

Differential Gray and White Matter Losses in Different Brain Lobes in Alzheimer's Disease

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Objectives:

- To determine gray matter (GM) and white matter (WM) losses in the main brain lobes in AD and normal aging;
- To compare GM losses of lobes with hippocampal volume loss
- To determine the relationship of lobar GM losses with dementia severity

Methods:

- Thirty patients with AD and Twenty-seven cognitive normal (CN) subjects were studied; See **Table 1** for demographics;
- MRI scans included a T1 weighted volumetric MPRAGE sequence (1x1x1.5 mm³) and double spin echo (DSE) sequence (1x1x3 mm³)
- MRI data of each subject were classified into cortical gray matter (cGM), subcortical gray matter (sGM), white matter (WM), sulcal CSF (sCSF), ventricular CSF (vCSF) and white matter hyperintensity (WMH) using previously described segmentation software.¹ In addition, a mutual entropy driven nonlinear warping algorithm² was used to transform MPRAGE data of each subjects into a reference space that had the main brain lobes (frontal, parietal, temporal, occipital) labeled (**Figure 1**), yielding tissue segmentation by lobes. Volumes were calculated by summing the voxels.

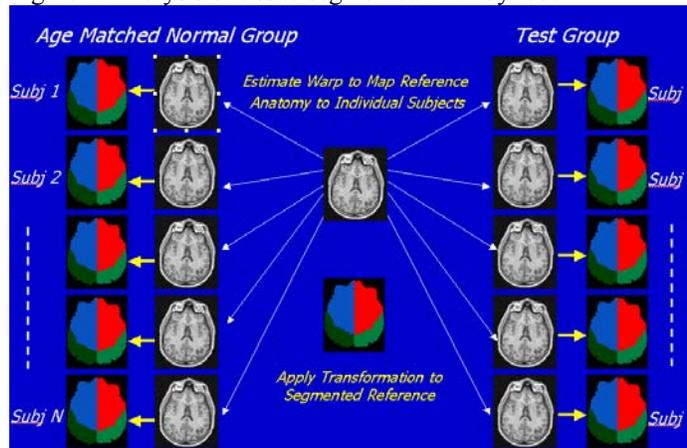
	No. (%F)	Age	MMSE
CN	27 (63%)	72 ± 8	29 ± 1
AD	30 (63%)	73 ± 6	22 ± 6

- Volume of the hippocampus was measured using high dimensional fluid transformations (SNT Inc., Boulder Co.).
- MANOVA, adjusted for age, was used to compare cGM and WM volume differences between AD and CN in each lobe. ANOVA, followed by Scheffe tests with adjustments for multiple comparisons was used to compare lobar GM losses with hippocampal volume losses in AD.

Results:

- **Figure 2** depicts differences between AD and controls of cGM volumes by lobes and hippocampal volume Compared to CN, AD had significant cGM losses in frontal (F[1,55] = 24, p < 0.001), parietal (F[1,55] = 17, p < 0.001), temporal (F[1,55] = 37, p < 0.001), and occipital lobe (F[1,55] = 7, p < 0.05). Furthermore, compared to occipital cGM, AD had significantly higher cGM loss in the frontal (F[1,58] = 16, p < 0.01), parietal (F[1,58] = 18, p = 0.01) and temporal lobe (F[1,58] = 28, p = 0.01). Differences

Figure 1. Analysis of tissue segmented MRI by lobe



between frontal, parietal and temporal cGM losses were not significant. In addition, AD patients had smaller hippocampi than CN subjects ($F[1,55] = 40, p < 0.001$). Furthermore, the hippocampal losses were significantly greater than cGM losses in AD (all $p < 0.01$).

- **Figure 3** depicts differences between AD and CN of WM by lobes. AD had significant WM losses in the temporal ($F[1,54] = 11, p < 0.01$) and occipital ($F[1,54] = 5, p = 0.03$) lobe compared to controls. WM losses in the frontal ($F[1,54] = 4, p = 0.06$) and parietal lobes ($F[1,54] = 4, p = 0.06$) of AD were a trend.
- Dementia severity (as measured with Mini-Mental State Examination) correlated with hippocampal and cGM losses of frontal, parietal and temporal lobes (all $p < 0.01$), but not of occipital lobe.

Conclusion:

- cGM and WM losses in AD occurred in frontal, parietal, temporal and occipital lobes, which is consistent with previous segmentation studies^{3,4}
- Hippocampal loss exceeded lobar cGM losses in AD, consistent with the theory that AD pathology involves initially the hippocampus before spreading to the cortex.
- Assessment of atrophy in different lobes, in addition to hippocampal atrophy, might aid diagnosis of AD and help monitoring treatment response, once medication becomes available.

Reference:

1. Tanabe JL et al. AJNR 1997; 18:115-123.
2. Studholme, C., D.L.G. Hill, and D.J. Hawkes. Pattern Recognition, 1999; 32: 71-86.
3. Kidron D et al. Neurology 1997;49:1504-1512.
4. Rusinek H et al. Radiology 1991; 178:109-114.

Figure 2. Losses of cGM and hippocampus in AD (■), relative to CN (■=100%)

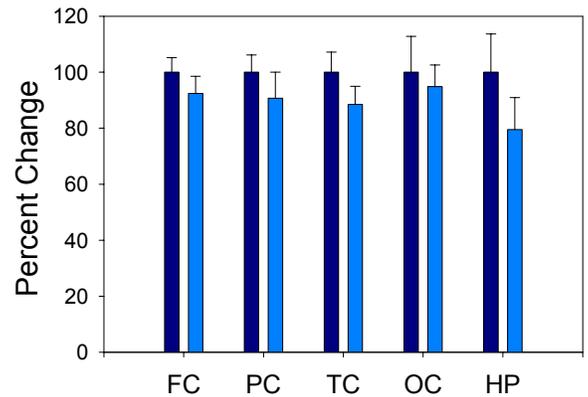


Figure 3. Losses of WM in AD (■), relative to CN (■=100%)

