Regional Changes of Cortical Mean Diffusivity with Ageing and Alzheimer Disease after Correction of Partial Volume Effects

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Introduction

DTI-derived metrics, mean diffusivity (MD), can be used to effectively quantify cortical architecture. Normal ageing is featured with higher cortical MD [1]. In addition, comparison of cortical MD between normal old control and patients with mild cognitive impairment (MCI) which is associated with an increased risk of progression to Alzheimer disease (AD) shows that higher MD was found in temporal lobe [2]. However, partial volume effects (PVE) which cause the averaging of signals from cortex and cerebrospinal fluid (CSF) usually lead to bias of the measured MD. So far few studies have been conducted to measure the regional MD at gyral or lobe level due to difficulty of parcellating the cortex into gyral level directly from DTI-derived contrasts. In this paper, we developed a novel technology to measure the regional cortical MD while reducing the bias caused by PVE. Our method integrates cortical parcellation based on T1 weighted images from freesurfer, fast marching to transfer the cortical labeling to MD map and CSF contamination model to eliminate CSF effects. This method was applied to study the effects to regional MD changes of normal ageing and AD. High resolution DTI and MPRAGE data of 39 subjects (13 young adults, 17 normal old controls and 9 AD) were acquired for this study. In contrast to conventional understanding of MD in normal ageing, significant increase of MD was only found in frontal lobe after PVE correction rather than all over the cortex before PVE correction. Our analysis also indicated no significant MD difference between old control and AD before and after PVE correction.

Methods

Subjects and data acquisition: 39 subjects including 13 young controls (age: 22.3±4.4), 17 normal old controls (age: 65.7±7.2) and 9 AD (age: 68.9±5.6) participated this study. AD subjects had been diagnosed by NINCDS/ADRDA criteria [3] as probable AD. A 3T Philips Achieva MR system was used. DTI data were acquired using a single-shot EPI with SENSE. DWI parameters were: FOV=224/224/143mm, in plane imaging matrix = 112× 112, axial slice thickness = 2.2 mm, 30 independent diffusion-weighted directions with b-value = 1000 sec/mm^2, TE=97ms, TR=7.6s. To increase signal noise ratio (SNR), two repetitions was performed. T1-weighted (MPRAGE) image with FOV=256/256/160mm and resolution 1x1x1mm was also acquired.

Parcellation of cortical MD into gyral level: As demonstrated in Fig. 1, segmenting the cortex of MD map into gyral level integrates freesurfer and fast marching. All MD values were measured in native DTI space to reduce the measurement bias caused by interpolation during image transformation. Fig. 1a and 1b show the b0 map and gray matter (GM) segmentation of b0 with SPM. With freesurfer, the cortex from T1-weighted image was segmented and parcellated into 70 gyral labeling as shown in Fig. 1g and 1h. Linear affine transformation was applied to reorient and transform T1 weighted image and the parcellated cortical ribbon into DTI. Irregular small yet significant offsets between cortical ribbon from transformed T1-weighted image (d) and GM segmentation of b0 map (b) were all over the cortex, due to cortical segmentation from images of two different contrasts (T1 and b0) and distortion of DTI space caused by B0-inhomgeneity. This offset is corrected by fast marching with GM segmentation of b0 map (b) as a template. In this way, the parcellated cortex in MD (Fig. 1f) is perfectly aligned with MD map (Fig. 1e). *PVE correction:* CSF contamination model $S(b)=S(0)\cdot[\lambda_{app\text{-}gm}\exp(-bD_{gm})+\lambda_{app\text{-}csf}\exp(-bD_{csf})]$ was used where S(b) and S(0) are diffusion weighted and non-weighted signals, $\lambda_{app\text{-}gm}$ and $\lambda_{app\text{-}csf}$ are the signal fraction weightings of GM and CSF compartments [4]. In the result below, corrected MD is D_{gm} in the equation (1) of PVE correction model.

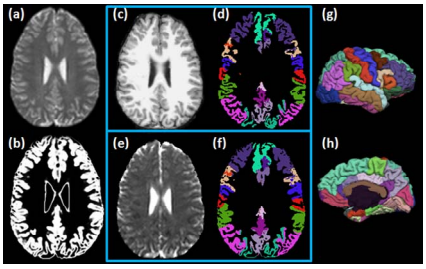

Fig. 1: Axial slice of b0 map (a), GM segmentation of b0 map (b), the same axial slice of T1 weighted image after affine transformation to native DTI space (c), the gyral parcellation map (d) from T1 weighted image by freesurfer and completely aligned with T1 weighted image, MD map (e), the elastically morphed gyral parcellation map (f) completely aligned with MD map. (g) and (h) show the gyral parcellation in 3D with T1 weighted image for anatomical guidance. (d), (f), (g) and (h) use same color scheme to represent gyral labeling.

Results

Regional cortical MD change with normal ageing: From Fig. 2a and 2c, comparison between MD values of old and young controls indicates statistically (FDR-corrected) significantly higher MD measurements at almost all cortical compartments except left temporal lobe, if there is no PVE correction. However, after PVE correction, statistically higher (FDR-corrected) MD can be only found in frontal lobe cortex of both hemispheres (Fig. 2b and 2d).

Regional cortical MD difference of AD versus old control and young control: From all panels of Fig. 2, there is no significant difference of MD values of AD compared to those of old control before and after PVE correction. The pattern of uncorrected MD or corrected MD difference between AD and young control is similar to that between old control and young control. *Effects of PVE to MD measurements:* It is clear that PVE caused higher MD values for all groups shown in Fig. 2a and 2c, compared to those after correction, shown in Fig. 2b and 2d. The MD measurement of young controls was less biased by PVE, compared to those of old controls or AD patients (Fig. 2a-2d).

Conclusion and discussion

We developed a novel approach including freesurfer parcellation, fast marching and CSF contamination model to measure regional cortical MD values. It has a great potential to reveal the unbiased regional cortical MD changes with ageing or AD affection. Our results of uncorrected cortical MD for young controls (Fig. 2a,2c) agree with previously reported MD profile across the cortex, namely highest MD at parietal lobe cortex and lowest MD at temporal lobe cortex [5]. Corrected MD measurements indicate that only frontal lobe cortex has significant MD difference between young and old control and between young control and AD patients. Due to cortical thinning with ageing and AD affection, CSF takes more space in the cortical sulcal area, leading to extra high uncorrected MD values in these two groups. In contrast to previous finding on MCI [2], we could not find any significant difference of either uncorrected MD or corrected MD at temporal cortex between AD and old control. Instead, lower corrected MD values at temporal cortex were found in AD than control (Fig. 2b, 2d). Histological slides (data not shown) suggest the sticky beta-amyloid in AD cortex may play a role to reduce MD. Fast marching was used to conduct elastic morphing. This is a key step to ensure the accuracy of our MD measurements. Direct application of freesurfer cortical parcellation to MD map in DTI space after affine registration lead to as high as averaged 70% offset. Especially the mismatched voxels in CSF or outside of the brain will lead to big bias of MD measurements.

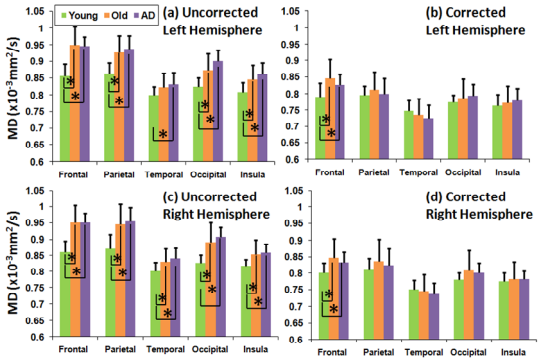

Fig. 2 Regional MD measurement of left (a,b) and right (c,d) hemispheres before (a,c) and after (b,d) PVE correction. Asterisks show statistical difference after FDR correction.

References: [1] Abe, O et al (2008) Neurobiology of Aging 29: 102. [2] Ray, KM et al (2006) Radiology 241:197. [3] McKhann, G et al (1984) Neurology 34: 939. [4] Koo, B et al (2009) Neuroimage 44:136. [5] Liu, T et al (2006) Neuroimage 31: 51. **Acknowledgement:** This study is sponsored by NIH/NIA P30AG12300, NIH RR014982 and NIH EB009545.