Changes in Functional Connectivity Associated with Treatment Gains in Aphasia

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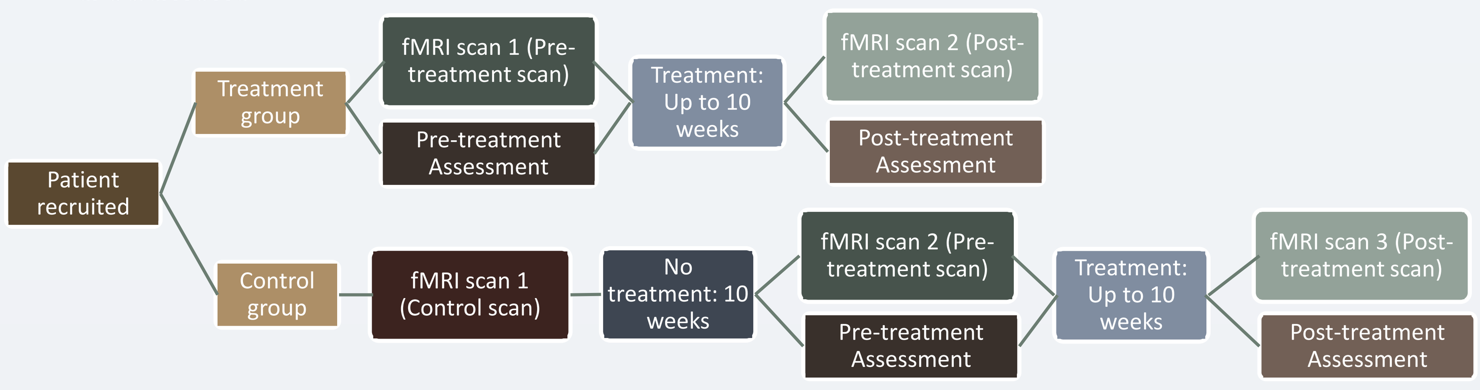
Introduction

- Persons with aphasia (PWA) who are trained to generate abstract words (e.g., justice) in a specific context-category (e.g., courthouse) have been shown to improve not only on the trained items, but also on concrete words (e.g., lawyer) in the same context-category (Kiran, Sandberg, & Abbott, 2009).
- However, the underlying neural mechanism of this generalization effect is unknown.
- The current study examined the neural activation and functional connectivity patterns of abstract and concrete word processing in PWA before and after training abstract word retrieval to shed some light on this phenomenon.

Methods

Participants

- Eight right-handed persons with chronic aphasia (> 6 mos post) secondary to left hemisphere stroke (3 F, mean age: 58)
- All participants were scanned using fMRI before and after a theory-based treatment

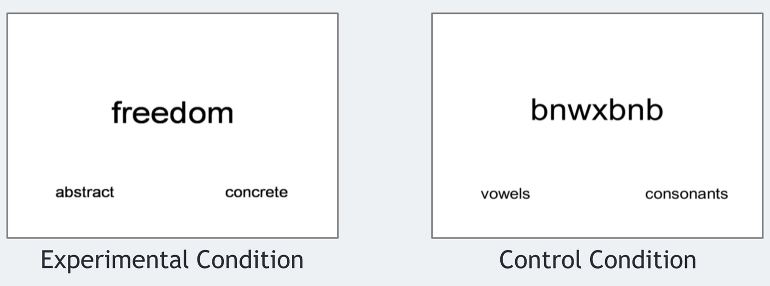


Treatment

- Based on the Complexity Account of Treatment Efficacy (Thompson, Shapiro, Kiran, & Sobecks, 2003)
- Consisted of training abstract words in a specific context-category for up to 10 weeks
- Criterion for stopping treatment before 10 weeks = 80% accuracy for 2 weeks in a row

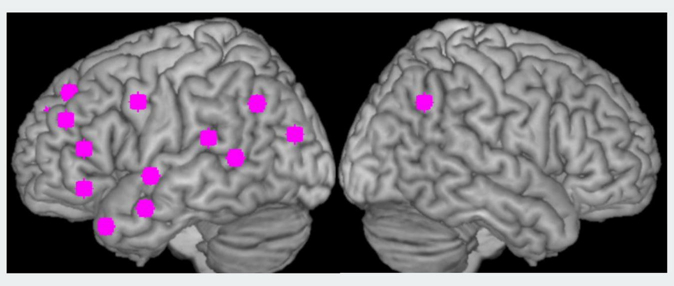
fMRI Task

- Word Judgment



Data Analysis

- GLM in SPM8
  - Contrasts
    - Post-treatment Abstract > Pre-treatment Abstract
    - Post-treatment Concrete > Pre-treatment Concrete
- Task-related functional connectivity
  - CONN toolbox for SPM8
  - Functional ROIs = 5 mm sphere around peak activation voxels elicited during general word processing (i.e., abstract + concrete > control)
    - Used meta-analyses of abstract and concrete word processing (Binder, Desai, Graves, & Conant, 2009; Wang, Conder, Blitzer, & Shinkareva, 2010), our own work in healthy older adults (Sandberg & Kiran, 2013), and patients' own activations as a guide



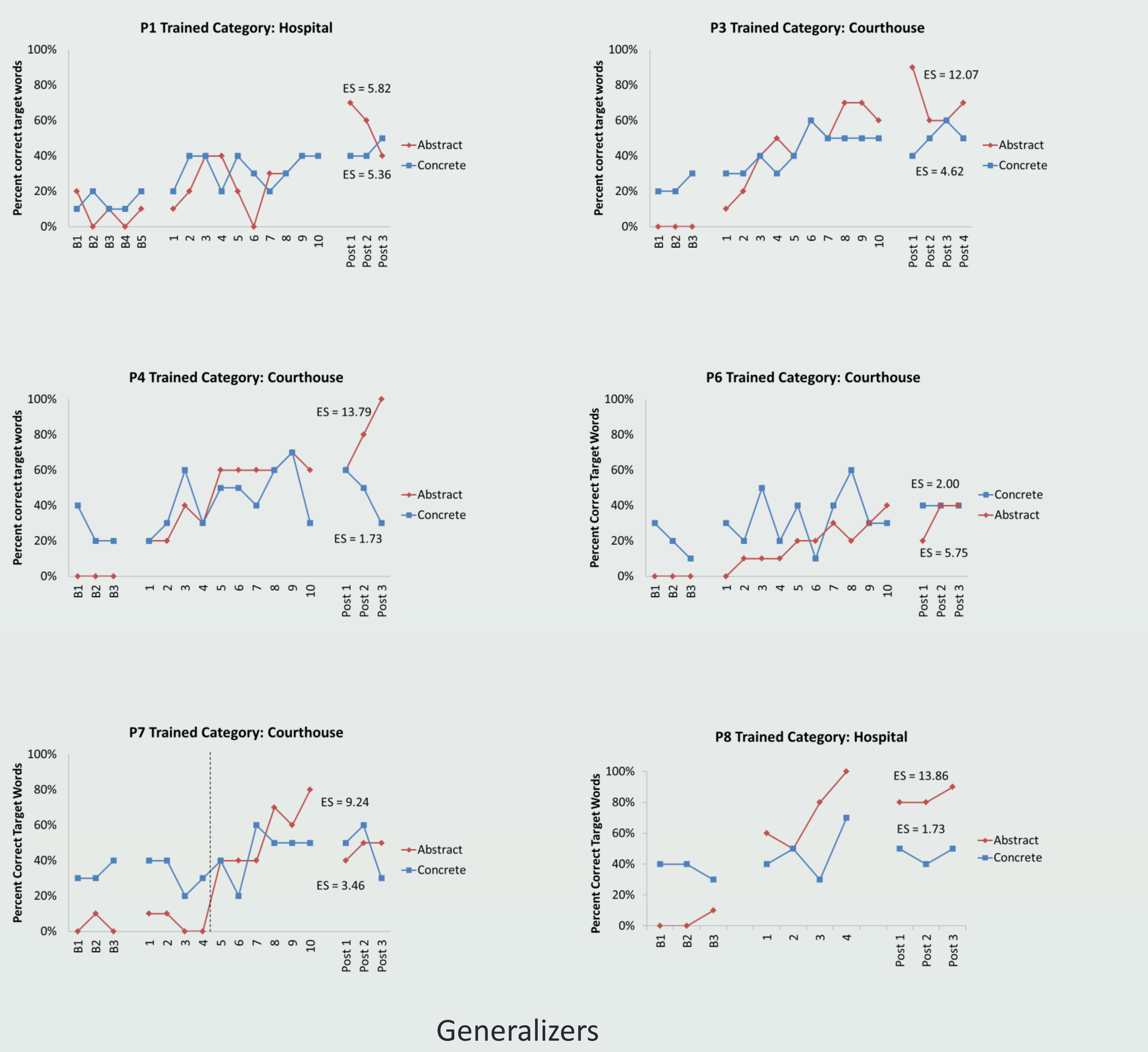
  - Conducted semipartial ROI-ROI correlations individually for each patient to create 4 networks:

Pre-treatment	Post-treatment
1. Abstract	3. Abstract
2. Concrete	4. Concrete

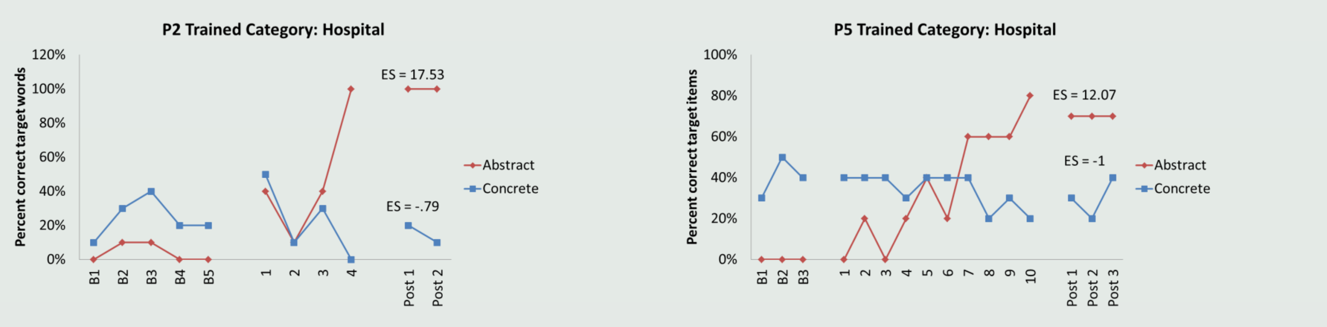
  - Pre-treatment matrix subtracted from post-treatment matrix to obtain increases in connectivity
    - Thresholded changes at 2 SD away from the mean

Treatment Results

- All eight patients improved on the trained abstract words
- Six patients also improved on the untrained concrete words in the same context-category = Generalizers
- Two patients did not improve on the untrained concrete words = Non-generalizers



Non-generalizers



fMRI Results

All eight patients showed increases in activation from pre to post

- Areas included those normally activated for abstract and concrete word processing
- The highest agreement among PWA was 3/8
- There is a high level of overlap for increases in activation for abstract and concrete words

Abstract Regions	Binder	Wang	NHOA	PWA
Left Superior Medial Gyrus			✓	3
Left Middle Frontal Gyrus			✓	1
Left SMA			✓	1
Left Precentral Gyrus			✓	3
Left Inferior Frontal Gyrus p. Triangularis	✓	✓	✓	1
Left Inferior Frontal Gyrus p. Orbitalis	✓	✓	✓	3
Left Middle Occipital Gyrus			✓	2
Other Active Regions				
Left Superior Frontal Gyrus				3
Left Postcentral Gyrus				3
Left Precuneus				3

Concrete Regions	Binder	Wang	NHOA	PWA
Left Superior Medial Gyrus	✓		✓	1
Left Superior Frontal Gyrus	✓			2
Left Middle Frontal Gyrus	✓		✓	2
Left SMA			✓	1
Left Inferior Frontal Gyrus p. Triangularis			✓	2
Left Inferior Frontal Gyrus p. Orbitalis			✓	3
Left Angular Gyrus	✓			1
Right Angular Gyrus	✓			1
Left Middle Occipital Gyrus			✓	3
Left Precuneus		✓		2
Left Calcarine				2
Other Active Regions				
Left Precentral Gyrus				3
Right Postcentral Gyrus				3
Right Superior Parietal Lobule				3
Right Inferior Temporal Gyrus				3

Figure 1. **Tally of PWA who show increases in predetermined abstract and concrete regions (and consensus of other regions) after treatment**

Functional Connectivity Results

Across patients, there appear to be more intra- than inter-hemispheric connections changing as a function of treatment

- Of these, there appear to be more LH-LH than RH-RH changes

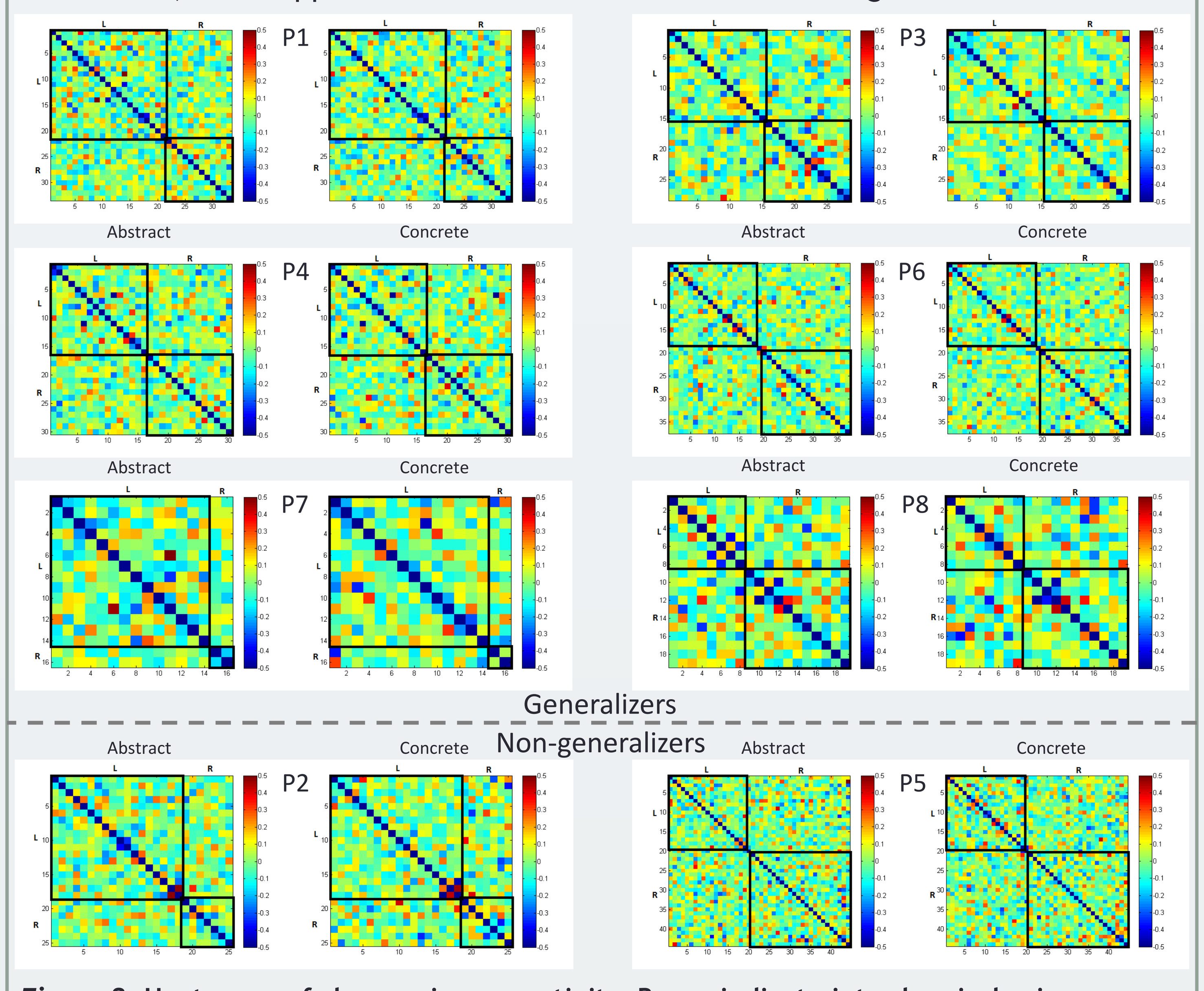


Figure 2. **Heat maps of changes in connectivity. Boxes indicate intra-hemispheric connections. Red indicates increases in connectivity, blue indicates decreases in connectivity. 2 SD away from mean ≈ .25**

When changes that cross threshold (2 SD) are tallied and averaged across patients,

- LIFGtri appears to be an important node for positive changes, especially in the trained abstract network
- Differences between generalized and non-generalized networks surface:

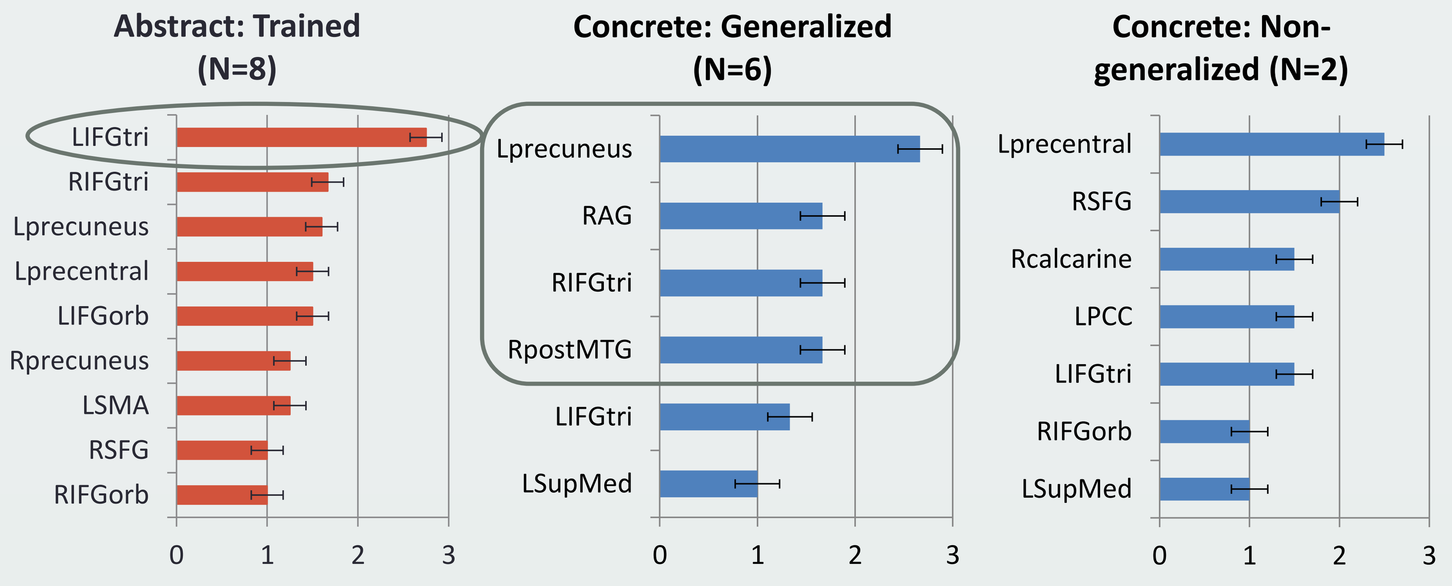


Figure 3. **Average number of connections that increase for each seed region.**

When connectivity change magnitude is calculated and averaged across patients,

- LH-LH > LH-RH LH-LH > RH-RH
- RH-LH > RH-RH RH-LH > LH-RH

This pattern is more prominent in the trained and generalized networks

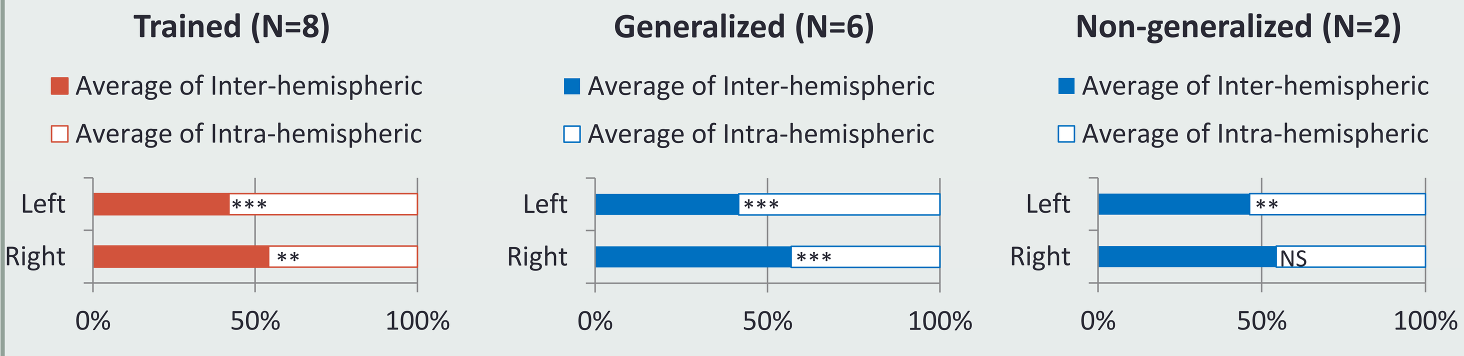


Figure 4. **Connectivity change magnitude (averaged within hemisphere) for trained (abstract), generalized (concrete), and non-generalized (concrete) networks.**

Conclusions

- Overall, behavioral gains in treatment are measurable as specific neural changes in fMRI and task-related functional connectivity in PWA (Figures 1 and 2).
- Furthermore, specific nodes in each network show changes in connectivity after treatment.
  - LIFGtri appears to be important for changes related to direct training, or abstract word training, for which all patients improved (Figure 3).
- Additionally, there is a higher degree of change in within-hemisphere connections in the left hemisphere and a shift to a higher magnitude of change in the right- to left- hemisphere connections for both the trained (abstract) and generalized (concrete) networks (Figure 4).
- Generalizers and non-generalizers appear to show different patterns of change in the untrained concrete network (Figures 3 and 4).

Acknowledgments

This work was supported by an NIDCD F31 NRSA and the Dudley Allen Sargent Research Fund

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