FINDING CRITICAL LANGUAGE CONNECTIONS ACROSS MULTIPLE TRACTOGRAPHY ALGORITHMS: A NEW ANALYTIC APPROACH

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INTRODUCTION

- Significant discrepancies exist across diffusion MRI studies regarding the functional contributions made by each of the major fiber pathways, particularly as they relate to language pathology (Bajada et al., 2015; Dick et al., 2014; Fridriksson et al., 2018; Ivanova et al., 2016; Vaidya et al., 2019). These variations are partly due to the tractography methods employed (e.g., Auriat et al., 2016).

Aims of the current study

- ***Methodological*** – Develop a new approach for evaluating the functional role of different tracts by minimizing the possible method-specific impact of different tractography algorithms on observed patterns of tract-behavior associations.
- ***Conceptual*** – Provide a more definitive answer on the role that white matter pathways play in language processing by simultaneously investigating four different iterative tractography algorithms and analytically combining their results.

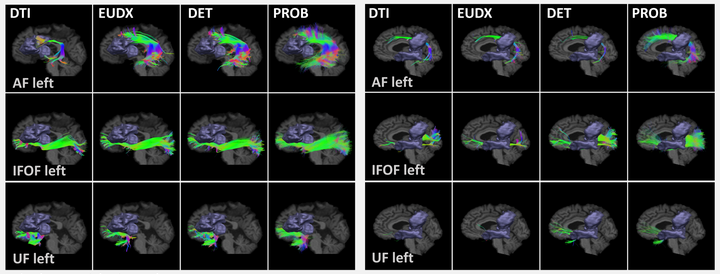
RESULTS

TRACTS RECONSTRUCTED:

- **AF** – arcuate fasciculus (3 segments)
- **IFOF** – inferior frontal-occipital fasciculus
- **ILF** – inferior longitudinal fasciculus
- **UF** – uncinate fasciculus
- **FAT** – frontal aslant tract
- **CST** – cortical-spinal tract (control tract)

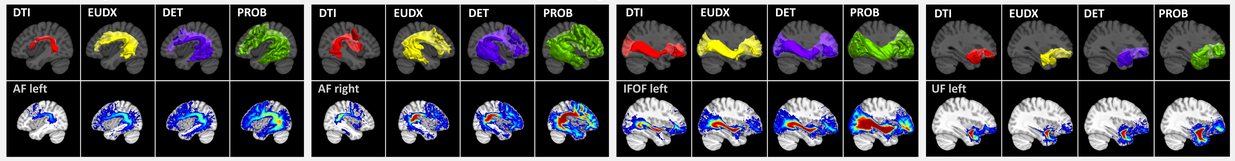
For each tractography algorithm and each tract volume (normalized by hemisphere volume) and mean fractional anisotropy (FA) were extracted.

Example of tract reconstructions in two individual patient cases



Lesion mask is shown in grey

- **Discrepancies in tract reconstructions between the four algorithms were observed**



- *Top row – 3D isosurface rendering, representing the average shape of the tract across the 33 participants (thresholded at 3).*
- *Bottom row – heatmap, representing the probability distribution from the 33 participants for the same tract (from 1 to 33).*

ANALYTICAL APPROACH FOR ESTABLISHING ROBUST BRAIN-BEHAVIOR RELATIONSHIPS

1. Normalized tract volume and mean FA values of each tract for each tracking algorithm were correlated with language measures while accounting for lesion volume *(see Correlation heatmaps on the right, first four rows)*.
   - This generated four different correlation matrices for mean normalized volume and for mean FA.
   - Some results (tract-language associations) were highly method-specific (observed only for 1-2 algorithms), while a select number of patterns were all significant, irrespective of the tracking method employed.
2. Significant correlations were then combined to determine which were observed systematically across the different algorithms *(see Correlation heatmaps on the right, bottom "Overlap" row)*.
   - We deemed correlations appearing in at least 3 out of 4 methods as reliable and amenable to further interpretation.

CONCLUSIONS

- The proposed method of analysis is highly replicable and reliable. It should be used in future studies to minimize the impact of algorithm-specific artifacts and help to solidify and verify detected brain-behavior relationships.
- Language-tract associations
  - Consistent correlations were observed for the AF posterior branch as critical for naming, repetition and comprehension, while the AF anterior branch was related to spontaneous speech, and the AF MTG branch, to naming.
  - The temporal lobe associative fibers (IFOF & ILF) were related to naming, repetition and comprehension.
- The current approach helps to robustly outline the crucial language connections that need to be represented in future models of language processing and further explored as predictors of clinical outcome.

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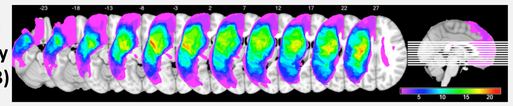
METHODS

Participants – 33 right-handed individuals with post-stroke aphasia (24 males; M_{age} = 63.7 ± 10.4 years, age range: 40 - 83 years; $M_{months\ post\text{-}onset}$ = 96.6 ± 93.1 months, post-onset range: 2 - 327 months).
Language testing – Western Aphasia Battery-Revised (Kertesz, 2007)

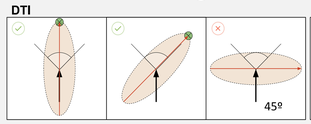
Lesion overlay (n = 33)



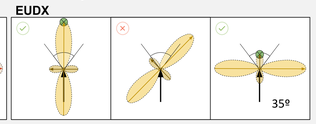
Neuroimaging – Structural and diffusion-weighted MRIs (64 directions, 2mm isovoxel, b=2000s/mm^2, 10 b0 volumes) were acquired on a Siemens Verio 3T scanner. DWI data processing was done with the tractoflow pipeline (local models, i.e., tensor and fiber orientation distribution function (fODF), tractography) using the *DIPY library* (Garyfallidis et al., 2014). For each tracking algorithm the tracts were automatically segmented from the whole brain tractogram in both hemispheres using *Recobundle* with multiple execution followed by labels fusion (Garyfallidis et al., 2018) .

TRACTOGRAPHY ALGORITHMS

Algorithms based on peaks

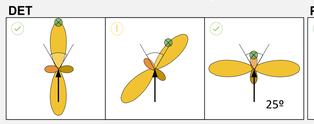


DTI - single-peak tractography based on the tensor (45º angular threshold)

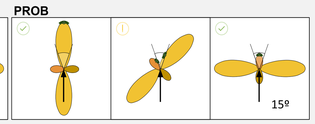


EUDX - multi-peaks eudx tractography based on the fODF (up to three peaks in each voxel, 35º angular threshold)

Algorithms based on fODF



DET - deterministic tractography based on the fODF (25º angular threshold)



PROB - probabilistic tractography based on the fODF (15º angular threshold)

Correlation heatmaps. Measures of spontaneous speech, speech fluency, naming and word finding abilities, repetition, and auditory comprehension are correlated with normalized volume and mean FA of each tract for each tractography algorithm.