Age-Related Changes In Structural Integrity Of The Corpus Callosum Demonstrated By Diffusion Tensor Tractography

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Introduction: One of the leading hypotheses relating to brain changes in normal ageing is the frontal ageing hypothesis (1,2), and is supported by reports of preferential age-related decline of the frontal lobes (3,4). Previous diffusion tensor imaging (DTI) studies of the corpus callosum (CC) report age-related changes in the genu that are not apparent in the splenium (5,6). In addition age-related changes in the splenium have been shown to be smaller than in the genu (7) although there are reports of similar changes in these structures (8,9). Here we investigate age-related changes in CC white matter structural integrity as measured by DTI and streamline diffusion tensor tractography (DTT) by application of a fully automatic CC tractography segmentation technique.

Methods: *MRI data acquisition:* Ninety-nine healthy older adults aged between 50 and 90 years old were scanned on a 1.5T GE Signa MRI system (max. field gradient strength 22mTm^{-1}). DTI was achieved using a single shot echo planar sequence with 12 diffusion sensitised directions as described previously (10). Two interleaved acquisitions comprising 25 slices each provided whole brain coverage (resolution: in plane 2.5mm; through plane 2.8mm). Each DTI was normalised to standard space by affine transformation (11). The transformation was computed in FSL tools (12).

Tractography: Subvoxel streamline DTT was performed as described previously (10). Streamlines (vector step length 1.0mm, termination criteria FA < 0.1) were initiated from every voxel centre of each DTI in standard space. Streamline termination coordinates were computed.

Commissural pathway segmentation: Frontal, temporal, parietal and occipital lobes in the left and right cerebral hemispheres were segmented from the normalised DTI data by application of the Talairach Daemon (13). The frontal lobe was further separated into the prefrontal (delineated as anterior to y = +18 mm in standard space, referred to here as the prefrontal region) and remaining regions of the frontal lobe (termed the frontal region). These segmentations were used to determine the streamlines that pass between the left and right cerebral hemispheres that terminate in these regions for each subject. This process retains the commissural pathways.

Callosal segmentation: In order to isolate the CC and remove the AC the following was performed. Each commissural streamline was separated into sections near the mid-sagittal plane (i.e. in the domain -7.5 mm ≤ x ≤ +7.5 mm in standard space) and those away from it. Streamline sections near the mid-sagittal plane were converted into a binary image. A flood fill was performed on this binary image and the largest connected component was extracted. This image corresponds to the location of the CC. Only the streamlines passing through the binary CC image were retained. Figure 1a illustrates the automatically segmented CC of a single subject coloured by the directionally encoded colour scheme (14). Pathways through the CC between different cortical regions are shown for the same subject in Figure 1b (Key: prefrontal, frontal, temporal, parietal, occipital). Figure 1c shows segmented CCs of two subjects. Pathways were separated into those passing through the CC (i.e. streamline sections in the domain -7.5 mm ≤ x ≤ +7.5 mm in standard space) and pathways passing between the CC and the cerebral cortex. Average mean diffusivity (MD) and fractional anisotropy (FA) values were computed along streamlines in each region.

Figure 1

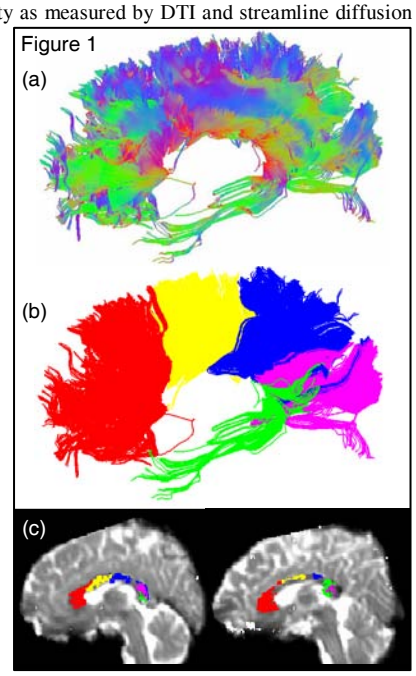
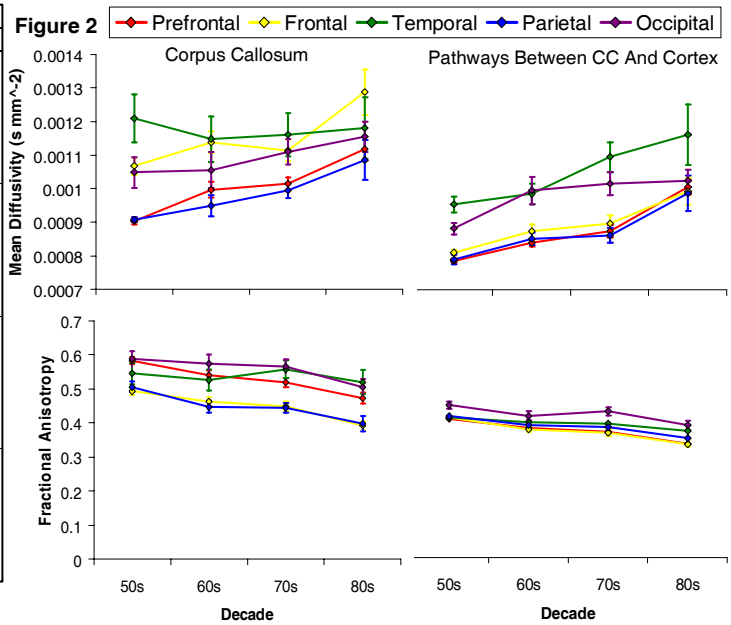


Table 1

Region	Correlation with age
MD: Corpus callosum	
Prefrontal	r = .597, p < .001
Frontal	r = .319, p = .002
Temporal	r < .001, p = 1
Parietal	r = .464, p < .001
Occipital	r = .207, p = .045
FA: Corpus callosum	
Prefrontal	r = -.546, p < .001
Frontal	r = -.497, p < .001
Temporal	r = -.030, p = .773
Parietal	r = -.405, p < .001
Occipital	r = -.255, p = .012
MD: Between CC and cortex	
Prefrontal	r = .722, p < .001
Frontal	r = .478, p < .001
Temporal	r = .381, p < .001
Parietal	r = .447, p < .001
Occipital	r = .364, p < .001
FA: Between CC and cortex	
Prefrontal	r = -.713, p < .001
Frontal	r = -.597, p < .001
Temporal	r = -.226, p = .026
Parietal	r = -.545, p < .001
Occipital	r = -.294, p = .003

Figure 2



Results: Line graphs of average MD (top row) and FA (bottom row) with standard errors are illustrated in Figure 2 for each region across the 4 decades. These show that average MD and FA values differ across CC regions (left column) and pathways between the CC and cortex (right column). In general, MD increases and FA decreases with age in all regions representing decline in structural integrity.

MD and FA measures in all regions of the CC were significantly correlated with age except for the temporal area (see Table 1). Correlations between the occipital CC region and age were less significant than for the prefrontal, frontal and parietal CC regions. Pathways passing between the CC and the cortex demonstrated significant decline with age in all regions (see Table 1).

When MD and FA measures for all regions (including the CC and the pathways between CC and cortical regions) were entered into a step-wise regression only the measures pertaining to white matter pathways between the CC and the prefrontal cortex (MD: beta = .353, p = .002; FA: beta = -.452, p < .001) were included in the model (F (2,83) = 55.50, p < .001). This model accounted for 57.2% of the variance in the data.

Discussion: We have applied a fully automatic CC segmentation technique based on streamline DTT. All areas of the CC except the temporal region showed significant reduction in white matter integrity with increasing age. This is in contrast to some previous studies that have demonstrated a reduction in the integrity of the genu but not the splenium (5,6), although some studies have demonstrated age-related decline in the splenium (8,9). Age-related decline in FA and increase in MD was apparent in all pathways between the CC and the cortex, with the strongest correlations between age and prefrontal measures. In keeping with the frontal ageing hypothesis pathways connecting the prefrontal area to the CC showed the strongest association with age.

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