Interaction of cortex and white matter during development accessed by cortical thickness and microstructure of projected axons

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Introduction

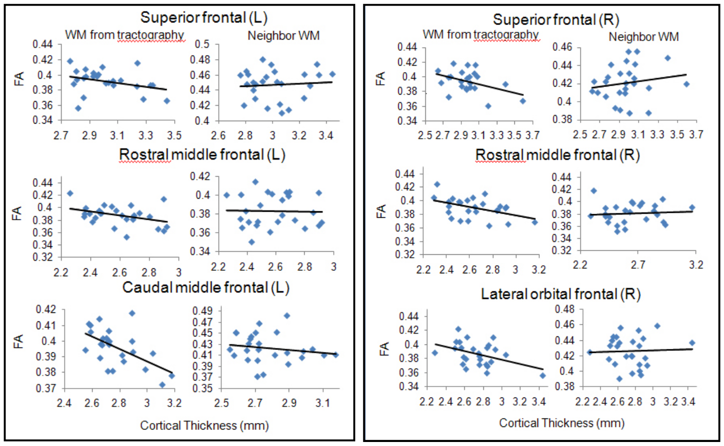
Cortical thinning during brain development is due to complicated cellular and molecular processes including increased proliferation of myelin into the cortical neurophil, synaptic pruning, trophic glial and vascular changes and cell shrinkage [e.g.1-3] during development. Age-dependent microstructural changes of brain white matter have also been found [e.g. 4-7]. Complicated cellular activities occurring in the cortex during development can drive the structural changes of not only cortex but also white matter, as most brain white matter is essentially axons from the neurons in the cortex. The correlation of gyral cortical thickness and the DTI metrics of anatomically adjacent white matter based on its geometric closeness to a cortical gyrus has been studied recently [8]. However, with the thickness change of a certain cortical area, the interaction between cortex and white matter may be better accessed with microstructural measurements of white matter traced from this cortical region rather than those of anatomically adjacent white matter areas. In this paper, we hypothesized that strong interaction exists during development between the thickness of a local cortical area and microstructure of projected axons with cortical areas as seeds for DTI-based axonal tractography. After acquiring DTI and T1 weighted images from 26 normal children and young adults with age range 8 to 25 years, we parcellated the cortex into 66 gyri and measured the fractional anisotropy (FA) of white matter tracts projected from the local cortex with a certain gyral label. Cortical gyri in frontal lobe were focused on as this is the area most related to cognitive and executive maturation. For comparison, FA of anatomically adjacent white matter of a cortical gyrus was also measured.

Methods

Subjects and data acquisition: DTI data of 26 normal children (13 Male and 13 Female; age 15.4±5.9; age range 8 to 25 years) were acquired from Philips 3T scanners of two institutions with identical imaging protocol. DTI data were acquired using a single-shot EPI with SENSE. The image parameters were: resolution=2x2x2 mm, 30 directions; b=1000 sec/mm^2, repetition=2. T1-weighted (MPRAGE) image with FOV=256/256/160mm and resolution 1x1x1mm was also acquired. *Identification of anatomically adjacent white matter:* The cortical surface was parcellated into 33 gyral labels in each hemisphere using FreeSurfer. Based on the cortical parcellation, 33 corresponding white matter regions were delineated by assigning a surface label to each neighboring white matter voxel within a 5mm distance limit. Linear affine transformation was applied to reorient and transform the T1-weighted image and parcellated white matter labels into DTI space using a b0 image as a template. The white matter labels were eroded by one voxel to remove the bias of partial volume effects near the grey and white matter boundary. The FA was measured using the eroded white matter labels as a mask in DTI. *Identification of axons projected from a cortical gyrus:* The cortical labels were dilated by 5 voxels in order to touch the white matter and then transformed into DTI space as tracking seeds. FSL probtrackx was used for tractography. *Measurements of cortical thickness and DTI metrics:* The mean cortical thickness was calculated for each gyral based label by using representations of the GM-WM boundary and the pial surface then computing the distance in between these surfaces at each point across the cortical mantle. FA was calculated with identified anatomically adjacent white matter and axons projected from a cortical gyrus as a binary mask. Pearson's correlations between cortical thickness and FA were performed to test the relationships between cortical thickness and the white matter microstructure.

Results

Effects of FA to thickness measurements: From Fig. 1, the results from multiple regressions with cortical thickness as the independent variable are shown. There is no significant trend with cortical thickness in the neighborhood white matter approach in 3 representative white matter regions, unlike white matter tractography, which has a strong negative correlation in these regions. *Regional FA change with anatomically adjacent white matter:* From Fig 1 and Table 1, Pearson's correlations between cortical thickness in each frontal lobe region and FA show no significant correlations (FDR-corrected). The strongest associations were found in the lateral orbitofrontal (r=0.21) and precentral (r=0.23) regions. *Regional FA change from white matter tractography:* From Fig 1 and Table 1, FA is significantly (FDR-corrected) negatively correlated to cortical thickness in all frontal lobe regions with the exception of pars opercularis. The strongest association was in the right hemisphere superior frontal region (r=-0.41) and left hemisphere caudal middle frontal (r=-0.50). There were fewer and smaller significant correlations with FA for the neighborhood white matter approach.



Region	rN	rT	|rT-rN|
lh-superiorfrontal	0.084344	**-0.31353**	0.397877
lh-medialorbitofrontal	0.105533	-0.1553	0.260829
lh-rostralmiddlefrontal	-0.01918	**-0.38955**	0.370376
lh-caudalmiddlefrontal	-0.16817	**-0.57178**	0.403611
lh-parsopercularis	0.10708	**-0.33354**	0.440615
lh-parsorbitalis	0.048038	**-0.29098**	0.339021
lh-parstriangularis	0.110382	-0.13551	0.245893
lh-lateralorbitofrontal	0.413837	0.002091	0.411746
lh-precentral	0.141505	**-0.26533**	0.40684
rh-superiorfrontal	0.168615	**-0.38348**	0.552091
rh-medialorbitofrontal	-0.12462	-0.15879	0.034169
rh-rostralmiddlefrontal	0.071467	**-0.45275**	0.524215
rh-caudalmiddlefrontal	0.088752	**-0.30112**	0.389868
rh-parsopercularis	-0.00521	-0.02444	0.019231
rh-parsorbitalis	0.129459	**-0.17007**	0.299532
rh-parstriangularis	0.055456	-0.11738	0.172837
rh-lateralorbitofrontal	0.033448	**-0.40888**	0.442324
rh-precentral	0.06538	**-0.38314**	0.448523

Fig. 1: Scatter plots for FA vs. cortical thickness using white matter tractography method and neighborhood white matter for 3 selected frontal lobe regions in the left and right hemisphere. Which are shown from top to bottom counterclockwise: left superior frontal lobe, left rostral middle frontal lobe, left caudal middle frontal, right superior frontal lobe, right rostral middle frontal, and right lateral orbitofrontal lobe.
Table: 1 Pearson's Correlations between cortical thickness and FA of the neighborhood white matter (rN) and between cortical thickness and FA of traced white matter (rT). The absolute differences of the two correlation coefficients are also shown. Bold characters represent FDR corrected p <0.05.

Conclusion and discussion

Significant negative correlations of thickness and FA of traced white matter were found in most of frontal gyri, showing a strong sensitivity of detecting interaction between cortex and white matter. The age-dependent cortical thickness decreases and FA increases are significant for most cortical areas (data not shown), consistent to previous findings [1-2, 4-7]. Increased myelination (2, 5-7) may cause the increased FA of axons projected from the frontal cortex. Higher sensitivity between cortical thickness and DTI metrics of projected axons may be partly caused by the fact that neuron bodies in the cortex and projected axons biologically belong to the same neurons. Therefore, the morphological changes of neuron bodies and microstructural changes of axons are intrinsically related. Data from more child and adolescent subjects will be added.

References: [1] Shaw et al (2008) J Neurosci 28:3586. [2] Gotay et al (2004) PNAS 101:8174. [3] Morrison and Hof (1997) Science 278:412. [4] Lebel et al (2007) Neuroimage 40:1044. [5] Gao et al (2009) AJNR 30:290. [6] Giorgio et al (2010) 49: 94. [7] Westlye et al (2010) Cereb Cortex 20: 2055. [8] Tammes et al (2010) Cerebral Cortex 20:534. **Acknowledgement:** This study is sponsored by NIH EB009545 and NIH MH092535.