alzheimer's disease. Imaging using single photon emission tomography (SPECT) enables us to determine the amount of beta-amyloid present in the brain. This imaging could serve as a tool to make a more accurate or definitive diagnosis and measure the progression of changes in the brain.

Imaging Methods

During the past decade, neurochemical imaging has emerged as a tool to help us understand the changes in the brain that my result in memory loss. Unlike MRI or CT scans which allow us to look at the brain structure, neurochemical imaging uses specific radioactively labeled ligands or tags to show abnormalities in the brain function. Specifically, these tags are tools that provide a window into the brain and enable us to evaluate abnormal deposits of proteins in individuals with Alzheimer's disease. These radioactively labeled ligands are visualized using Positron emission tomography (PET) or single photon emission tomography (SPECT) imaging.

Clarifying the Diagnosis in Memory Loss

The first question of a marker is whether it reliably distinguishes between subjects with Alzheimer's disease and those with other causes for memory loss. Several studies using beta-amyloid binding ligands suggest that this imaging technology can discriminate individuals with Alzheimer's disease from healthy subjects of similar age. The increase in beta-amyloid binding in patients with Alzheimer's

disease can be seen in Figure 2. Importantly the pattern of beta-amyloid deposits occurs in the brain regions most affected by Alzheimer's disease. This imaging pattern is important because it is consistent with the known changes that occur in the brain pathology from post-mortem studies.

Another important question is whether the amount of beta-amyloid protein detected in the brain reflects the severity of symptoms of memory loss. Studies are underway to evaluate if beta-amyloid imaging may serve as a marker for disease severity in Alzheimer's disease.

Measuring Disease Progression

A major goal of research is to develop therapies which slow or stop the progression of memory loss in Alzheimer's disease. An attractive therapeutic strategy to slow the progression is to prevent, reduce or reverse beta-amyloid deposition in the brain. Several small chemical compounds, made up of synthetic peptides and natural proteins have been described. These compounds inhibit beta-amyloid formation in animal models. The effect of these and other compounds now needs to be tested for safety in humans and the ability of these beta-amyloid inhibitors to halt the progression of Alzheimer's disease in humans needs to be evaluated.

The rate of Alzheimer's disease progression is variable and somewhat unpredictable. Several large clinical studies have followed cohorts of Alzheimer's patients for several years using memory and other cognitive tests, but these studies lack an objective measure of disease progression. Imaging studies provide the opportunity to evaluate patients from early to late in the disease using an objective measure of beta-amyloid deposition. Studies evaluating sequential beta-amyloid imaging scans obtained over time are underway to determine the expected rate of progression of beta-amyloid deposition in Alzheimer's disease over the course of the disease.

These studies of disease progression will provide important new insights into the onset and natural history of Alzheimer's disease. Imaging studies also provide a tool to objectively assess the affect of potential neuroprotective therapies on the deposition of beta-amyloid in Alzheimer's disease. Prior studies of potential neuroprotective agents have relied entirely on clinical

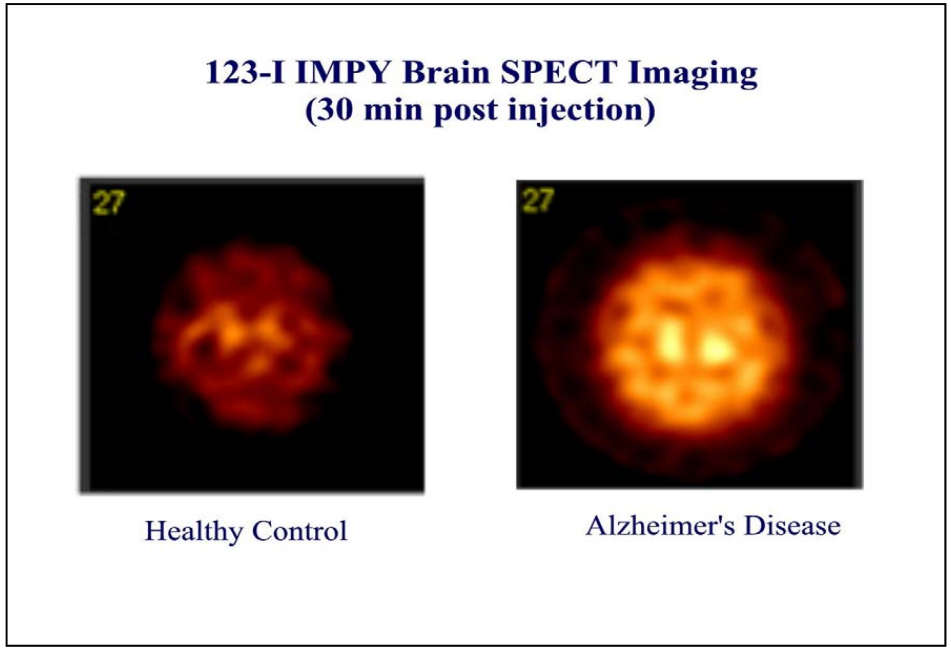

Figure 2