Effective connectivity of the naming network in post-stroke chronic aphasia

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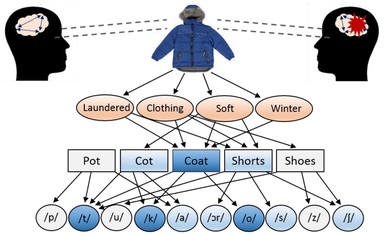
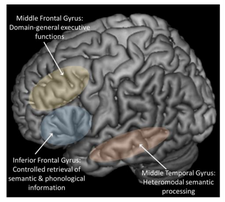
Introduction

- 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)
- Specifically, in the context of oral picture naming, the left middle temporal gyrus (LMTG) has been implicated in conceptual processing and the left inferior prefrontal gyrus (LIFG) has been found to be critical in controlled processing of semantic and phonological information (e.g., Indefrey & Levelt, 2004; Thompson-Schill et al., 1997; Wagner et al., 2001)
- Additionally, activation in regions associated with domain-general cognitive control, such as left middle frontal gyrus (LMFG), has been found for demanding language tasks, including picture naming (e.g., Fedorenko & Thompson-Schill, 2014; Murtha et al., 1999)
- During naming, multiple lexical and sub-lexical representations may be activated, and the cooperation of all aforementioned regions is required to generate a correct response
- Focal lesions to critical brain regions within this distributed network disrupt retrieval processes (Jefferies & Lambon Ralph, 2006)





- While it is known that a picture naming task would activate regions involved in cognitive control such as LMFG, lexical selection such as LIFG, and semantic processing regions such as LMTG, little is known about the dynamic connectivity of this activation in persons with aphasia (PWA)

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 also 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)

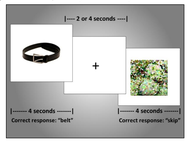
ID	Age	Gender	Handedness	MPO	WAB-R Aphasia Quotient (AQ)	Picture Naming Screener (%avg)	BNT (%)
PWA1	56.28	M	R	17	87.2	47.22	81.67
PWA2	50.62	F	L	33	25.2	1.54	1.67
PWA3	78.39	M	R	13	74.1	65.12	86.67
PWA4	67.88	M	R	10	30.8	7.41	6.67
PWA5	55.32	M	R	138	48.0	14.81	10.00
PWA6	49.92	M	R	59	82.8	68.21	85.00
PWA7	72.01	F	R	39	95.2	46.60	75.00
PWA8	53.25	F	R	14	80.4	57.10	61.67
PWA9	42.75	M	R	19	92.7	46.60	71.67
PWA10	71.35	F	R	75	87.2	41.05	71.67
PWA11	50.00	M	R	71	33.6	0.93	1.67
PWA12	61.40	M	R	155	74.3	45.99	1.67
PWA13	79.39	M	R	12	26.9	6.48	n/a
Mean	60.66			50.38	64.5	34.54	46.25
Stdev	11.95			48.38	27.2	24.72	37.65

ID	Age	Gender	Handedness
C1	66.13	F	R
C2	66.83	M	R
C3	40.76	M	R
C4	54.76	F	R
C5	63.12	F	R
C6	68.97	F	R
C7	46.34	M	R
C8	75.94	M	R
C9	59.00	M	R
C10	73.49	M	R
Mean	61.53		
Stdev	11.41		

fMRI Methods

Data Acquisition and Analysis

- 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*)
- Lesion masks were hand-drawn in MRIcron
- SPM8 was used for fMRI analysis
- ART Repair within the SPM toolbox applied for volume displacement > 0.5mm



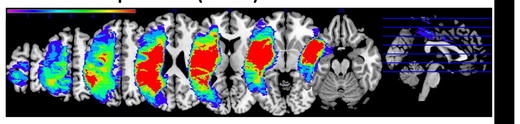
Preprocessing
- Slice timing correction: reference to middle slice
- Realignment: registration to mean
- Coregistration:
  - Structural to mean functional image
  - For PWA only, lesion mask (lesion deleted) and lesion map (lesion preserved)
- Segmentation:
  - Structural image
  - For PWA only, lesion mask
- Normalization: Subject > MNI

Statistical Analysis in SPM
- GLM: 1st level analysis:
  - 3 experimental conditions: 1) pictures, 2) scrambled & 3) fixation
  - Realignment parameters included as multiple regressors
  - Canonical HRF with its temporal derivative
  - Contrast of interest: pictures – scrambled

% Spared Tissue Calculation
- For each PWA, subtracted normalized lesion maps from the anatomical AAL maps
- ROI volumes calculated using MRIcron
- Calculated % spared tissue as (Anatomical AAL ROI volume – normalized lesion volume)/ (Anatomical AAL ROI volume) in MarsBaR

Lesion Information

Lesion Overlap in PWA (n = 13)



% Spared Tissue per Region in PWA

	LIFG	LMFG	LMTG
PWA 1	96.60	100.00	79.36
PWA 2	65.51	96.26	68.09
PWA 3	99.05	100.00	33.51
PWA 4	80.25	100.00	14.16
PWA 5	92.47	96.44	70.38
PWA 6	89.59	100.00	78.15
PWA 7	99.98	100.00	93.91
PWA 8	100.00	100.00	91.80
PWA 9	99.98	100.00	97.09
PWA 10	80.77	73.95	99.66
PWA 11	49.15	51.04	12.55
PWA 12	58.68	98.66	46.11
PWA 13	53.89	98.75	99.92
TOTAL AVG	81.99	93.47	68.05

- The values above reflect the amount of spared tissue in each cortical region of interest and were used in subsequent analyses

Dynamic Causal Modeling (DCM)

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

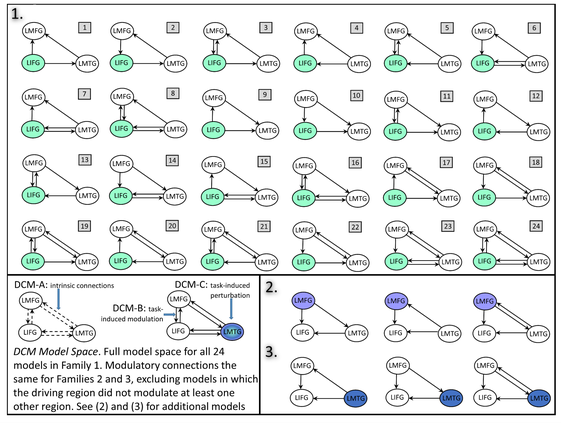
Model specification
- Bilinear, two-state, center input & non-stochastic
- All regions interconnected (A)
- Effect of pictures on regions (C) and connections (B)

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)

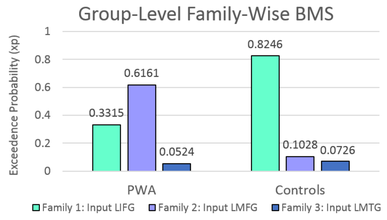
BMA
- Bayesian Model Averaging (BMA) within each family
- Yields values reflecting task-induced input (Ep.C) and connection (Ep.B) strength

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

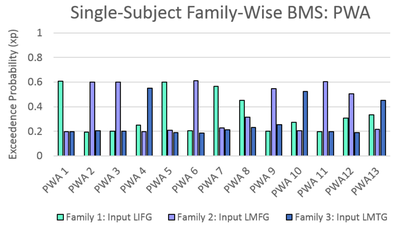


DCM Model Space. Full model space for all 24 models in Family 1. Modulatory connections the same for Families 2 and 3, excluding models in which the driving region did not modulate at least one other region. See (2) and (3) for additional models

Results: Differences between PWA & Controls



- Best-fit model family differed between groups



- Variability seen at individual level in PWA

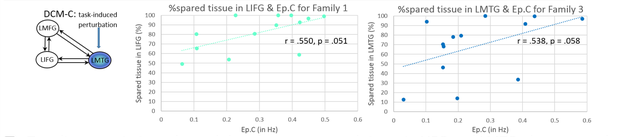
- No significant differences between groups in perturbation strength (Ep.C)
- For connections, PWA had significantly less task-induced coupling from LMTG to LIFG (Ep.B) relative to controls ($F(1,63) = 6.75$, $p = .012$); this effect was observed across families

Ep.B = -.009Hz for PWA

Ep.B = -.031Hz for Controls

Results: Results within PWA Group

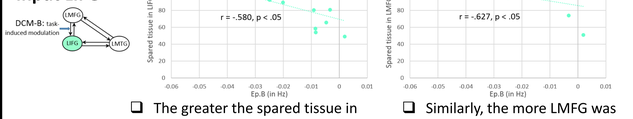
Correlations between % spared tissue and input strength



- Trending associations showed that the more spared tissue in LIFG and LMTG, the greater the effect of the task on those regions

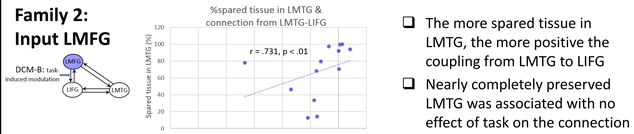
Correlations between % spared tissue and connection strength

Family 1: Input LIFG



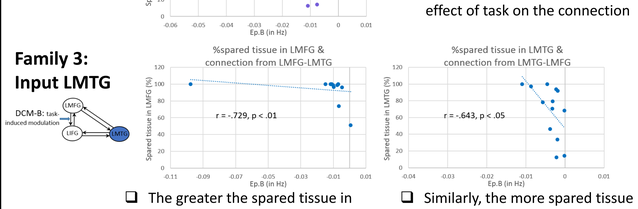
- The greater the spared tissue in LIFG, the more negative the task-induced coupling from LMFG to LIFG
- Similarly, the more LMFG was preserved, the more negative the coupling from LMFG to LIFG

Family 2: Input LMFG



- The more spared tissue in LMTG, the more positive the coupling from LMTG to LIFG
- Nearly completely preserved LMTG was associated with no effect of task on the connection

Family 3: Input LMTG



- The greater the spared tissue in LMFG, the more negative the coupling from LMFG to LMTG
- Similarly, the more spared tissue in LMTG, the more negative the coupling from LMTG to LMFG

Correlations between % spared tissue and behavior

	%LIFG spared tissue	%LMFG spared tissue	%LMTG spared tissue
WAB-R AQ	0.669*	0.412	0.489
BNT	0.665*	0.641*	0.427
Picture Naming Screener	0.741**	0.748**	0.195

* = p significant at < .05 ** = p significant at < .01 *** = p significant at < .001

- Greater spared tissue in LIFG was significantly associated with higher scores on all behavioral measures while greater spared tissue in LMFG was related with higher naming scores
- The amount of spared tissue in LMTG was not related to any of the behavioral measures

Conclusions

- The best-fit model families for each group indicate that PWA rely on more preserved LMFG to modulate other regions (e.g., Turkeltaub et al., 2011) while healthy older controls rely on regions associated with increased semantic control demands to drive naming (e.g., Velanova et al., 2006)
- Significantly less task-induced coupling between LMTG and LIFG was seen for PWA relative to controls, which may have been influenced by the amount of damage to LMTG across the group
- Greater spared tissue in a given region was typically associated with a reduction of information flow between regions, excluding the relationship between spared tissue in LMTG and the LMTG-LIFG connection
- Significant associations were found between behavioral accuracy and spared tissue in prefrontal regions but surprisingly, not with LMTG

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