Regional Pattern of Medial Temporal Lobe Atrophy in Mild Alzheimer's Disease Compared with Mild Vascular Dementia and Normal Aging

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Purpose

Medial temporal lobe structures (MTL), including hippocampus, parahippocampal gyrus (PHG), and amygdala and related structures, have been reported to be relevant to human memory [1]. Subjects with vascular dementia (VaD) also present significant deficits in memory. Yet, the specificity of the structure and function of MTL in AD has not been fully investigated when relative to VaD. MTL structures are reported to be involved earliest and most extensively in the pathology of AD [2]. These data provide a rationale for quantitative MRI-based MTL volumetric measurement. However, the extent of atrophy and the specificity of MTL regional measures in mild AD when compared to mild VaD is not well established. The present study was designed, firstly to compare the MRI-based volumetry of MTL regional structures among mild AD, mild VaD and healthy controls, and secondly using ROC curve analysis, to investigate the difference in extent of MTL regional atrophy in mild AD.

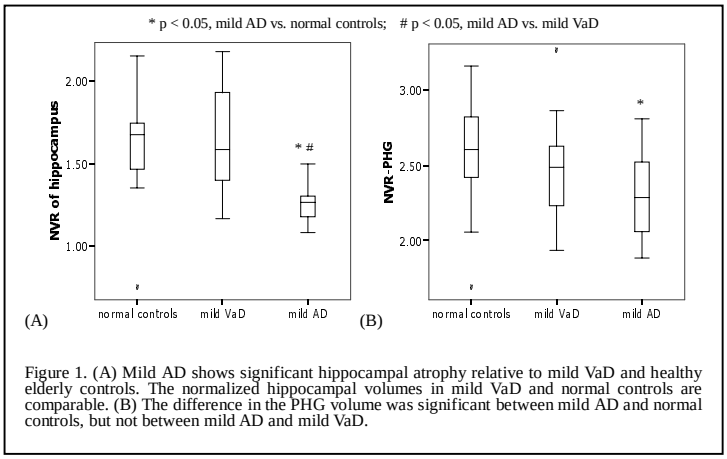

Figure 1. (A) Mild AD shows significant hippocampal atrophy relative to mild VaD and healthy elderly controls. The normalized hippocampal volumes in mild VaD and normal controls are comparable. (B) The difference in the PHG volume was significant between mild AD and normal controls, but not between mild AD and mild VaD.

Methods

Fourteen patients with mild AD (65 ± 10 years), 10 patients with mild VaD (64 ± 7 years) and 31 age-matched healthy elderly controls (64 ± 7 years) participated in this study. All subjects provided their informed consent prior to entering the study. All scans were performed on a 1.5-Tesla Siemens Magnetom MRI Scanner (Siemens Medical, Germany). Spin echo sequence was used to acquire the oblique coronal T1-weighted images (T1WI). The slices were perpendicular to the long axis of hippocampus (TR/TE = 500ms/15ms, matrix 256 x 256, slice thickness = 5mm, no gap). The oblique coronal T1WI covered the hippocampus, amygdala, and PHG. On the oblique coronal T1WI, the volumes of hippocampus, amygdala, and PHG were obtained as described previously [3]. Briefly, an experienced investigator (intrarater reliability ICC = 0.98) obtained the ROIs of hippocampus, amygdala and PHG and calculated the volumes with an in-built program. The normalized volumetric ratio (NVR) to intracranial volume (ICV) was used for analysis. In addition to between-group comparison of NVRs with ANOVA, with the method described by Hanley et al [4, 5], we analyzed the area under receiver operating characteristic (ROC) curves (AUC) to directly compare the extent of regional atrophy of hippocampus, amygdala, and PHG in mild AD when comparing to mild VaD and normal controls.

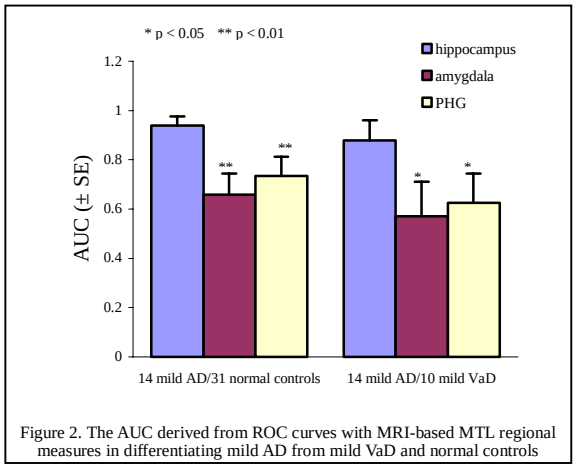

Figure 2. The AUC derived from ROC curves with MRI-based MTL regional measures in differentiating mild AD from mild VaD and normal controls

Results

We observed significant hippocampal atrophy in mild AD group relative to mild VaD and normal controls ($p < 0.001$, Fig. 1A). Mild AD also exhibited significant PHG atrophy compared to normal controls ($p < 0.05$, Fig. 1B). The normalized hippocampal and PHG volumes in mild VaD and normal control groups were comparable. The group difference in the normalized amygdala volume did not reach a significant level ($p > 0.05$).

We calculated the AUC for the hippocampus, amygdala, and PHG when comparing mild AD, mild VaD and normal controls. As shown in Fig. 2, the AUC of the hippocampus was greater than amygdala and PHG for the comparison between mild AD and normal controls ($p < 0.01$), and between mild AD and mild VaD ($p < 0.05$), suggesting more pronounced hippocampal atrophy than amygdala and PHG in mild AD.

Discussion

In the present study, we investigated differences in regional patterns of MTL atrophy in mild AD patients compared to mild VaD and healthy elderly controls within the framework of ROC analysis. First, we assessed the group differences for the size of hippocampus, amygdala, and PHG among three groups. We found significant reductions of normalized hippocampal and PHG volumes in mild AD relative to normal controls. These observations agree with previous reports. The normalized hippocampal volume was also smaller in mild AD when compared to mild VaD. This adds some evidence that mild AD and VaD probably have different neural mechanisms accounting for the memory loss in these two different cerebral pathological conditions. MTL might play different roles in the development of AD and VaD.

Using AUC analysis, we found that the hippocampal atrophy was more pronounced than atrophy of amygdala and PHG in mild AD compared to normal controls and mild VaD. This further support that hippocampus plays a key role in the development of mild AD. The results imply that the atrophy of amygdala and PHG might be consequent to the advanced degeneration of hippocampus in AD. These findings warrant further investigations on the temporal cascade of MTL regional atrophy in the progression from normal aging to mild AD via mild cognitive impairment.

References

1. Petersen RC, Jack CR, Jr., Xu YC, et al. Memory and MRI-based hippocampal volumes in aging and AD. Neurology 2000; 54:581-7.
2. Armstrong RA. beta-Amyloid (A beta) deposition in elderly non-demented patients and patients with Alzheimer's disease. Neurosci Lett 1994; 178:59-62.
3. Wang H, Shu L, Xie J, Zhang H, Zhang D. Diagnostic utility of neuropsychological performance and quantitative MRI-based measurement in Alzheimer's disease. Alzheimer Dis Assoc Disord 2004; 18:163-170.
4. Hanley JA, Mcneil BJ. The meaning and use of the area under a receiver operating characteristic (ROC) curve. Radiology 1982; 143:29-36.
5. Hanley JA, Mcneil BJ. A method of comparing the areas under receiver operating characteristic curves derived from the same cases. Radiology 1983; 148:839-843.