Diffusion-Tensor Imaging Tractography: Correlation with Processing Speed in Aging

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Objective

- To determine the relative contribution of interhemispheric vs. cingulum bundle fibers to psychomotor processing speed ability in the elderly using quantitative DTI tractography.

Background

- Prior studies using diffusion-tensor imaging (DTI) demonstrated an age-related decline in the integrity of white matter, mostly in anterior regions (e.g., 1-3).
- Processing speed has been shown to be correlated with vascular white matter injury (4) and recent DTI studies suggests involvement of the cingulum bundle in executive functions (5) and corpus callosum in processing speed (6)
- We developed a DTI tractography-based metric for assessing the relationship between the structural integrity of specific white matter pathways and cognitive functioning (7).
- The *normalized total weighted length* (NTWL) metric is the summed length of all computer-generated fibers (streamtubes) of a tract-of-interest (TOI) weighted for average linear anisotropy and then normalized for estimated intracranial volume.
- White matter tracts with reduced structural integrity from age-related changes or injury should have lower linear anisotropy.
- Local reductions in linear anisotropy that fall below a pre-specified threshold cause the computerized streamtube generation algorithm to terminate prematurely resulting in shorter streamtubes and lower values of NTWL.
- To examine the ability of our metrics to detect associations between the structural integrity of certain TOIs and cognitive functioning we examined the relative contribution of interhemispheric fibers (passing through the corpus callosum) vs. cingulum bundles to psychomotor processing speed.

Hypotheses

- Based on the prior studies we anticipated that NTWL in the interhemispheric fibers and cingulum bundle would have differential relationships with measures of psychomotor processing speed and executive function.

Participants

- Participants were 12 cognitively normal adults (mean age = 68.63 ± 11.25 years, range = 49-83; mean education = 14.6 ± 3.8, range 9-20).

DTI Acquisition Protocol

- Three interleaved sagittal acquisitions offset in slice direction by 0.0mm, 1.7 mm and 3.4 mm, 5mm thick slices, 0.1mm inter-slice spacing, matrix=128x128mm, FOV=21.7x21.7cm, TR=7200, TE=156, b= (0, 1000 mm/s^2), 12 directions, no partial echoes, final voxel dimension=0.85 mm^3.

Tractography Measurements

- Tractography models of whole-brain white matter were produced in which fibers were represented as streamtubes (8) (Figure 1).
- TOIs were selected manually by a trained rater using customized software modeled after a method proposed by Akers et al. (9) and NTWL was calculated based on a prespecified algorithm. Streamtubes that were anatomically questionable were manually culled from each TOI. See Figure 1 for examples

Cognitive Tests

- Trail Making Test parts A & B (TMT-A, TMT-B) (10) were used to assess processing speed and executive functions respectively.

Statistics

- Separate multiple linear regression models were used to test the association between TMT-A and TMT-B NTWL in the three TOIs.
- In each model age was entered at step 1 and the TOI variables were entered at step 2.

Results

- Table 1 provides descriptive statistics for the tractography and cognitive variables.
- Processing speed: There were trend level findings for step 1 (age, p = .079) and step 2 (TOIs, p = . 058).
- Age accounted for 28% of the variance in TMT-A performance (p =.079, trend). NTWL for the three TOIs accounted for an additional 41% of the variance (p = .101, trend for F change).
- Examination of standardized beta weights for the individual TOIs showed that NTWL in the right cingulum bundle was the strongest predictor (beta = – 585, p = .044 ; p > .05 for all other variables).
- Executive function: Step 1 was not significant (age, p = .46) and there was a trend level finding for step 2 (p = .08).
- Examination of standardized beta weights for the TOIs showed that NTWL in the interhemispheric fibers was the strongest predictor of TMT-B performance (beta = – .70, p = .01; p > .05 for all other variables).

Table 1: Descriptives (Mean ± SD)

Variable	
Interhemispheric Fibers (mm)	4437 ± 1893
Right Cingulum Bundle (mm)	472 ± 187
Left Cingulum Bundle (mm)	394 ± 139
TMT-A (s)	36.8 ± 14.4
TMT-B (s)	101.0 ± 46.3

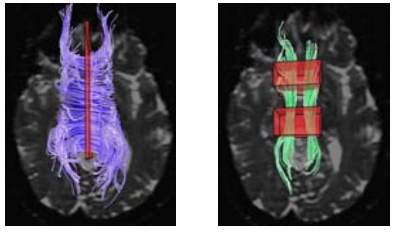

Figure 1: Left: Interhemispheric fibers. Right: cingulum bundle

Conclusions

- Our new quantitative DTI tractography metric appears to capture information about the structural integrity of specific white matter pathways that is relevant to cognitive function in aging.
- The results suggest tentatively that after accounting for age, performance on TMT-A and TMT-B have differential associations with the interhemispheric fibers and the right cingulum bundle, respectively, but not with the left cingulum bundle.
- The results are limited by the small sample size, which may well have limited our statistical power. Also, the results are likely to be affected specific method used for TOI selection and editing.
- The incremental validity of these metrics for predicting cognitive function over and above volumetric measures of conventional MRI images and scalar DTI maps needs to be determined in a larger sample.

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