Shape Analysis of the Corpus Callosum in Alzheimer's disease

Li Shuyu, Pu Fang, He Xiangqi, Deyu Li
Department of Bioengineeringline
Beihang University
Beijing, P. R. China
shuyuli@buaa.edu.cn

Li Shuyu, Jiang Tianzi
National Laboratory of Pattern Recognition
Institute of Automation, CAS
Beijing, P. R. China
jiangtz@nlpr.ia.ac.cn

Abstract—**Alzheimer' disease (AD) is a neurodegeneratetive disease characterized by progressive dementia. The corpus callosum (CC) is the biggest association fiber in the cerebral hemisphere. Many structural neuroimaging studies have found the atrophy of the CC. Most studies focused on analyzing the areas of subdivisions of CC. But the shape change of the CC may reflect a midline neurodevelopmental or neurodegenerative abnormalities. The purpose of this study was to investigate the abnormal shape changes of CC in the AD compared to the normal aging. The two measurements, area and radial distance, were extracted to characterize the regional and local atrophy of CC in AD. The results showed that the CC of AD appeared global atrophy, but the atrophy of posterior part was more evident than that of other parts. The lower edge showed more extension than the upper edge of the CC in AD. These findings confirmed the pathology characteristic in AD.**

Keywords- shape analysis, corpus callosum, Alzheimer's disease

I. INTRODUCTION

Alzheimer's disease (AD) is a neurodegenerative disease characterized by progressive dementia. Many electrophysiological and neuroimaging studies have suggested functional disconnections between the cerebral hemisphere in AD [1]. The corpus callosum (CC) is the major white matter tract that crosses the interhemispheric fissure in the human brain. Several in vivo brain morphometric studies using magnetic resonance imaging (MRI) have shown the atrophy of CC [2,3,4]. Such callosal abnormatlities are thought to be due mainly to Wallerian degeneration, secondary to AD-related pathological changes in the cortical association areas interconnected by CC fibers [5,6,7].

Most MRI studies of the CC in AD were performed using voxel-based morphometry (VBM) methods and region-of-interest (ROI) analysis. VBM [8] is an automated unbiased analysis of the differences in tissue concentration throughout the brain on structural MRI scans. Recently, it has been used to examine AD-related changes in white matter density [9]. However, some AD-related studies using VBM suggested that the atrophy of callosal white matter tracts probably reflected an interface shift due to the adjacent enlarged lateral ventricle [10,11,12]. Compared with VBM, ROI analysis based on manual segmentation could precisely outline the regions in anatomy and was represented the gold standard in the detection of atrophic changes. Many ROI-based MRI studies on CC have shown more severe abnormalities in the rostrum and splenium of CC [2,4,13]. Most of such studies focused on analyzing the areas of subdivisions of the CC. However, the shape change of the CC may reflect a midline neurodevelopmental or neurodegenerative abnormalities. Despite Thompson et al. [14] have reported the CC shape alterations in association with the diagnosis using high-dimensional warping techniques, investigations of CC shape abnormalities have been scarce.

In this study, we firstly analyzed the regional area atrophy of CC in AD. And then we used radial distance to represent the shape of CC, and conducted a detailed assessment of CC shape changes in 19 AD patients compared to 20 healthy controls matched for age, gender and educational level. These findings confirmed the pathology characteristic in AD.

II. MATERIALS AND METHODS

A. Subjects

Nineteen AD patients and twenty healthy controls volunteers participated in this study. All patients with AD were subject to neurologic, neuropsychologic and psychiatric examinations. The examination results fulfilled the National Institute of Neurological and Communicative Disorders and Stroke-ADRDA work group criteria [15]. All subjects' cognitive status had been evaluated using the Mini-Mental State Exam (MMSE) [16]. The MMSE scores of AD were 18.9 ± 3.9, those of healthy controls were 29.5 ± 0.9. Subjects were excluded if they presented with symptoms of other neuropsychiatric disorders that could confound the diagnosis of dementia of the Alzheimer type. All subjects were right-handed, and all gave informed consent before being scanned. The details of the ages, genders, education levels and MMSE scores of the two groups are depicted in Table 1.

TABLE I.   DEMOGRAPHICS AND CLINICAL FINDINGS

	AD(n=19)	Controls(n=20)	P value
Sex (F/M)	9/10	10/10	>0.95*
Age (mean±SD)	72.6±6.9	70.7±6.4	0.38♦
Education (mean±SD)	11.3±4.0	10.9±4.5	0.76♦
MMSE score (mean±SD)	18.9±3.9	29.5±0.9	<0.0001♦

MMSE, Mini-Mental State Examination; *, the P value was obtained by Pearson $\chi 2$ two-tailed test, with continuity correction for n < 5; ♦, the P value was obtained by a two-sample two-tailed t test.

B. Image acquisition

All scans were acquired on a 1.5 T GE Signa Twin Speed scanner. A standard head coil was used for radio frequency (RF) transmission and reception of the nuclear magnetic resonance (NMR) signal. Head motion was minimized with restraining foam pads offered by the manufacturer. High-resolution 3-D T1-weighted images were obtained using the following parameters: TR = 11.3 ms; TE = 4.2 ms; FOV = 24 24cm; matrix = 256 224; slice thickness = 1.8 mm; NEX = 2.

C. Image analysis

1) Image preprocessin.

The images were preprocessed using statistical parametric mapping (SPM2) software [17]. Initially, images were spatially normalized to the standard SPM T1-MRI template, using linear 12-parameter affine transformations. Then each spatially normalized image was scaled to an isotropic voxel resolution of 1mmolution of 1mm.

The sagittal slice best representing the midsagittal plane (few or absent grey matter and a visible septum pellucidum) was selected. Manual CC dileanation was performed using the manual segmentation function of MRIcro software (http://www.sph.sc.edu/comd/rorden/mricro.html). Boundaries of the CC were manually outlined by one rater who was blind to the diagnosis. Pixels of high signal intensity were assigned to the CC. To evaluate the measurement reproducibility, 10 images were independently outlined by a second rater. The correlation coefficient was 0.92.

2) Area analysis of CC subregions

Then a rectangle was constructed round the CC and divided into five parts of the same size as suggested by Weis et al. [18]. The five subsections called CC1-CC5 correspond approximately to the five anatomical subdivisions of the CC (CC1 = rostrum and genu; CC2 = rostral body; CC3 = midbody; CC4 = isthmus; CC5 = splenium) as shown in Figure 1. Then the area of each subsection was calculated.
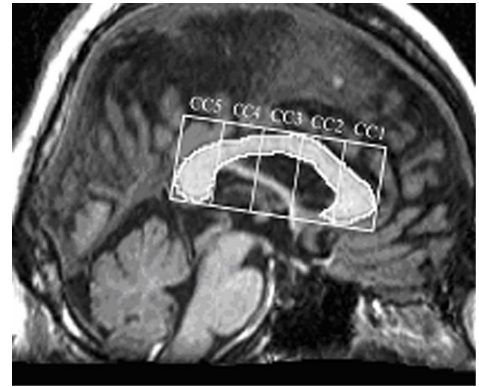

Figure 1.   The manual outlining of callosal segments

3) Shape analysis of CC

We explored the radial distance to represent the shape of CC. The center of the lower edge of the rectangle was considered as the origin. The radial distance was defined as the distance between each point on the contour of CC and the origin. Then, we drawn one ray from the origin each one degree (the lower edge of the rectangle was thought as 0 degree, that is, the horizontal direction). Thus there were two intersections between each radial and the contours of CC. The detailed is shown in Figure 2. We arranged the radial distances of all intersections in clockwise sequence. Thus, each shape of CC was represented by one feature vector consisted of the arrayed radial distance.
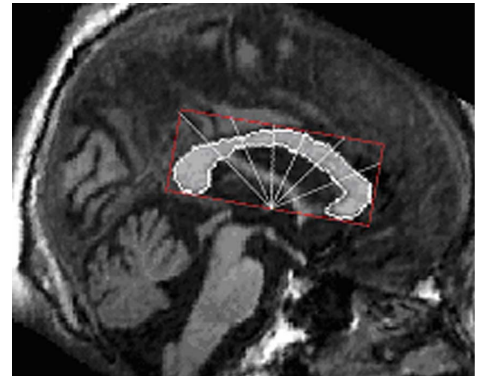

Figure 2.   The radial distance for each point on the contour of CC

D. Statistical analysiss

The two-sample t-test was used to detect regional area and local radial distances differences between the AD and controls groups. The statistical results from the radial distance was overlapped onto the average CC template.

III.   RESULTS

A. Differences of five sub-regions areas

The five subdivisions of the CC showed significantly smaller in patients with AD relative to healthy controls. The comparisons of regional callosal area are shown in Table 2. The p value was obtained by a two-sample two-tailed t test.

TABLE II.   DIFFERENCES OF FIVE SUB-REGIONS AREAS

	AD(mm^2)	NC(mm^2)	Differences	
	Area (mean±std)	Area (mean±std)	t	p
CC1	215.82±40.15	244.67±28.30	-2.594	0.0136
CC2	85.24±19.68	107.90±16.01	-3.917	0.00038
CC3	91.59±18.94	113.38±23.88	-3.061	0.00416
CC4	110.18±30.75	133.10±30.96	-2.276	0.02889
CC5	209.59±33.34	237.10±25.28	-2.894	0.00643

B. Differences of radial distances

The statistical results are shown in the average boundary of the CC. The significance was represented by different color. The warmer colors (i.e., orange to red) represented the outward variations of the upper boundary of CC, while the cooler colors (i.e., blue to purple) represented the outward variations of the lower boundary of CC. From Figure 3, the posterior regions of the CC showed significantly outward expansion in AD patients compared to healthy controls. But the lower edge showed more extension than the upper edge of the CC in AD. So the posterior regions of the CC demonstrated the significant atrophy in AD. These results were in accordance with previous ROI, VBM and DTI studies. Moreover, the result showed that there was a upper bending pattern of the CC in AD, which was similar to the study by Thompson et al.[19].
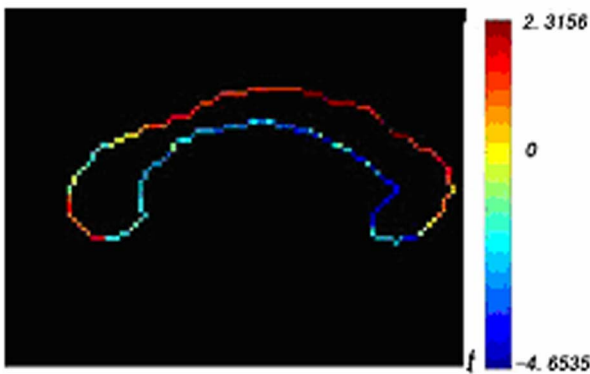

Figure 3.   Shape abnormal pattern of CC in AD

IV.   DISCUSSION

In this paper, we examined the regional area and local radial distances differences between the AD and controls groups. Compared with the healthy controls, the five subdivisions of the CC showed significantly smaller in patients with AD. In addition, the posterior regions of the CC showed significantly outward expansion in AD patients compared to healthy controls. But the lower edge showed more extension than the upper edge of the CC in AD. So the posterior regions of the CC demonstrated the significant atrophy in AD.

The CC is the major white matter tract that crosses the interhemispheric fissure in the human brain. An anatomically-specific relationship has been observed in some studies [2,4,20] between putative fiber loss in callosal regions and the dynamic progression of cortical and lobar atrophy characteristic of AD. Severe and regionally-selective area loss and focal shape inflection at the isthmus observed in our study may reflect disease-related disruption of the commissural system connecting bilateral temporal and parietal cortical zones, since these regions are known to be at risk for early metabolic dysfunction, perfusion deficits and selective neuronal loss in AD [21]. These finding on the abnormalities of the posterior regions of the CC could also provide the structural basis for the functional disconnections of homologous regions. For example, Horwitz et al [22] and Azari et al. [23] have consistently found weaker functional neocortical interactions in mild to moderate AD patients, especially between frontal association and both parietal association and paralimbic areas using PET. Our results can be further supported by previous diffusion tensor imaging (DTI) studies. Rose et al. [24] have found a significant reduction in the structural integrity of the white matter tracts in the splenium of AD patients. Moreover, the findings in shape inflection of CC in AD may be associated with temporo-parietal neuronal loss, the early perfusion and cognitive performance deficits in AD.

Our results on regional area atrophy and shape inflection were accordance with the previous studies. They further confirmed the pathology characteristic in AD. These methods may also be applied in other psychiatry diseases.

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