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Meier, Erin L.
Boston University

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The relationship between frontotemporal effective connectivity during picture naming, behavior, and preserved cortical tissue in chronic aphasia

Erin L. Meier¹, Kushal J. Kapse², & Swathi Kiran¹

Boston University, Sargent College of Health and Rehabilitation Sciences¹; Children’s National Medical Center, Washington D.C.²

Introduction

- The integrated functioning of anatomically segregated anterior and posterior left-lateralized brain regions is vital for successful language processing (e.g., Friston, 2011; Price, 2012; Vigneau et al., 2006)

- Damage secondary to stroke forces neural reorganization of brain function and brain structure in persons with aphasia (PWA)

- In PWA, damage impacts the degree to which PWA recruit “classic” language regions such as LMTG and LlFG yet PWA recruit regions outside the traditional language network, such as LMFG, regardless of the extent of damage (Turkeltaub et al., 2011)

- Language is processed in a network but… very little is known about:
  - The dynamic interactions between these regions for picture naming or how
  - Task-based connectivity relates to structural damage and naming abilities

Study Aims

1) To investigate the nature of task-specific left hemisphere cortical reorganization in PWA relative to intact language networks in healthy individuals by examining effective connectivity via Dynamic Causal Modeling (Friston, Harrison, & Penny, 2003)

2) To examine the relationship between connectivity parameters, cortical structural damage and behavioral performance

Participants

- 13 participants with chronic aphasia secondary to left hemisphere CVA and 10 neurologically-intact controls participated in the study

- PWA were administered a battery of tests assessing overall aphasia severity (Western Aphasia Battery-Revised, WAB-R) and naming skills (e.g., Boston Naming Test, BNT; picture naming screener)

<table>
<thead>
<tr>
<th>ID</th>
<th>Age</th>
<th>Gender</th>
<th>Handedness</th>
<th>MPO</th>
<th>WAB-R</th>
<th>AQ</th>
<th>Picture Naming Screener (%avg)</th>
<th>BNT (%)</th>
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<tbody>
<tr>
<td>PWA1</td>
<td>56.28</td>
<td>M</td>
<td>R</td>
<td>17</td>
<td>87.2</td>
<td></td>
<td>47.22</td>
<td>81.67</td>
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<tr>
<td>PWA2</td>
<td>59.52</td>
<td>F</td>
<td>L</td>
<td>33</td>
<td>25.2</td>
<td></td>
<td>1.54</td>
<td>1.67</td>
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<td>78.39</td>
<td>M</td>
<td>R</td>
<td>13</td>
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<td>65.12</td>
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<td>R</td>
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<td>M</td>
<td>L</td>
<td>138</td>
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<td></td>
<td>14.81</td>
<td>10.00</td>
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<td>M</td>
<td>L</td>
<td>59</td>
<td>82.8</td>
<td></td>
<td>68.21</td>
<td>85.00</td>
</tr>
<tr>
<td>PWA7</td>
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<td>F</td>
<td>R</td>
<td>39</td>
<td>95.2</td>
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<td>46.60</td>
<td>75.00</td>
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<td>53.25</td>
<td>F</td>
<td>R</td>
<td>14</td>
<td>80.4</td>
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<td>R</td>
<td>19</td>
<td>92.7</td>
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<td>46.60</td>
<td>71.67</td>
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<tr>
<td>PWA10</td>
<td>71.25</td>
<td>F</td>
<td>R</td>
<td>75</td>
<td>67.2</td>
<td></td>
<td>41.05</td>
<td>71.67</td>
</tr>
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<td>50.00</td>
<td>M</td>
<td>R</td>
<td>71</td>
<td>33.6</td>
<td></td>
<td>0.93</td>
<td>1.67</td>
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<tr>
<td>PWA12</td>
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<td>M</td>
<td>R</td>
<td>155</td>
<td>74.3</td>
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<td>45.99</td>
<td>1.67</td>
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<tr>
<td>PWA13</td>
<td>79.39</td>
<td>M</td>
<td>R</td>
<td>12</td>
<td>26.9</td>
<td></td>
<td>6.48</td>
<td>n/a</td>
</tr>
</tbody>
</table>

Mean: 60.66 M 50.38 F 64.5 34.54 49.25

Stdev: 11.95 11.5 8.38 7.2 7.24 6.67

Table 1. Demographic & behavioral information for PWA and controls

MRI Data Acquisition

- MR images were acquired on a Siemens Trio TIM with a 20-channel head+neck coil

- T1 images were acquired with the following parameters: TR = 2300ms, TE = 2.91ms, 176 sagittal slices, 1x1x1mm voxels

- Functional images were acquired with the following parameters: TR = 2570ms, TE = 30ms, 40 axial slices, interleaved with 2x2x3mm voxels

- All participants completed 2 runs of an overt picture-naming task including experimental stimuli from 3 of 5 categories (i.e., birds, vegetables, fruit, clothing, and furniture)
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fMRI Data Analysis
- SPM8 was used for fMRI analysis; lesion masks were hand-drawn in MRICron

Preprocessing
- Slice timing correction
- Realignment with registration to mean
- Coregistration:
  - Structural to mean functional image
  - Lesion mask and lesion map coregistered to PWA’s structural image
- Segmentation
- Normalization
- ART Repair as needed

Statistical Analysis in SPM
- 1st level GLM analysis:
  - Modeled three conditions:
    - Canonical HRF + TD
    - Contrast of interest: pictures – scrambled
- 2nd level analysis:
  - Within-group one-sample t-tests
  - Contrast of interest: pictures – scrambled

Spared Tissue Calculation
- Required preserved lesion via normalized lesion maps
- Percentage of spared tissue = (Anatomical AAL ROI volume – normalized lesion volume) / (Anatomical AAL ROI volume) in MarsBaR

fMRI Results: Whole Brain Activation
- Results of group one-sample t-tests for pictures (experimental) > scrambled pictures (control) at an uncorrected for (A) PWA and (B) Controls
- Similar activation seen in bilateral frontal, temporal and parietal regions in each group
- Results of single-subject overlays for the same contrast in (C) PWA and (D) Controls → peak maxima per region used in DCM analysis

Dynamic Causal Modeling (DCM)

VOI Selection
- VOIs selected in 3 regions: LIFG, LMFG & LMTG
- VOI = 8mm sphere eigenvariate

Model Specification
- Bilinear, two-state, center input & non-stochastic
- All regions interconnected (A)
- Effect of pictures on regions (C) and connections (B)

Partitioning
- 3 families, each with driving input to 1 of the 3 regions
  - Family #1: Input LIFG
  - Family #2: Input LMFG
  - Family #3: Input LMTG

Family-wise BMS
- Family-wise Bayesian Model Selection (BMS) performed to determine which set of models best fit the data (Penny et al., 2010)

BMA
- Bayesian Model Averaging (BMA) within each family yields values reflecting task-induced input (Ep.C) and connection (Ep.B) strength

Inference
- ANOVAs to examine group differences in Ep.C & Ep.B
- Spearman correlations run between Ep.C/Ep.B, %spared, & behavioral measures

MRI Results: Lesion Characteristics

Table 2. %Spared Tissue per Region in PWA

<table>
<thead>
<tr>
<th>Region</th>
<th>LIFG</th>
<th>LMFG</th>
<th>LMTG</th>
</tr>
</thead>
<tbody>
<tr>
<td>PWA 1</td>
<td>96.60</td>
<td>100.00</td>
<td>79.36</td>
</tr>
<tr>
<td>PWA 2</td>
<td>65.51</td>
<td>96.26</td>
<td>68.09</td>
</tr>
<tr>
<td>PWA 3</td>
<td>99.05</td>
<td>100.00</td>
<td>33.51</td>
</tr>
<tr>
<td>PWA 4</td>
<td>80.25</td>
<td>100.00</td>
<td>14.16</td>
</tr>
<tr>
<td>PWA 5</td>
<td>92.47</td>
<td>96.44</td>
<td>70.38</td>
</tr>
<tr>
<td>PWA 6</td>
<td>89.59</td>
<td>100.00</td>
<td>78.15</td>
</tr>
<tr>
<td>PWA 7</td>
<td>99.98</td>
<td>100.00</td>
<td>93.91</td>
</tr>
<tr>
<td>PWA 8</td>
<td>100.00</td>
<td>100.00</td>
<td>91.80</td>
</tr>
<tr>
<td>PWA 9</td>
<td>99.98</td>
<td>100.00</td>
<td>97.00</td>
</tr>
<tr>
<td>PWA 10</td>
<td>80.77</td>
<td>73.95</td>
<td>99.66</td>
</tr>
<tr>
<td>PWA 11</td>
<td>49.15</td>
<td>51.04</td>
<td>12.55</td>
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<tr>
<td>PWA 12</td>
<td>58.68</td>
<td>98.66</td>
<td>46.11</td>
</tr>
<tr>
<td>PWA 13</td>
<td>53.89</td>
<td>98.75</td>
<td>99.92</td>
</tr>
<tr>
<td>TOTAL AVG</td>
<td>81.99</td>
<td>93.47</td>
<td>68.05</td>
</tr>
</tbody>
</table>

- Across PWA, most spared tissue was in LMFG
- Least spared tissue was in LMTG yet the relative preservation of LMTG and LIFG different from PWA to PWA
- The values to the left reflect the amount of spared tissue in each cortical region of interest and were used in subsequent analyses
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**DCM Results**

RQ1: Differences in effective connectivity between PWA and controls

- Group-Level Family-Wise BMS
  - PWA: Controls
  - Family 1: Input LIFG, Family 2: Input LMFG, Family 3: Input LMTG

RQ2: Relationship between input strength (Ep.C), behavior, & spared tissue in PWA

- No significant differences between groups in perturbation strength (Ep.C)
  - Ep.C = .009Hz for PWA
  - Ep.C = .031Hz for Controls

- For connections, PWA had significantly less task-induced coupling from LMTG to LIFG (Ep.B) relative to controls (F(1,63) = 6.75, p < .05); this effect was observed across families

**Conclusions**

- Differences between groups in network connectivity
  - Controls: family #1 best-fit indicative of...
    - Greater demands on top-down control processes for healthy older adults (Meinzer et al., 2009, 2012; Park & Reuter-Lorenz, 2009) OR
    - The need to rely on LIFG to resolve competition between many active lexical representations (e.g., Thompson-Schill et al., 1997)
  - PWA: family #2 best-fit indicative of...
    - The functional role of LMFG
    - The relative preservation of LMFG compared to LIFG and LMTG

- Relationship between connectivity parameters, spared tissue & behavior
  1) > tissue in “classic” language regions related to > task-induced perturbation of these regions
  2) > task accuracy related to > task-induced perturbation of LIFG and LMFG
  3) > spared tissue significantly related to > modulatory effects for a connection that included the region
  4) > preserved tissue & > task performance, the more inhibitory the connections between regions
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References


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