Multivariate analysis on hemispheric asymmetry alterations in differentiating mild cognitive impairment and Alzheimer's disease from healthy aging

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Introduction

Converging evidences have shown that hemispheric asymmetry alters in healthy aging and neurological disorders with impairment of structural and functional integrity [1]. Independent analysis of the morphological variates including volume, cortical thickness, surface area, and curvature index has manifested discrepancies in the outcome [2-4]. As changes in any individual variate may alter the other, it is necessary to explore the hemispheric asymmetry based on the compositive effect of the morphological indices. In this study, we developed a method to collectively explore relevant variates for a more comprehensive morphological assessment on brain hemispheric asymmetry alterations in subjects of healthy aging, mild cognitive impairment (MCI) converters, and Alzheimer's disease (AD).

Materials and methods

151 subjects were grouped as "healthy young" (n=35, average age=30.1±10.4 years, male=18, female=17), "healthy elderly" (n=44, average age=75.48±6.34, male=23, female=21), "MCI converters" who had progressed to AD latter (n=33, average age=75.44±7.31, male=27, female=12), and "AD patients" (n=39, average age=77.88±7.51, male=17, female=16). T1 weighted images of the entire brain were obtained for each subject with the MPRAGE sequence. Subjects of the healthy young group were scanned on a 3T Scanner (Siemens Trio, Erlangen, Germany) with a high-resolution 32-channel head coil. Typical imaging parameters were: TR/TE=1900/2.53ms, FA=9°, FOV=256×256, in plane resolution=1mm×1mm×1mm. Data of the other subjects were retrieved from the Alzheimer's disease Neuroimaging Initiative (ADNI) database (http://www.loni.ucla.edu/ADNI).

Cerebral cortex and the corresponding white matter (WM) of each subject were parcellated into gyral-based regions of interest (ROIs) for each hemisphere using FreeSurfer (http://surfer.nmr.mgh.harvard.edu/). Surface area, mean curvature index, cortical thickness, and subjacent WM volume were calculated from the constructed surface on each ROI. MANCOVA was performed on the combination of the four variates using SPSS 17.0 (SPSS Inc., Chicago, IL, USA) to compare the shape characteristics between left and right hemispheres. Subject gender and age were introduced as covariates. Regions of significant asymmetry (SARs) were identified as $p<0.05$. The lateralization index of each significant region was defined as $LI=\Sigma_i (L_i-R_i)/(L_i+R_i)$, where L_i and R_i were the mean value of the left and right hemisphere for the ith variate. $LI>0$ indicates a leftward asymmetry, and $LI<0$ a rightward asymmetry. Multiple-comparison correction was performed to control false discovery rate (FDR) at a significance level of 0.05.

Results

Multivariate asymmetry analysis of the four groups was shown in Figure 1. The number of SARs significantly reduced from young to AD ($p<0.05$). The healthy elderly lost asymmetries in the superior frontal gyrus, the supramarginal gyrus and the insula cortex, in comparison with the healthy young group. The SARs almost matched between the healthy elderly and the MCI group, except for the entorhinal cortex. The number of SARs further reduced as MCI advanced to AD in which profound asymmetries disappeared in the caudal middle frontal gyrus, the calcarine sulcus, the middle temporal gyrus, the parahippocampal gyrus, and the temporal pole. Compared with that of healthy elderly, *LI* reversed in regions of parahippocampal gyrus, entorhinal cortex, and temporal pole in MCI converters, while lateralization disappeared in the aforementioned regions in AD patients.

Conclusion

Preservation, reduction or reverse of hemispheric asymmetries were detected in healthy aging, MCI and AD patients compared with healthy young. Hemispheric asymmetry significantly reduced over normal aging in brain regions involving working memory, language processing, emotion, and the regularization of body homeostasis. Further decline of hemispheric asymmetry occurred in regions associated with memory encoding and retrieval, distance contemplation, recognition of known face, social and emotional processing and behavior with the onset of AD. Alteration of asymmetry in the entorhinal cortex was manifested as an early sign as MCI advanced to AD. Compared with healthy elderly, lateralization of MCI converters featured reverse rather than disappearance in AD patients in regions associated with episodic and spatial memory, emotion, and attention.

Compositive morphological markers of brain asymmetry derived in this study were region-specific, which may provide useful information for disease diagnosis, differentiation and monitoring of MCI and AD.

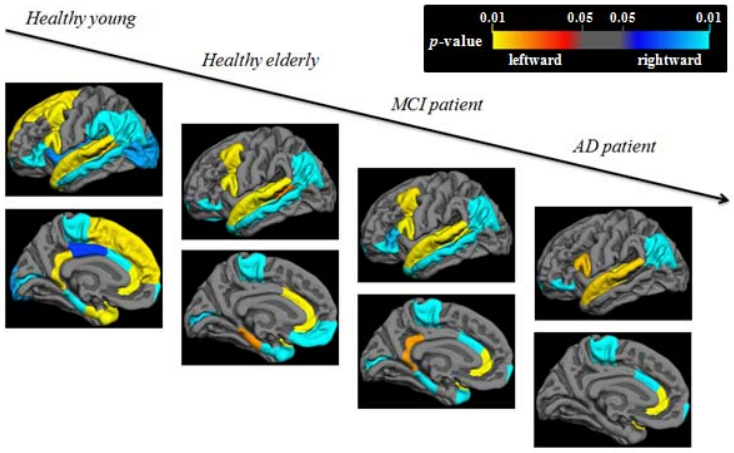

Figure 1. MANCOVA results of the four groups. The number of significantly asymmetric regions reduced from young to AD ($p<0.05$). Reverse of lateralization was detected in MCI converters compared with healthy elderly.

Reference

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