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Mapping the human direct and indirect motor descending pathways using high-resolution tractography with diffusion imaging

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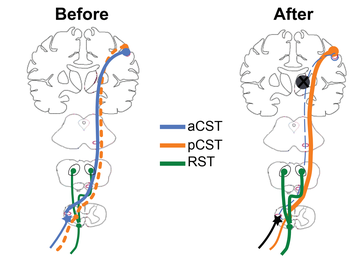
Introduction

Dexterous hand movements are essential for daily activities. Fine finger control and hand strength have been found supported by separable descending pathways: the corticospinal (CST) and the reticulospinal tracts (RST)[1-3]. Research in non-human primates also suggests that after lesions to the direct corticomotoneuronal projections within the CST, the indirect, propriospinal pathway within the CST also contributes to hand dexterity recovery[4]. Mapping these descending pathways in humans will be crucial for understanding functional recovery after neurological insults. Here we attempt to delineate these pathways using existing knowledge from comparative fiber tracking suggesting that studies across species suggest that the majority of the monosynaptic pathway in humans originates from the anterior bank of precentral gyrus (aCST)[5], and the indirect CST projections mainly originate from the ventral premotor cortex (pCST)[6].

This preliminary study investigated the feasibility of using a high-resolution whole-brain tractography method to separate aCST, pCST, and RST in healthy and stroke populations.



Hypothesized Model

A hypothesized model of three descending pathways (aCST, pCST and RST) showing disruption of the neural pathway before and after the stroke incident.

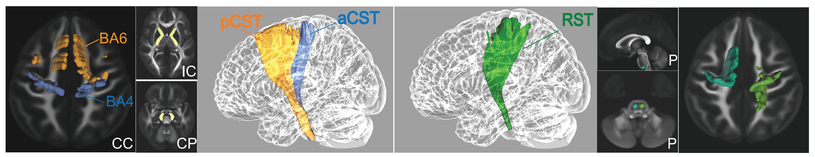
In stroke: after a disruption of the aCST, pCST and RST may be upregulated to compensate the loss of the direct pathway.

Methods

Participants: Healthy younger adults (YA) (N= 13; 9 females; 4 males; mean age 22), older adults(OA) (N = 8; 4 males; mean age of 71 years) and individuals with stroke(SP) (N = 9; 3 females; 6 males; mean age 62 years).

Diffusion Imaging: The diffsusion Magnetic Resonance imaging (dMRI; 60 directions, b=2000 and 4000 s/mm², slice thickness of 2mm) was collected from each participants using a 3T GE Discovery MR750 scanner. We used readout-segmented echo-planar imaging with parallel imaging[7] and a multi-shell diffusion spectrum imaging sequence. The dMRI images were reconstructed to the MNI space using q-space diffeomorphic at an output resolution of 2 mm isotropic[8] in a standard atlas space for easy comparison across subjects using DSI studio.

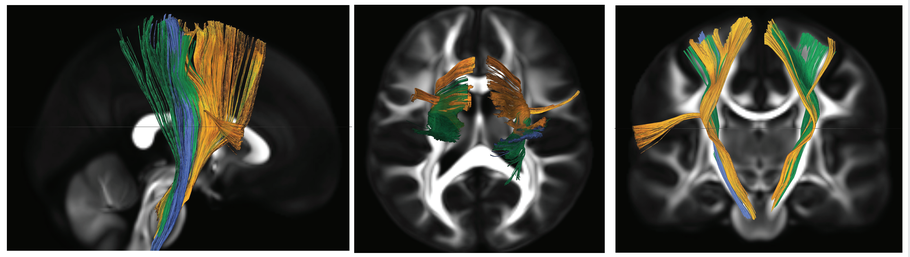
Fiber Tracking: To access the integrity of three different pathways (aCST, pCST and RST) affected by lesion, we generated the three different ROI masks to approximate these pathways in the HCP atlas.



ROIs Masks: Cerebral Cortical(CC) ROIs were approximated using Brodmann's Area BA4 and BA6 for aCST and pCST, respectively. Fibers were restricted by BA4 and BA6, and traced between the cortex, internal capsule (IC), and cerebral peduncle (CP)[9]. For the RST pathways, seeds were placed in the anterior segment of the brainstem and dorsal pons (P) to approximate medial and lateral RSTs, respectively, based on prior voxel-space locations[10].

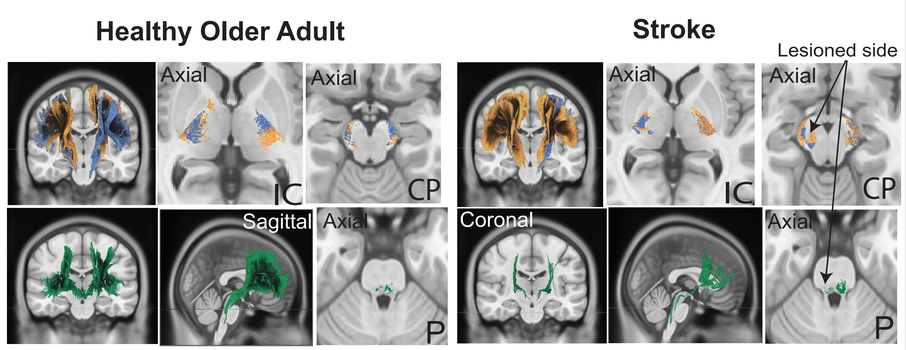
Tract ROIs Template: Tract ROI masks generated in the Human Connectome Project (HCP) atlas were used to assess tract integrity of the three different pathways affected by the lesion. The average quantitative anisotropic (QA) values of the descending fibers in these masks were extracted for each participant and compared between patients and controls.

Atlas: aCST, pCST RST



The decending tracts, aCST, pCST, and RST are mapped in the HCP1065 average data as shown in sagittal, axial and coronal plane

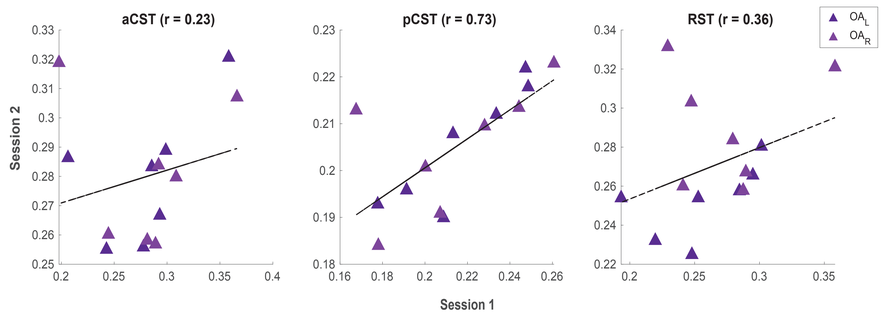
Tracts Visualization (single subjects)



Friber tracking visualization in two single subjects' International Consortium for Brain Mapping (ICBM) template showing CST tracts (aCST and pCST) restricted using ROI masks starting at IC and CP, and RST ROI mask at P. Tractography performed in the patient's template reveals decreased fiber density on the lesioned side in both the corticospinal tract (CST) and reticulospinal tract (RST).

Repeated Sessions Reliability

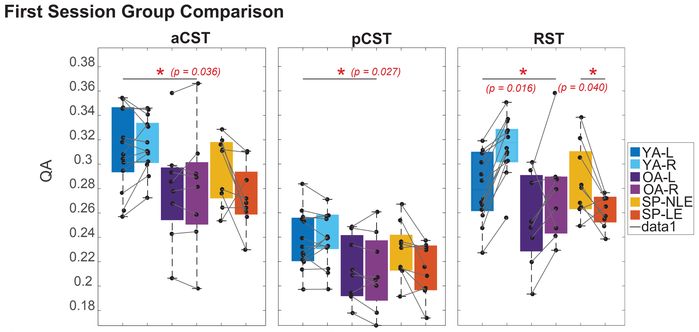
Participants were invited for a second session to repeat the assessment using the same imaging protocol. The 2nd session was conducted between 1-24 months.



We accessed whether QA values of healhty older adults in session 1 (QA1) and tract specific predictors (aCST, pCST, RST) could explain QA values in session 2 (QA2), using linear mixed-effects model with subject as a random factor. Our results shows that QA1 was a significant predictor of QA2 across all models (p<0.01). pCST was a significant predictor of QA2 (t = -6.031, p < 0.001). aCST and RST did not significantly predict QA2 (p < 0.05).

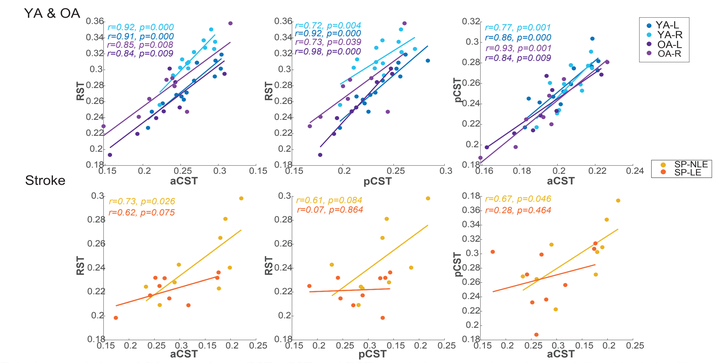
Voxel QA Results

First Session Group Comparison



QA values extracted from both hermispheres of YA, OA and non-lesioned (NLE) and lesioned (LE) of the SP are plotted for all three pathways (aCST, pCST, RST). Our results comparing QA values between YA and OA revealed significantly higher values in YAs' aCST, pCST and RST tracts. QA values in the LE and NLE hemispheres among stroke survivors yielded significant differences in RST tracts but not in aCST and pCST tracts (pCST: p=0.1781; aCST: p=0.124). No other significant differences were found among YA, OA, and SP groups.

Correlation Between Tracts



Pairwise correlations of QA values from aCST, pCST, and RST revealed strong and consistent relationships in healthy participants (YA & OA), with all correlations reaching significance (r = 0.72~0.98, p < 0.01). In contrast, participants with stroke (SP) showed weaker and more variable correlations, with only NLE RST–aCST (r = 0.73, p = 0.026) and pCST–aCST (r = 0.67, p = 0.046) reaching significance. QA values among all tracts in the lesioned side are not correlated.

Discussions

- Our study evaluated the reliability of white matter intregity indicated by QA values across repeated sessions. Linear mixed-effects models showed QA1 was a strong predictor of QA2, indicating test-retest reliability.
- Group comparisons highlighted age-related QA decline, with significantly higher QA values in younger adults across all tracts. Higher QA values in healthy younger adults within aCST, pCST and RST tracts underscore the integrity of intact pathways.
- Among stroke survivors, only the RST showed significant asymmetry between lesioned and non-lesioned hemispheres, indicating its potential vulnerability or role in recovery.
- Correlation analysis between tracts revealed robust inter-tract coherence in healthy adults, but disrupted patterns in stroke participants.
- This pattern highlights the sensitivity of our method to fiber loss due to aging, and lesion after a stroke.

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