

**Purpose:** Optimized Voxel based morphometry (VBM) has been increasingly applied to investigate differences in brain morphology between a group of patients and control subjects. VBM permits comparison of gray matter (GM) volume at voxel-level from the entire brain, thus is an efficient method for assessing regional differences. The purpose of this study was to assess the regional GM volume loss measured by VBM in Alzheimer's disease (AD) compared to controls, and to measure hippocampal volume using manually delineated volumetry and compare the results to VBM findings.

**Method and Materials:** Twenty-three AD (mean age  $70 \pm 8$ y; m/f= 7/16, Mini-Mental State Exam [MMSE]= 22.2) and 20 cognitively normal elderly control subjects (mean age  $69 \pm 4$ y; m/f= 10/10) were included in this study. The 20 sets of images were first normalized and create the probability maps for segmentation. Normalized hippocampal volume to the intracranial volume was compared between AD and control groups.

**Results:** The AD group had a lower GM %, and a higher CSF% compared to controls. The total intracranial volumes analyzed using SPM and our own ROITool program were very close ( $p < 0.0001$ ). The hippocampal volume of AD patients was significantly lower than that of controls ( $P < 0.001$ ). The region includes parahippocampal gyrus, cingulate, insula, frontal lobe and middle temporal complex. Despite the high significance in manual ROI analysis, hippocampus was not revealed in the VBM.

**Conclusions:** We found that the hippocampal volume in AD was significantly smaller than in controls using ROI-based volumetry. However, although our VBM results demonstrated that AD patients had a significant atrophy in middle temporal lobe, parahippocampus and insula, the hippocampus was not revealed. While VBM can be applied to assess global atrophy efficiently, manual volumetry is needed to study irregularly-shaped subcortical structures.