A Study of Corpus Callosum Size and Shape in Early Alzheimer's Disease

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Introduction

The corpus callosum (CC) is the largest fiber bundle connecting the two cerebral hemispheres. Atrophy of the CC may lead to functional disability because of reduced inter-hemispheric integration. Therefore, CC has been examined extensively for indications of pathology in various disorders including Alzheimer's disease (AD). Almost all previous studies of CC in AD have been concerned with the size of its mid-sagittal cross-sectional area (CCA). The aim of this study was to examine the CC *shape* in AD using *circularity* (CIR) as a descriptive parameter. CIR which is defined as $4\pi\times\text{Area}/\text{Perimeter}^2$ reflects not only area changes due to CC atrophy but also changes in the CC perimeter due to deformation which may be a consequence of the general age- or disease-related atrophic process in the brain. Thus, we hypothesized that CIR may be a more sensitive indicator of AD progression than CCA. We tested this hypothesis by measuring the CIR and CCA on structural scans from the Open Access Series of Imaging Studies (OASIS) MRI database. Our CC segmentations and corresponding CCA and CIR measurements are publicly available at www.nitrc.org/projects/art.

Methods

MRI volumes: The OASIS structural MRI scans are 3D sagittal T1-weighted volumes of matrix size: 256×256×128 and voxel size: 1×1×1.25 mm^3. Each volume is the post registration average of 3 or 4 independently acquired MP-RAGE scans with TR: 9.7 ms; TE: 4.0 ms; TI: 20 ms; TD: 200 ms; and flip angle: 10˚; obtained using a 1.5 Tesla Siemens Vision scanner (Erlangen, Germany). Subjects: We analyzed scans from *all* subjects in the OASIS cross-sectional database aged 60 years or above classified as normal controls (NC; n=98; M/F=26/72) with a clinical dementia rating (CDR) scale of zero; patients clinically diagnosed with very mild AD (AD-VM; n=70; M/F=31/39; CDR=0.5); or with mild AD (AD-M; n=28; M/F=9/19; CDR=1). CC Segmentation: We used a fully automated method to find the mid-sagittal plane (MSP) of the MRI volumes to bring the head yaw and roll angles as close as possible to zero. In addition, the anterior commissure (AP) and posterior commissure (PC) were located on the MSP using a fully automated model-based method. Using this information, the original MRI volume was re-sliced to obtain a single 2D image of matrix size: 512×512 and pixel size: 0.5×0.5 mm^2 representing the true AC-PC aligned MSP (Figure 1). Using *a priori* information a rectangular CC search region was indentified on the MSP as shown in Figure 1. Finally, a multi-atlas model-based segmentation method using the Automatic Registration Toolbox (ART) non-linear registration algorithm was used to locate the CC within the search region as shown in Figure 1. Our serial implementation of the entire segmentation process with 38 atlases takes less than one minute on a Linux workstation with 2.4 GHz clock speed. Statistical analysis: Two-way factorial analysis of covariance (ANCOVA) was performed using the SPSS 15.0 for Windows software with sex (F or M) and diagnostic group (NC, AD-VM, or AD-M) as fixed between-subject factors, age and *intracranial* capacity as covariates, and CCA or CIR as the dependent variable. Post-hoc pairwise tests were planned to ascertain any group differences. Statistical significance was tested at the level of $\alpha=0.05$ (two-tailed).

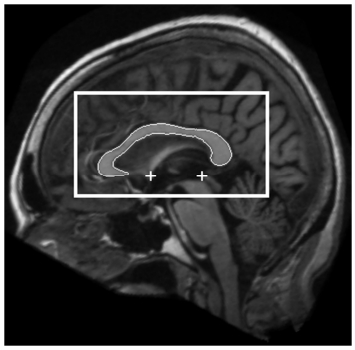

Figure 1: Automatically detected mid-sagittal slice, AC/PC landmarks, and rectangular CC search region.

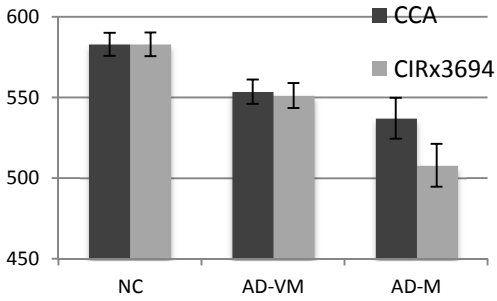

Figure 2: Mean (±Std. Error) CCA and CIR for the three diagnostic groups. 3694 is an arbitrary scaling factor used to allow side-by-side display of CCA and CIR.

Results

CCA: The marginal CCA means (adjusted for age and intracranial capacity) of the three diagnostic groups are shown in Fig. 2. CCA decreases with dementia severity. Post-hoc pairwise comparisons showed a significance difference between the marginal means of the NC and AD-VM groups ($p=0.005$), and the NC and AD-M groups ($p=0.002$). However, there was no statistically significant difference between the AD-VM and AD-M groups ($p=0.266$). CIR: The corrected CIR means of the three diagnostic groups are shown in Fig. 2. CIR decreases with dementia severity. Post-hoc pairwise comparisons showed a significance difference between the corrected means of the NC and AD-VM groups ($p=0.004$); NC and AD-M groups ($p<10^{-5}$); and AD-VM and AD-M groups ($p=0.006$). Both CIR and CCA showed statistically significant linear relationships with age and intracranial capacity.

Discussion and Conclusions

This study for the first time examined the circularity of the CC in AD alongside its size. Our analysis indicates that: (a) both CIR and CCA decrease with age; (b) CIR decreases and CCA increases with intracranial capacity; (c) the CIR is reduced and CCA is larger in females; and (d) CIR is more sensitive than CCA in distinguishing between the three groups of NC, AD-VM, and AD-M, thus, it appears to be a better measure for tracking AD progression. CC circularity could be used as an objective measure for evaluating the efficacy of treatments that aim to arrest the progression AD.