Corticospinal tract diffusivity is related to motor cortex surface area in healthy controls

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Target audience: This research is aimed at researchers and/or clinicians seeking to better understand the relationship between cortical gray matter morphology and associated white matter tracts in healthy controls.

Background/purpose: The relationship between measures of white matter (WM) integrity and associated gray matter (GM) morphology has been studied in pathological conditions (1). Their association in healthy controls (HC) though has been less frequently investigated. Diffusion tensor-based tractography allows for the identification of specific WM tracts and obtain quantitative measures of structural integrity (e.g. fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD), radial diffusivity (RD)). The freely available FreeSurfer software package provides advanced reconstruction algorithms for obtaining fine-grained morphological measures of the cortex (e.g. thickness, surface area, curvature). In this work, we have assessed in HCs the relationships between cortical morphology and associated WM tracts, using the primary motor cortex (MC) for the former and the corticospinal tract (CST) for the latter.

Methods: This was a cross-sectional study of 24 HCs that were examined using 1.5T MRI. The MRI protocol included a 3D T1-weighted MP-RAGE with 1mm isotropic resolution, a dual-echo turbo spin echo, and a DTI acquisition (2 runs with 12 non-collinear diffusion gradients (b=900 s/mm2) and 1 volume without diffusion weighting). FreeSurfer was used to obtain measures of cortical thickness, surface area and curvature from the MP-RAGE (2). We used the DKT40 parcellation to identify the precentral gyrus(corresponding to the MC) (3). Cortical morphology measures were estimated separately for the left and right hemispheres. DTI-based indices within the CST were calculated using two different approaches: 1) application of a previously in-house generated probabilistic CST atlas (4); 2) Tract-Based Spatial Statistics (TBSS) (5), with the resulting maps masked with the CST tracts provided as part of the JHU White-Matter Tractography Atlas. In order to reduce the number of comparisons, we combined left and right measures into a single metric. The dual-echo image was used to check for WM abnormalities. Mean CST and MC metrics were compared between males and females using Student's t-test. Partial correlations, controlling for age and sex, were used to assess the relationship between CST DTI indices and cortical measures. For tests with surface area comparisons, correlations were repeated with total intracranial volume (TIV) added as an additional covariate. To exclude the possibility of a residual non-linear effect of sex after covariate correction, additional exploratory analyses were performed separately for males and females. A p-value of $< .05$ was deemed significant while $< .1$ was considered a trend.

Results: Our study included 24 HCs with a mean (SD) age of 41.7 (11.6), 14 of which were female. All HC were free of T2 abnormalities. Mean age was not significantly different between males and females. With the exception of MC surface area ($p = .027$), mean values for all other indices did not significantly differ between males and females. Neither MC thickness nor curvature correlated with any of the DTI indices. For MC surface area, trends were found with atlas-derived CST MD ($r = -.365$, $p = .095$) and TBSS-derived AD ($r = -.419$, $p = .052$). When including TIV as an additional covariate, MC surface area correlated with atlas-derived CST MD ($r = -.556$, $p = .009$), AD ($r = -.477$, $p = .029$), RD ($r = -.434$, $p = .049$) and TBSS-derived MD ($r = -.525$, $p = .015$), AD (-.612, $p = .003$) and trend for RD ($r = -.392$, $p = .079$). Similar results were obtained when investigating males and females separately.

Discussion: Our preliminary analysis shows that increased diffusivities within the CST are related to reduced cortical surface area but not thickness nor curvature. We controlled for age as it has been to shown to correlate with both surface area reductions (6) and diffusivity changes (7). The results from the probabilistic atlas approach were generally in line with those obtained from TBSS. The neural underpinnings of the connection between WM-tract diffusivity and corresponding cortical surface area remain to be elucidated. Assessing connectivity measures as well, which was not done for the present work, may also help shed light on the relationship. Longitudinal studies in a larger sample of HCs are warranted to better understand the temporal evolution of changes in the WM and anatomically/functionally connected GM regions.

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