White matter matters in the recovery of language in post-stroke aphasia

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Background
- Lesion size has been highlighted as a critical predictor of language outcome in persons with stroke-induced aphasia (PWA)1-2
- Lesion symptom-mapping studies have implicated specific gray matter (GM) structures in certain language skills (e.g., naming, lexical-semantics)3-4
- Due to structural disconnects, metrics of regional white matter (WM) integrity may be more powerful predictors of language skills in PWA than GM metrics alone5-10
- However, the potential compensation by remaining GM and WM left hemisphere (LH) structures, and their right hemisphere (RH) homologues11-12 has received little attention in the context of naming in patients with anoma

Research Questions (RQs)

**RQ #1:** To what extent does the integrity of core LH WM regions differ from RH homologues in PWA?
- Hypothesis: Fractional anisotropy (FA): LH < RH; mean diffusivity (MD): LH > RH

**RQ #2a:** What is the relationship between bilateral GM and WM integrity and (a) aphasia severity and (b) naming skills in PWA?
- Hypothesis: All LH ROIs will predict aphasia severity whereas the strongest predictors of naming will be middle temporal and inferior frontal areas and their RH homologues13-14

**RQ #2b:** What type of LH model is best for predicting language?
- Hypothesis: GM+WM model will better predict language than either GM only or WM only models10

Participants
- 27 PWA (17M, 24 right-handed, mean age = 62.3 ± 10.5 years, time post CVA onset = 55.0 ± 52.1 months)
- The Western Aphasia Battery-Revised15 was used to index overall aphasia severity via the Aphasia Quotient (AQ)
- A 180-item non-standardized picture naming probe was administered to assess naming abilities
- PWA ranged in severity of aphasia and naming impairment as well as size and location of lesion

Lesion overlap (n = 27 PWA)

**Methods: MR Data Acquisition**
- Images acquired on a 3T Siemens Trio Tim scanner with a 20-channel coil
- T1-weighted (TR/TE = 2300/2.91ms, slice thickness = 1mm, 176 sagittal slices), TR-FLAIR (TR/TE = 9000/90ms, slice thickness = 5mm, 36 slices, acceleration x2) and DTI (TR/TE = 900ms/92ms, slice thickness = 2mm, 70 interleaved slices, b = 1000 s/mm²) scans collected
- Eight regions of interest (ROIs, i.e., ACC; superior, middle, and inferior frontal gyri [SFG, MFG, IFG]; middle and inferior temporal gyri [MTG, ITG]; and supramarginal and angular gyri [SMG and AG]) were identified and masks were extracted from the Harvard-Oxford (H-O) cort-maxprob-thr0,1mm template

**Methods: MRI Data Processing**
- Cortical gray matter
  - Lesion masks (lesion = 0) & maps (lesion = 1) manually drawn for each patient in MRcron
  - Lesion masks & maps used in segmentation and normalization
- GM integrity metrics:
  - Lesioned LH ROIs generated for each patient
  - Cortical integrity calculated by % spared tissue (H-O ROI volume – normalized lesion volume) / (H-O ROI volume) in MarsBar

**RQ #1 Results: WM Metrics by Hemisphere**
- FA by Hemisphere
  - FA significantly lower in LH than RH ROIs (F(1,52) = 10.15, p < .001) except for ACC (F(1,52) = 0.32, p = 0.58)
- MD by Hemisphere
  - MD was significantly higher in LH than RH ROIs (F(1,52) = 5.77, p < .001)

**RQ #2 Results: Language Predictions**
- Six components resulted from the PCA including all LH metrics (i.e., FA, MD, and %spared tissue)
- Metrics from certain adjacent regions loaded together

**Conclusions**
- Integrity metrics of LIFG and LH dorsomedial prefrontal regions were the strongest predictors of both aphasia severity and naming
- LMSG and LAG—highly damaged regions in this sample—also predicted AQ
- GM metrics (per PCA components) did not independently predict language skill
- For naming, the WM only and GM+WM models did not differ in predictive power
- WM integrity of LIFG and LACG is likely most critical for word retrieval16
- WM integrity of cortical ROIs (e.g., LAG, LMSG, and LMTG) aligns with established WM tracts like the arcuate fasciculus
- Next steps include determining the utility of regional versus en masse integrity metrics in predicting language therapy outcomes

**Selected References**

Acknowledgments

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**Images and Data**

- [Image 58x400 to 414x495](image1.png)
- [Image 339x58 to 627x197](image2.png)
- [Image 974x862 to 1281x1014](image3.png)
- [Image 982x787 to 1272x847](image4.png)
- [Image 983x471 to 1263x687](image5.png)

**Table 1:**
<table>
<thead>
<tr>
<th>Region</th>
<th>FA (LH)</th>
<th>FA (RH)</th>
<th>MD (LH)</th>
<th>MD (RH)</th>
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<td>ACC</td>
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<td>0.84</td>
<td>0.91</td>
<td>0.87</td>
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<tr>
<td>SFG</td>
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<tr>
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<tr>
<td>IFG (LH)</td>
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<td>0.86</td>
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<tr>
<td>MTG</td>
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<tr>
<td>ITG</td>
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<tr>
<td>SMG</td>
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**Table 2:**
- **Research Questions (RQs)**
  - **Background**
  - **Participants**
  - **Methods: MR Data Processing**
  - **RQ #1 Results: WM Metrics by Hemisphere**
  - **RQ #2 Results: Language Predictions**
  - **Conclusions**

**References**