Topographical relationships between arcuate fasciculus connectivity and cortical thickness



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Introduction

White matter connectivity and neural integrity constitute critical components of brain function, though how fiber coherence and organization relates to cortical gray matter structure remains under-explored. Gray matter thickness reflects the size, density and arrangement of neurons, glial cells and nerve fibers. Variations in cortical thickness identified using structural magnetic imaging (sMRI) data occur in association with normal brain maturation and aging and relate to individual differences such as sex, cognitive ability and disease status. Fractional anisotropy (FA), which is measured in diffusion tensor imaging (DTI) data and reflects the degree to which water diffusion is directionally biased in brain tissue, is also shown to vary in accordance with demographic and clinical characteristics of individuals. Diffusion tractography methods allow FA and other diffusion metrics such as axial and radial diffusivity to be estimated within discrete fiber pathways to determine the structural connectivity of particular cortical networks.



The arcuate fasciculus (AF) is a white matter tract that has received particular attention for its role in language. This tract projects from the superior temporal gyrus and Wernicke's area (Brodmann's area (BA) 22, involved in speech comprehension), curves around the Sylvian fissure connecting with Broca's area (BA 44, 45, involved in speech production) in the inferior frontal cortex. Arcuate fibers also link association cortices in caudal dorsolateral prefrontal cortex (BA 6, 8) and the inferior parietal lobule (BA 39, 40). However, it remains unknown whether the connectivity of the arcuate fasciculus relates to regional cortical gray matter structure. The current investigation sought to address this hypothesis.

Methods

Imaging data was acquired from 36 (24 male, age: 29.7±10.7 and 12 female, age: 34.4±10.7) healthy subjects on a 1.5T Siemens Sonata scanner. The DTI acquisition included 3 averages of a whole brain sequence with 30 non-collinear diffusion directions, 5 b0's and 55 brain slices (TR=6400 ms, TE=83 ms, b=0, 1000 sec/mm², FOV: 240x240 mm, matrix: 96x96, voxel size: 2.5 mm³). High-resolution T1-weighted sMRI data was acquired using a 3D MPRAGE sequence with four averages (TR=1900 ms, TE=4.38, FOV: 256x256 mm; voxel size: 1 mm³, flip angle: 15°). For DTI data, the diffusion gradient table was corrected for slice prescription and the images were corrected for eddy current distortions and motion artifacts. The diffusion tensor was then estimated within each voxel (Pierpaoli and Basser, 1996). Three-dimensional tract reconstruction of the AF was performed in DTIstudio using a previously validated method (Phillips et al., 2009; Wakana et al., 2007) [Figure. 1]. Average intra-voxel FA, and axial and radial diffusivity were computed for the left and right arcuate separately in each subject.

A B C D D

Figure 2. Statistical maps showing topographic associations between arcuate fasciculus fractional anisotropy, and cortical thickness encoded in color. Uncorrected probability values and partial correlation coefficients (age and gender controlled) are shown in the left and right panels respectively. Far left insets: The AF mapped in different orientations. The bottom left inset shows the gyral regions of interest from the LPBA40 atlas mapped onto the average representation of the cortex.



Figure 3. Relationships between arcuate fasciculus fractional anisotropy (FA) and cortical thickness averaged within gyral regions of interest for the left and right hemispheres respectively.





Figure 1. Locations of the seed regions used for extracting the arcuate fasciculus. (A) The coronal section showing the middle of the internal capsule posterior limb used to identify the core of the arcuate fasciculus (intense triangular shaped area), (B) fiber tracts projecting from A, (C) fiber tracts selected from the level of the anterior commissure in the axial plane that project laterally to the sagittal striatum, and (D) fiber bundles crossing both A and C.

Preprocessing of the T1-weighted MPRAGE images included signal inhomogeneity correction, skull stripping, correction for head tilt and alignment using 6-parameter registrations, tissue classification and cortical surface extraction. Cortical pattern matching methods (Narr et al., 2007; Thompson et al., 2004) were then employed to spatially relate homologous cortical surface locations between individuals. These procedures allow relationships between measures of AF connectivity and cortical thickness, reflecting the distance between the cortical white/gray matter and gray matter/CSF boundaries, to be assessed at high spatial density (65,536 spatially matched vertices) across subjects. Gyral regions of interest (ROI) were generated using the Laboratory of NeuroImaging Probabilistic Brain Atlas (LPBA40) (http://www.loni.ucla.edu/Atlases/LPBA40) to determine relationships in regions through which the AF traverses.



Male and female subjects did not differ significantly in age, F (1,34)=.16, p>.68. Relationships between arcuate FA examined within each hemisphere separately, (mean left FA: .47±.03 SD and mean right FA: .47±.05 SD), and cortical thickness assessed at each vertex are mapped to the average surface representation of the cortex shown in Figure 2. Partial correlation coefficients and uncorrected probability values are shown in the left and right panels. False Discovery Rate (FDR) correction indicated that 90% of the uncorrected p-values thresholded at p<.01 (orange, red and magenta) are expected to reflect true positive findings. These statistical maps revealed highly significant associations between FA and cortical thickness along the trajectory of the AF encompassing Broca's area (BA 44, 45) and proximal prefrontal cortex (BA 6), Wernicke's area (BA 22), and inferior parietal (BA 39 and 40), superior and middle temporal (BA 41, 42) and inferior temporal cortices (BA 37). Effects were pronounced in the left hemisphere particularly in primary language areas (BA 44, 45 and 22).

Figure 4. Statistical maps showing associations between arcuate fasciculus axial diffusivity (top panel) and radial diffusivity (bottom panel) and cortical thickness encoded in color. Uncorrected probability values and partial correlation coefficients (age and gender controlled) are shown on the left and right respectively.



Graphs in Figure 3 show the relationships between arcuate FA and cortical thickness (controlling for age and gender) averaged across each gyral region of interest. These relationships were not significant for cortical thickness averaged across the entire hemisphere or for the superior occipital gyrus that was used as a control region.

Relationships between left and right AF axial and radial diffusivity and cortical thickness measured at each vertex are shown in Figure 4. Negative associations between cortical thickness and radial diffusivity (bottom panel) and positive associations between cortical thickness and axial diffusivity (top panel) are seen in a similar spatial pattern to the regional associations observed for arcuate FA and cortical thickness shown in Figure 2. However, only left hemisphere radial diffusivity exceeded FDR thresholding to indicate that >90% of uncorrected findings at .01 represent true positives. Associations between axial and radial diffusivity and cortical thickness averaged across each hemisphere and within each gyral region showed significant effects for radial diffusivity in the bilateral postcentral and right supramarginal gyrus and middle temporal gyrus only (p>.05) although trends were observed for other regions.

Converging evidence supports that the arcuate is major fiber pathway that connects cortical regions important in language processing. By examining how arcuate fiber coherence and organization relates to gray matter macrostructure using cortical pattern matching and diffusion tractography methods, we revealed positive and highly topographical associations between arcuate connectivity indices and cortical thickness within anterior and posterior language regions and surrounding cortices, more prominently in the left hemisphere. Regional cortical thickness/FA associations were more attributable to variations in radial diffusivity that might indicate variations in the degree of myelination form the basis of such relationships. Notwithstanding, topographical relationships between independent measures of white matter and gray matter integrity suggest that rich developmental or environmental interactions influence brain structure and function where the presence and strength of such associations may help elucidate pathophysiological processes influencing language systems. The present findings may thus provide new insight towards understanding the underlying disturbances of neurodevelopmental disorders such as dyslexia or schizophrenia for which language dysfunction represents a primary feature.



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