Corpus Callosum Partitioning Schemes and Their Effect on Callosal Morphometry

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Introduction

The Corpus Callosum (CC) is the main fiber tract connecting the two hemispheres in the brain. It functions to communicate e.g. cognitive and learned information between the hemispheres. The lack of evident landmarks that delimit anatomical and functionally distinct callosal regions has spawned several geometric partitioning schemes to subdivide the CC into regions where the fiber topography is expected to be different. These regions might be affected differently in development of disease and their structural parameters (such as size and shape) might correlate with cognitive and functional tests that evaluate different channels of interhemispheric communication. The aim of this work was to investigate the statistical impact of six common partitioning schemes for regional analysis of CC. We hypothesize that conflicts among different CC studies may partially arise from hidden methodological differences.

Methods

The CC was delineated in a set of stereotactically normalized MPRAGE images stemming from 569 non-disabled elderly subjects (age: 64-85, F/M: 312/257) with Age-Related White Matter Changes (ARWMC) from the *Leukoaraiosis And DISability* study (LADIS) [1]. The two-dimensional outline of the CC was automatically localized in the mid-sagittal plane using the learning-based Active Appearance Models (AAMs) [2]. An expert reviewer subsequently corrected for any inaccuracies. Each CC was divided into five sub regions (e.g. Figure 1b), rostrum and genu (CC1), rostral body (CC2), midbody (CC3), isthmus (CC4) and splenium (CC5), using three different partitioning methods. See Figure 1. Each method was used in two variants, resulting in a total of six different subdivision schemes.

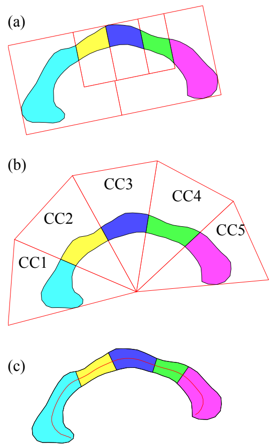

Figure 1: The three partitioning schemes, WP (a), radial (b) and MAP (c).

The first method, known as the Witelson Partitioning (WP) scheme [3], divides the CC along its first principal axis (FPA), roughly corresponding to the longest axis of the outline. For five sub regions, four division points need to be defined. These are referenced along the FPA, ranging from zero, the anterior CC part, to one, the posterior part. In variant 1 (equidistant) division points are [1/5, 2/5, 3/5, 4/5], whereas in variant 2 (according to Wittelson [3]) they are [1/3, 1/2, 2/3, 4/5]. Figure 1a shows WP using variant 2.

The second method, denoted radial partitioning (RP), exploits that the CC often approximates a circular section. The centre of this circle is found by translating the FPA such that it divides the CC into fractions containing the superior 95%, and inferior 5% of the total area. The CC centre of gravity is then projected onto this line. Each CC is partitioned using four radial dividers emanating from this point. As before, two variants were considered. The first uses equal angles producing dividers at [$\pi/5$, $2\pi/5$, $3\pi/5$, $4\pi/5$] (Figure 1b). The second set defines angles, similar to the WP fractions, at [$\pi/3$, $\pi/2$, $2\pi/3$, $4\pi/5$].

The third method seeks a curvilinear reference line that approximates the medial axis of the CC by using the chordal axis transform. Medial axis partitioning (MAP) can thus be carried out along this line based on its arc-length. Unlike the previous two methods, this results in a partitioning that is not biased by the CC shape being either near-circular, or very elongated. The two parameter sets used are identical to the ones used in the WP scheme, except that these parameterize arc-length rather than distance along the FPA. Figure 1c shows MAP using the second set.

The relationship of the CC area and the clinical status of the subjects were examined for each of the six subdivision schemes using the General Linear Model (GLM) with correction for age, gender, handedness and ARWMC load. The clinical status included the Mini Mental State Examination (MMSE) as a global measure of cognition, the Short Physical Performance Battery (SPPB) test, walking speed as a test of motor function, and the Geriatric Depression Scale (GDS-15) as a test for mood disturbance. Furthermore, a two-tailed, unpaired student's t-test was used to assess differences in subjects with or without subjective memory complaints, history of depression, subjective gait difficulty and history of falls.

Results

The GLM's revealed significant correlations between CC areas and MMSE, SPPB, and walking speed independent of the partition method. However, the pattern of associations between CC areas and clinical and functional data depends on the partitioning scheme used. The variability introduced by the choice of method became especially apparent with MMSE and SPPB data having borderline significance levels. For example, significant relationships between CC3, CC5 and MMSE were found using the WP method. In contrast, the radial method showed significant correlation between CC1, CC4 and MMSE.
All methods demonstrated that the CC areas were significantly different in subjects with subjective gait difficulty and history of falls. Subjects with a history of depression only had significantly different CC5 areas in three of the six methods.

Overall, the different partitioning schemes resulted in varying significance patterns depending on the choice of method.

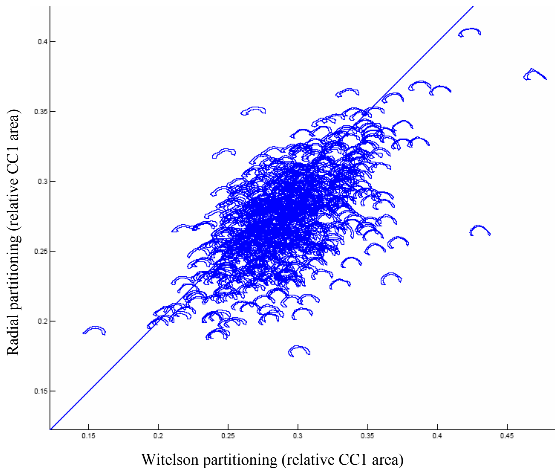

Figure 2: Relative CC1 area for two partitioning schemes.

The variation of the results using different methods may partially be explained by Figure 2 illustrating CC1 areas calculated using WP plotted against the corresponding areas using RP. The dependence of both approaches on the shape of the CC is apparent. Shapes exhibiting high curvature reside below the diagonal, where the WP scheme overestimates the area. More elongated shapes are found above the diagonal due to the overestimation in the radial scheme in this case. This shape-dependent variation may explain some of the contradictive results in CC-studies. Finally, we found that the strongest contribution to the bias in the measured area stems from the choice of parameter set, that is equidistant versus differing angles, regardless of whether we used the radial, vertical or the MA partitioning scheme.

Conclusion

Irrespective of the method used, CC atrophy was associated with impaired global cognitive and motor function in subjects with ARWMC. However, for some regions the pattern of associations between CC areas and clinical and functional data depends on the partitioning scheme used. Future studies employing diffusion tensor imaging and fiber tractography, establishing the topographic distribution of callosal connections at the cortex, may help to find the best and most robust way to partition the CC and thereby distinguish abnormalities form normal variants in the callosal structure.

References

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