VIII. 5. Voxel-Based Analysis of Cerebral Amyloid Deposition Using $[^{11}\text{C}]$BF-227 PET

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A PET study using $[^{11}\text{C}]$-labeled BF-227 successfully detected amyloid plaques in living Alzheimer’s disease (AD) patients. AD patients showed the preferential $[^{11}\text{C}]$BF-227 retention in the posterior neocortical region of the brain, which corresponded with an area containing a high density of neuritic plaques. In the previous studies, data analysis has been mainly based on region of interest (ROI) analysis. To eliminate any a priori hypothesis about ROI selection, we performed a voxel-based analysis of whole brain regions for the comparison between the groups. The purpose of this study is to understand the pattern of neocortical BF-227 uptake for early diagnosis of AD.

$[^{11}\text{C}]$BF-227 PET scans were performed in 12 normal healthy control subjects and 19 probable AD patients. AD patients were recruited through the Tohoku University Hospital Dementia Patients Registry. The diagnosis of AD was made according to the National Institute of Neurological and Communicative Diseases and Stroke/Alzheimer's Disease and Related Disorders Association (NINCDS–ADRDA) criteria.

Voxel-by-voxel comparisons between images from normal controls and AD patients were performed using SPM5 software. SUV summation images 20 to 40 min post injection were stereotaxically normalized using individual MR images into a standard space of Talairach and Tournoux. The normalized images were smoothed using a 12 mm×12 mm×12 mm Gaussian filter. The count of each voxel was normalized to the cerebellar ROI value. Images of AD patients were compared with those of aged normal controls for between-group analysis (P < 0.05 with false discovery rate (FDR) correction). For the
group analysis, a two sample t-test was used to detect differences between the groups.

We additionally created a Z score map by comparison with mean and standard deviation PET images of the aged normal controls for each voxel. A software program named the easy Z score imaging system (eZIS)\(^1\) was used for this analysis. Each PET SUV image of AD patients was compared with the mean and standard deviation (SD) of PET SUV images of 12 aged normal controls using voxel-by-voxel Z score analysis after voxel normalization to cerebellar ROI values; Z score = (\[control mean\]–\[individual value\])/(control SD). These Z score maps were displayed by projection with an averaged Z score of 14 mm thickness to surface rendering of the anatomically standardized MRI template.

SPM analysis of \[^{11}C\]BF-227 PET images demonstrated that patients with AD had significantly higher \[^{11}C\]BF-227 uptake in the neocortical region than aged normal controls (Fig. 1). Bilateral temporoparietal BF-227 uptake was evident in AD group. Compared to the lateral temporoparietal region, difference in the lateral frontal cortex was less evident. The Z-score maps of PET images were created by comparison with aged normal controls (Fig. 2). Most patients with AD showed a Z-score greater than 2 in the bilateral temporal and posterior cingulate cortices\(^2\).

\[^{11}C\]BF-227 PET can detect early A\(\beta\) load in the lateral temporal cortex of patients with AD. BF-227 would be less subjective to amyloid pathology during the process of aging since this probe is considered to bind selectively to dense A\(\beta\) plaques. Thus, \[^{11}C\]BF-227 PET offers unique information concerning AD pathology that cannot be obtained by other PET tracers.

References

Figure 1. Brain regions showing significantly higher uptake of $[^{11}]$C$\text{BF}$-227 in patients with AD.

Figure 2. Voxel-by-voxel Z-score analysis by comparison of $[^{11}]$C$\text{BF}$-227 PET images for 19 patients with AD with the mean and SD of PET images of the 12 aged normal controls.