

## Chapter 23

# Neuroimaging in Alzheimer's Disease

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### ABSTRACT

*The diagnosis of Alzheimer's disease (AD) is often based on clinical and pathological data. Positron emission tomography (PET) using the tracer 18F-FDG revealed findings specific to AD-mainly the posterior part of the brain and the association cortices of the parietal and occipital lobes were affected by a reduction in glucose metabolism. Recent advances in the development of tracers for amyloid protein, which is the key protein in the pathogenesis of AD, enables the pattern of deposition of amyloid protein in the brain to be visualized. Various tracers have been introduced to visualize other aspects of AD pathology. Recent clinical interests on dementia have focused on the early detection of AD and variation of Parkinson's disease, namely dementia with Lewy body disease (DLB), because the earlier the diagnosis, the better the prognosis. The differential diagnosis of mild AD or mild cognitive impairment (MCI) as well as DLB has been studied using PET and MRI as part of the NIH's Alzheimer disease Neuroimaging initiative (ADNI). At present, many countries are participating in the ADNI, which is yielding promising results. This chapter's study will improve the development of new drugs for the treatment of dementia patients by enabling the evaluation of the effect and efficacy of those drugs.*

### INTRODUCTION

Various aspects of Alzheimer's disease (AD) have been investigated from a variety of research fields, including genetics, biochemistry, behavior and imaging. Neuroimages of AD patients have been obtained by positron emission tomography (PET)

using different tracers and magnetic resonance imaging (MRI). Recently, the AD neuroimaging initiative (ADNI) has been started in U.S.A., and the J-ADNI started two years ago in Japan. These imaging modalities are regarded as not only diagnostic biomarkers, but also as a tool to investigate the pathophysiology of the disease, such as inflammation and amyloid protein accumulation.

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## PET AND SPECT IMAGING

### Fluorine-18 Labeled Deoxyglucose (FDG)-PET

In the early 1980's, FDG-PET was applied to neuro-degenerative disorders to clarify the energy metabolism of the brain. AD showed a typical reduction in glucose metabolism by FDG-PET as well as in cerebral blood flow (CBF) and oxygen metabolism in the posterior association cortices (Fukuyama, Ogawa, Yamauchi, Yamaguchi, Kimura, Yonekura & Konishi, 1994). Statistical analysis demonstrated the reduction of metabolism and CBF in the posterior cingulate cortex and precuneus (Minoshima, Frey, Koeppe, Foster & Kuhl, 1995). This finding is also specific to the early phase of AD, which involved mild cognitive impairment (MCI) of the amnesic type. These observations have been confirmed by single photon emission CT (SPECT) and FDG-PET, and they were clearly shown using statistical image manipulations, such as 3D-SSP (Figure 1) or SPM.

Based on this background work, AD can be diagnosed easily using PET or SPECT combined

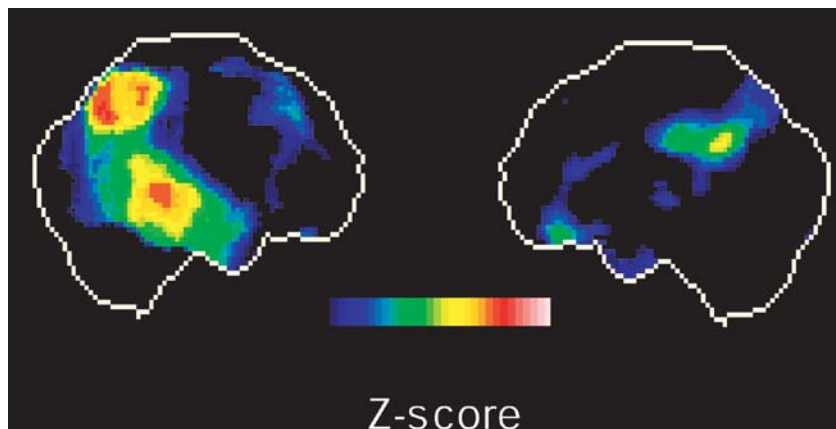
with clinical and psychological data. Because the functional state of the brain is damaged in several specific regions, this particular pattern of damage supports the correct diagnosis. These types of image analyses have been used in clinical trials for the early diagnosis on AD in studies performed all over the world.

## NEW TRACERS FOR AD DIAGNOSIS

### C11-Labeled PK11195 Imaging for Microglial Activation

McGeer et al. proposed that a mild inflammatory process was involved in the pathology of AD (Lee, Sparatore, Del Soldato, McGeer & McGeer, 2009). Their hypothesis was based upon the observation that the incidence of AD is relatively small in patients with rheumatoid arthritis who are administered aspirin compared with its frequency in the normal population and the pathology caused by activated microglial reactions in the affected brain. Based on that proposal, R. Banati attempted to visualize the activated microglia by PK11195 in

*Figure 1. CBF reduction in statistical images. The parietal and temporal lobes as well as the posterior cingulate cortex and precunes showed reduced CBF. These images were taken from statistical parametric mapping (Friston, Frith, Liddle & Frackowiak, 1991) and 3D-SSP (Minoshima, Frey, Koeppe, Foster & Kuhl, 1995). The use of these findings on SPECT CBF or FDG-PET makes the diagnosis of AD and MCI easy. The arrow indicates the posterior cingulate cortex and precuneus.*



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