Measuring Fractional Anisotropy of the Corpus Callosum Using Diffusion Tensor Imaging: Mid-Sagittal versus Axial Imaging Planes

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Objective: Many diffusion tensor imaging (DTI) studies of the corpus callosum (CC) have been performed with a relatively thick slice thickness in the axial plane, which may result in underestimating the fractional anisotropy (FA) of the CC due to a partial volume effect. We hypothesized that the FA of the CC can be more accurately measured by using mid-sagittal DTI. We compared the FA values of the CC between the axial and mid-sagittal DTI.

Materials and Methods: Fourteen healthy volunteers underwent MRI at 3.0 T. DTI was performed in both the mid-sagittal and axial planes. One 5-mm mid-sagittal image and twenty-five 2-mm axial images were obtained for the CC. The five regions of interest (ROIs) that included the prefrontal (I), premotor and supplementary motor (II), motor (III), sensory (IV) and parietal, temporal and occipital regions (V) were drawn along the border of the CC on each sagittal FA map. The FA values obtained from each region were compared between the two sagittal maps.

Results: The FA values of all the regions, except for region V, were significantly increased on the mid-sagittal imaging. The FA values in region IV were significantly underestimated on the mid-sagittal image from the axial imaging, compared with those in the regions I and V (p = 0.037 and p = 0.001, respectively).

Conclusion: The FA values of the CC were significantly higher on the mid-sagittal DTI than those on the axial DTI in regions I-IV, and particularly in the region IV. Mid-sagittal DTI may provide more accurate FA values of the CC than can the axial DTI, and mid-sagittal DTI may be more desirable for studies that compare between patients and healthy subjects.

Index terms:
Corpus callosum
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The corpus callosum is by far the largest white matter tract in the human brain. Due to its structural characteristics, many studies have focused on detecting the morphological changes that occur in the corpus callosum in various disorders (1–3). With the recent advent of diffusion tensor imaging (DTI), many DTI studies have been conducted to detect alterations in the white matter's integrity, and particularly in the corpus callosum (4–8).

Many comparative studies of the corpus callosum that examined the differences between patients and healthy subjects have been performed using DTI, and these have shownd different results for the fractional anisotropy (FA) of the corpus callosum in the healthy subjects. Most of the axial DTI studies showed that the highest FA was in the splenium, the next highest was in the genu and the lowest was in the body. However, a few studies have suggested that the FA in the genu is higher than that in the splenium (9, 10). Interestingly, the FA in the body of the corpus callosum was highest in the coronal DTI studies (11–14).

In most of the previous studies, the DTI has been obtained in the axial plane with a

slice thickness more than or equal to 2 mm. The body of the corpus callosum usually parallels the anterior-posterior commissure (AC-PC) line. Moreover, the width of the posterior midbody or isthmus is frequently lower than that of the other subregions in the sagittal plane, with a minimum width of 3.2 mm (15). Therefore, the partial volume effect with axial DTI may hamper accurately measuring the FA of the corpus callosum. We hypothesized that the FA of the corpus callosum can be more accurately measured using mid-sagittal DTI, rather than using axial DTI, and so the FA in the posterior midbody or isthmus may be different from that reported in the previous axial DTI studies. The purpose of this study was to compare the FA values for the corpus callosum of healthy subjects who underwent both axial and mid-sagittal DTI.

MATERIALS AND METHODS

Subjects

Fourteen healthy volunteers (7 males and 7 females), ranging in age from 25 to 35 years (mean age: 29.1 years), were enrolled in this study. All of them were right-handed. Any subjects with a brain abnormality detected by MRI were excluded from this study. This study was approved by our medical center's institutional review board. All the volunteers gave us their informed written consent.

MR Imaging

All the volunteers underwent MRI at 3.0 T (Intera Achieva, Philips Medical Systems, Best, the Netherlands) with using an eight-channel sensitivity-encoding (SENSE) head coil. Both the axial and mid-sagittal DTI were performed using single-shot spin echo-echo planar imaging. The axial images were obtained parallel to the AC-PC line. The parameters for axial DTI were as follows: a SENSE factor of 2, a matrix of 128×128 (in plane resolution: 1.72 mm $\times$ 1.72 mm), a bandwidth of 1534.6 Hz, a field of view of 220 mm, a slice thickness of 2 mm without gap, a repetition time of 5,000/an echo time of 60 ms, one signal acquired, 45 different diffusion gradient directions, b = 1,000 s/mm^2 and an acquisition time of 245 seconds. The parameters for mid-sagittal DTI were as follows: a SENSE factor of 3, a matrix of 256×256 (in plane resolution: 0.86 mm $\times$ 0.86 mm), a bandwidth of 768 Hz, a field of view of 220 mm, a slice thickness of 5 mm, a repetition time of 5,000/an echo time of 76 ms, the number of excitations 4, 45 different diffusion gradient directions, b = 1,000 s/mm^2 and an acquisition time of 372 seconds. The slabs for flow compensation (5 cm in thickness) were located below and posterior to the corpus callosum on the sagittal plane in order to reduce the artifacts from vascular pulsation. One 5-mm mid-sagittal image and twenty-five 2-mm axial images were obtained for the corpus callosum. All the axial images were resliced into a 256×256 in-plane dimension with isotropic voxels ($0.86 \times 0.86 \times 0.86$) with using a trilinear interpolation method.

Mid-sagittal DTI at 3.0 T may be more hampered by susceptibility artifacts and geometric distortion than the axial DTI. This may be reduced by using a higher SENSE factor. Therefore, we used a higher SENSE factor in the mid-sagittal DTI. However, a higher SENSE factor reduces the signal-to-noise ratio (SNR), which may cause overestimation of the FA (16). Therefore, the SNR for the mid-sagittal DTI should be set higher than or equal to that for axial DTI. It may be difficult to set the SNR of mid-sagittal DTI equal to that of axial DTI. Therefore, we performed mid-sagittal DTI with a higher number of excitations than those of axial DTI in order to obtain a higher SNR for the mid-sagittal DTI. The SNR was calculated by the following formula:

$$\text{SNR} \propto (\text{pixel volume}) \sqrt{\frac{Ny \times NEX}{BW \times R}}$$

where Ny is the matrix, NEX is the number of acquisitions, BW is the bandwidth and R is the reduction factor. We calculated the SNR of each imaging prior to obtaining the DTI in order to get a higher SNR for the mid-sagittal DTI than for the axial DTI. After acquisition of the DTI, the actual SNR was measured in the b=0 image of each DTI by using the following formula:

SNR = Signal intensity of the splenium/Standard deviation of air

Data Analysis

The FA maps were generated using the software installed on the workstation (Version, 1.1.5). The resliced axial images were viewed in the mid-sagittal plane using in-house Windows-based software (Neuroan version 1.0). The five regions of interest (ROIs) consisted of the prefrontal (I), premotor and supplementary motor (II), motor (III), sensory (IV) and the parietal, temporal and occipital regions (V), as suggested by Hofer and Frahm (17). These regions were carefully drawn along the border of the corpus callosum on each sagittal FA map (Fig. 1). The pixels crossing the border of the corpus callosum were eroded manually by using Neuroan. The ROIs were drawn independently by two neuroradiologists, and the average values of the FA from each ROI were used for statistical analysis. We measured the percentage of changes in the FA values between the two sagittal maps.

Statistical Analyses

The interrater agreement of the FA values was determined by using the intraclass correlation coefficient. A Wilcoxon signed-ranks test was performed to compare the FA values obtained from each region between the two sagittal images. Friedman's two-way ANOVA test was performed to test whether any significant percentage of change was present among the regions. If any significant percentage of change was found, a post hoc test was then done to find which region showed a significant percentage of change in the FA values. *P* values less than 0.05 were considered to indicate significant differences. All the analyses were performed using the SPSS for Windows software, version 12.0 (SPSS Inc, Chicago, IL).

RESULTS

No structural abnormalities were noted in the brains of any of the subjects. No distortion was found in any of the corpus callosums on the FA maps from the mid-sagittal or axial DTI. The calculated SNR of the mid-sagittal DTI was 1.77 times better than that of the axial DTI. The measured SNRs by using the b = 0 image in the axial and mid-sagittal DTI were 937.75 and 1690.44, respectively.

The intraclass correlation coefficients between the two neuroradiologists for the FA maps from the mid-sagittal and axial DTI were 0.974 (95% CI: 0.959, 0.984) and 0.906 (95% CI: 0.853, 0.941). The mean FA values of the regions I-V with the mid-sagittal DTI were 0.77 $\pm$ 0.04, 0.72 $\pm$ 0.04, 0.76 $\pm$ 0.03, 0.77 $\pm$ 0.03 and 0.80 $\pm$ 0.03, respectively. The mean FA values with axial DTI were 0.74 $\pm$ 0.04, 0.67 $\pm$ 0.03, 0.70 $\pm$ 0.05, 0.69 $\pm$ 0.06 and 0.78 $\pm$ 0.03, respectively. The FA values of all the regions except for region V were significantly higher with the mid-sagittal imaging than with the axial imaging (Table 1). The FA values in region IV (the isthmus) were significantly underestimated by the axial imaging, when compared to the FA values of regions I and V (p = 0.037 and p = 0.001, respectively; post hoc test after Friedman's two-way ANOVA test).

DISCUSSION

In our study, the FA was highest in the splenium with both the axial and mid-sagittal DTI, and this result is comparable with the previous axial DTI studies. Why are our FA values of the other regions different from those of the previous studies? We propose two possible explana-

Table 1. Comparison of FA values of Corpus Callosum between Axial and Mid-Sagittal DTI

Regions	FA from Axial DTI	FA from Mid-Sagittal DTI	% Change	*p* value*
I	0.74 $\pm$ 0.04	0.77 $\pm$ 0.04	3.98 $\pm$ 4.54	0.011
II	0.67 $\pm$ 0.03	0.72 $\pm$ 0.04	6.45 $\pm$ 4.42	0.002
III	0.70 $\pm$ 0.05	0.76 $\pm$ 0.03	6.96 $\pm$ 5.60	0.002
IV	0.69 $\pm$ 0.06	0.77 $\pm$ 0.03	10.06 $\pm$ 5.91	0.001
V	0.78 $\pm$ 0.03	0.80 $\pm$ 0.03	1.66 $\pm$ 3.87	0.087

Note.— * Wilcoxon signed-rank test. FA = fractional anisotropy, DTI = diffusion tensor imaging, I = prefrontal, II = premotor and supplementary motor, III = motor, IV = sensory, V = parietal, temporal and occipital regions

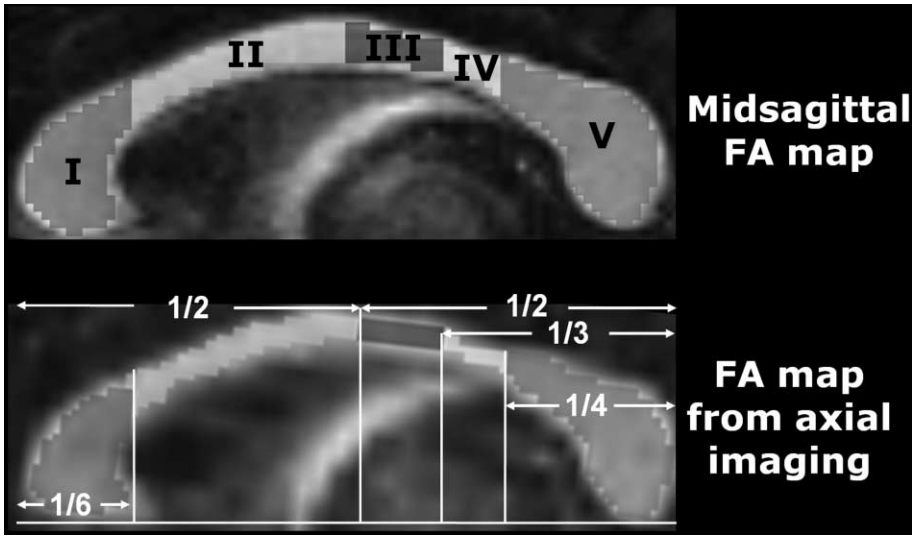

Fig. 1. Five regions of interest. Prefrontal (I), premotor and supplementary motor (II), motor (III), sensory (IV) and parietal, temporal and occipital regions (V) on mid-sagittal fractional anisotropy (FA) map (**A**) and the fractional anisotropy map from axial imaging (**B**).

tions. First, the axial DTI is usually obtained parallel to the AC-PC line. The body of the corpus callosum usually parallels this line. Therefore, axial DTI with a 2-mm or greater thickness cannot preclude a partial volume effect at the border of the corpus callosum. A lower FA in the body and isthmus may be due to this partial volume effect. This partial volume effect may even be present in the coronal DTI. In the previous coronal DTI studies (11–14), the authors suggested that the FA of the body is higher than that of the genu or splenium. They used a relatively thick, 4-mm coronal DTI. In the coronal plane, the partial volume effect might be less in the body than in the genu and splenium because the body is more perpendicular to the imaging plane. Second, many previous studies used the method of transferring the ROIs, which were manually drawn on 3-D volumetric imaging or the b = 0 image onto an FA map. This method may be more reliable than the method that directly draws ROIs on the FA map. However, transferring ROIs may be limited by a higher chance of the partial volume effect. In addition, manual drawing ROIs may be difficult and unreliable due to the low resolution of conventional DTI. The FA values of the corpus callosum that varied from those of the previous studies may be due to these limitations. We used mid-sagittal DTI with a higher resolution to overcome these limitations. In addition, we eroded the pixels that crossed the margin of the corpus callosum to minimize the partial volume effect.

Our mid-sagittal DTI showed no difference in the FA for regions III and IV as compared to that in region I. This might be due to a regional difference in axonal density and diameter. The regions III and IV have thicker axons with lower density whereas region I has thinner axons with higher density (18). The determinants of FA have been reported to be axonal diameter, density and coherence (19). When considering the axonal diameter alone, the FA in the regions III and IV may be highest. However, the axonal density of these regions is lower than that of the genu and the proportion of largest axons is small, which might offset an increase in FA. However, we still do not know which factor is the most powerful determinant for FA.

In this study, the percentage of change in the FA values was lowest in the splenium. It has been suggested that less coherence with the partial volume effect decreases anisotropy (20). Therefore, the higher coherence in the splenium might offset a decrease in FA with performing axial DTI. However, further studies are necessary to improve our understanding of the coherence of the axons in the human corpus callosum.

The corpus callosum is small in size in patients with disorders such as traumatic brain injury or dementia. When these patients are compared with healthy subjects on the axial DTI, the partial volume effect is expected to be greater in these patients, resulting in an underestimation of the FA values and a possible false positive result. Conversely, underestimation of the FA values can be observed on axial DTI in healthy subjects, which may cause a false negative result despite that there may be a significant difference. Therefore, mid-sagittal DTI with its smaller partial volume effect may be more appropriate for conducting comparative studies. However, further study using both mid-sagittal and axial DTI in patients should be performed to validate the utility of mid-sagittal DTI.

One may argue that the voxel size and shape of axial and sagittal DTI are different from each other, causing a potential bias when measuring the FA. However, it has been suggested that the effect of the voxel size/shape on the measurement of FA is significant in the regions that contain crossing fibers, and not in the corpus callosum (21). The different acquisition parameters between the two DTIs may cause a potential bias of measuring the FA as well. However, the SNR of the axial DTI was lower than that of the mid-sagittal DTI in our study. This may result in overestimation of the FA in the axial DTI, but not in the mid-sagittal DTI. Therefore, the higher FA of the corpus callosum in the mid-sagittal DTI may be justified.

This study was limited because the number of subjects was relatively small and the mid-sagittal DTI is not optimized for the whole brain. Moreover, no template is currently available for SPM (statistical parametric mapping) analysis. Therefore, the mid-sagittal DTI in this study cannot be used in a comparative study with voxel-based morphometry. Lastly, it is cumbersome to manually draw ROIs after obtaining the additional mid-sagittal DTI.

In conclusion, the FA values of the corpus callosum measured on mid-sagittal DTI were significantly higher than those on the axial DTI in regions I-IV, and particularly in the region IV. The mid-sagittal DTI may provide more accurate FA values of the corpus callosum than does the axial DTI, and it may be more suitable for studies that compare between patients and healthy subjects.

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