# Structural disconnections associated with language impairment in chronic aphasia


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## Introduction and aim

As language function relies on a complex network, analyzing residual white matter connections between brain regions is an important key to understand language impairment in post-stroke aphasia[1].

However, few studies investigated the relationship between seemingly spared but directly disconnected white matter pathways and language impairments in chronic aphasia. Probabilistic maps of disconnection based on anatomical connectomes of healthy controls are a complementary method to measure the impact of the lesion on neural circuits[2].

**Aim of this study**: to examine the relationship between the location and the degree of structural disconnection in white matter tracts and language deficits in persons with chronic aphasia (PWA).

## Methods

### Participants

- 76 PWA resulting from a single left-hemisphere stroke were recruited in 3 research sites (Boston, John Hopkins, and Northwestern Universities).

| Site | N | Gender | | AQ | | Age | | Education | | MPO | | Handedness* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | F | M | Mean | Std | Mean | Std | Mean | Std | Mean | Std | |
| BU | 34 | 10 | 24 | 62.5 | 24.7 | 62.0 | 10.8 | 15.1 | 2.1 | 61.6 | 86.3 | 31R-3L |
| JHU | 23 | 7 | 16 | 77.2 | 21.0 | 60.4 | 9.9 | 16.4 | 1.7 | 84.9 | 57.0 | 18R-3L-2A |
| NU | 19 | 7 | 12 | 74.2 | 13.1 | 49.3 | 10.6 | 16.6 | 2.5 | 47.1 | 32.4 | 16R-3L |

AQ = aphasia quotient, MPO = Months post-stroke onset
*R=right, L=left, A=ambidextrous

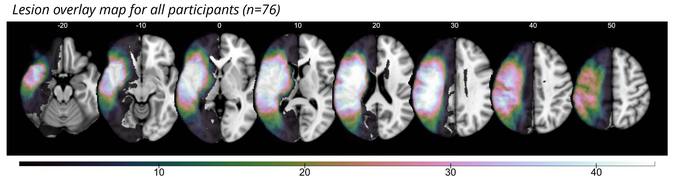
### Language testing

- Western Aphasia Battery-Revised (WAB)[3]
- Northwestern Assessments of Verbs and sentences (NAVS)[4]
- Psycholinguistic Assessments of Language Processing in Aphasia (PALPA)[5]

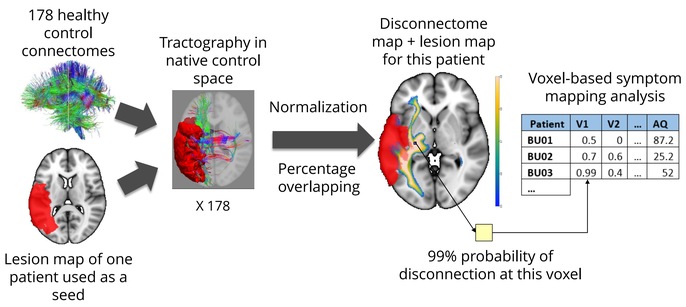
### Imaging data acquisition and processing

- 3T systems, high resolution T1-weighted 3D sagittal volumes using an MPRAGE sequence (TI/TE/TR = 900/2.91/2300ms, FOV = 256x256mm, voxel resolution = 1x1x1mm$^3$, 176 sagittal slices, phase encoding direction=A/P)
- Lesions were drawn manually slice-by-slice on T1-weighted images.

*Lesion overlay map for all participants (n=76)*




- A probability map of white matter tracts' disconnection was computed for each participant with the *Disconnectome map* tool of the BCBToolkit[2] using tractograms of 178 healthy controls from the Human Connectome Project (7T, www.humanconnectomeproject.org).

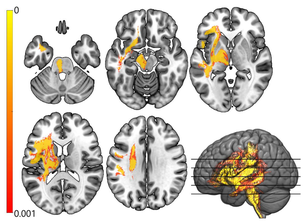



### Statistical analysis

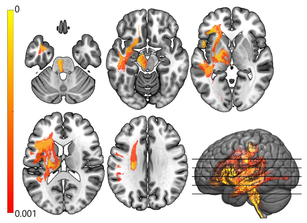
- Nonparametric permutation inference between:
  - **probability of white matter disconnection** (disconnectome maps)
  - each **language domain** (WAB: aphasia severity, auditory verbal comprehension, repetition, naming; NAVS: sentence comprehension test (SCT), sentence production priming test (SPPT); PALPA-subtest 40: spelling)
  - Demographic variables and lesion size included as covariates of no interest in the general linear model
- Family-wise error rate controlled at p<0.001 + Bonferroni correction at p<0.01 to control for multiple comparison.
- Identification of the proportion of each disconnected tract significantly correlated with each language score: *Tractotron* tool from the BCBToolkit[2].

## Results

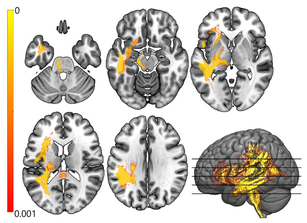
**WAB - Aphasia severity**



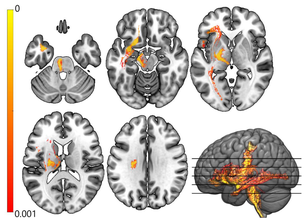

**WAB – Auditory verbal comprehension**



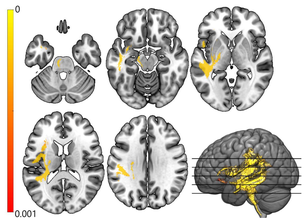

**NAVS – Sentence comprehension**



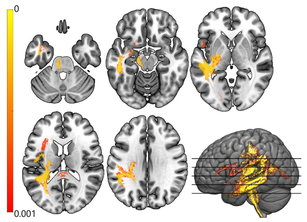

**WAB – Confrontation naming**



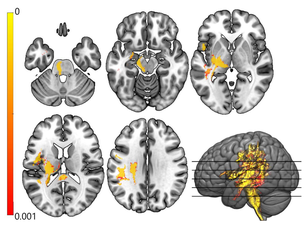

**WAB - Repetition**




**NAVS – Sentence production**




**PALPA40 - spelling**




**Statistical mapping of white matter disconnections associated with language scores in individuals with chronic aphasia**

These statistical maps show the result of **the mass-univariate correlation between the probability of white matter disconnection (disconnectome maps)** and each **language score**.
Disconnectome maps included in the model were thresholded at 50%, which means that, at each voxel, at least 50% of controls had a reconstructed fiber tract that entered the lesion mask of the patient. Color bars indicate p-values ranged from 0.001 to 0.

- All language scores were significantly negatively correlated with disconnections in left hemisphere white matter tracts. The higher the disconnection probability, the lower the language score.
- Disconnected tracts contributing most to all language impairments were left Fronto-insular tract 3, left corticospinal tract and pons left.
- Disconnection of left Arcuate fasciculi and Superior Longitudinal Fasciculus (SLF) III affected all language impairments except naming.
- Disconnection of left Inferior Longitudinal Fasciculus (ILF) and Inferior Fronto-Occipital Fasciculus (IFOF) seemed to contribute more to comprehension deficits (nouns and sentences).
- Disconnection of the left Uncinate Fasciculus seemed to affect more naming and comprehension.

**Proportions of disconnected tracts significantly correlated with aphasia severity and specific language impairments**

| Tracts | AQ | WAB naming | WAB repetition | WAB comp | NAVS SCT | NAVS SPPT | PALPA40 |
|---|---|---|---|---|---|---|---|
| Anterior Commissure | 19% | 20% | 5% | 22% | 21% | 12% | 8% |
| Anterior Thalamic Projections Left | 22% | 10% | 1% | 23% | 8% | 3% | 6% |
| Arcuate Anterior Segment Left | 19% | 1% | 9% | 10% | 15% | 10% | 12% |
| Arcuate Long Segment Left | 19% | 1% | 18% | 18% | 33% | 28% | 11% |
| Arcuate Posterior Segment Left | 9% | 0% | 15% | 12% | 27% | 23% | 7% |
| Cingulum Left | 2% | 1% | 0% | 2% | 3% | 1% | 2% |
| Corpus callosum | 4% | 1% | 2% | 4% | 5% | 3% | 2% |
| Cortico Spinal Left | 42% | 24% | 9% | 39% | 16% | 15% | 20% |
| Face U tract Left | 8% | 0% | 0% | 3% | 0% | 0% | 1% |
| Fornix | 8% | 10% | 2% | 13% | 13% | 9% | 3% |
| Frontal Aslant Tract Left | 18% | 3% | 2% | 19% | 6% | 3% | 3% |
| Frontal Commissural | 2% | 1% | 0% | 3% | 1% | 1% | 1% |
| Frontal Inferior longitudinal Left | 8% | 0% | 0% | 8% | 1% | 0% | 0% |
| Frontal Orbito Polar Left | 12% | 14% | 2% | 18% | 6% | 0% | 0% |
| Fronto Insular tract3 Left | 68% | 34% | 39% | 67% | 55% | 33% | 51% |
| Fronto Insular tract4 Left | 43% | 5% | 25% | 34% | 32% | 18% | 26% |
| Fronto Insular tract5 Left | 34% | 3% | 26% | 16% | 31% | 25% | 14% |
| Fronto Striatal Left | 21% | 10% | 3% | 22% | 9% | 4% | 6% |
| Hand inferior U tract Left | 13% | 0% | 2% | 3% | 3% | 2% | 14% |
| Hand superior U tract Left | 3% | 2% | 0% | 3% | 5% | 2% | 5% |
| IFOF Left | 16% | 10% | 7% | 19% | 18% | 10% | 2% |
| ILF Left | 6% | 5% | 4% | 10% | 13% | 10% | 1% |
| Optic Radiations Left | 7% | 9% | 6% | 12% | 22% | 18% | 7% |
| Pons Left | 39% | 21% | 9% | 39% | 20% | 15% | 20% |
| SLF III Left | 33% | 5% | 17% | 27% | 30% | 21% | 15% |
| SLF II Left | 10% | 2% | 4% | 7% | 16% | 11% | 10% |
| SLF I Left | 3% | 1% | 1% | 3% | 5% | 3% | 5% |
| Uncinate Left | 21% | 18% | 4% | 25% | 16% | 4% | 0% |

## Conclusion

In post-stroke chronic aphasia:

- **Disconnectome mapping is an informative tool to understand the impact of the lesion on seemingly intact but disconnected parts of the brain.**
  - Direct structural disconnections of left perisylvian fiber pathways seem to be associated with more severe language impairments in aphasia.
- **Disconnectome mapping is a complementary tool that could be further explored in order to be transferred in a clinical setting.**
  - It is based on lesion maps from T1-weighted images, which is a common imaging sequence acquired during stroke clinical evaluation.

Future studies should further investigate the role of disconnected regions and pathways on the functional reorganization of brain networks after stroke.

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## References


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