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Functional imaging of neuroplasticity in aphasia

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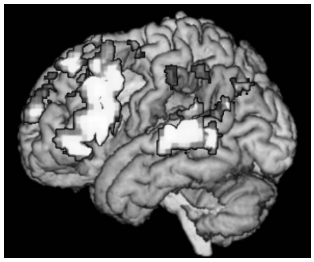
August 8, 2017

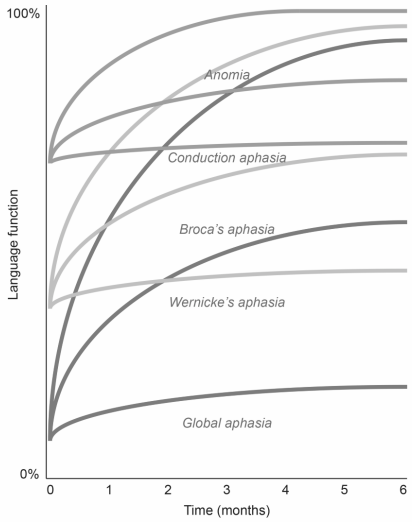


Learner outcomes

As a result of this course, participants will be able to:

1. Describe the neural substrates of language processing in the healthy brain.
2. Describe ways in which language processing is altered after brain damage.
3. Identify methodological challenges to research in neuroplasticity in aphasia.

In many patients with aphasia, language function improves over time.



Early improvements may reflect return to function of compromised brain areas.

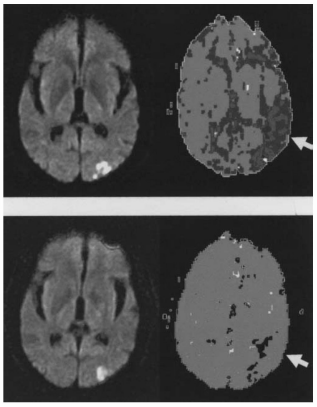
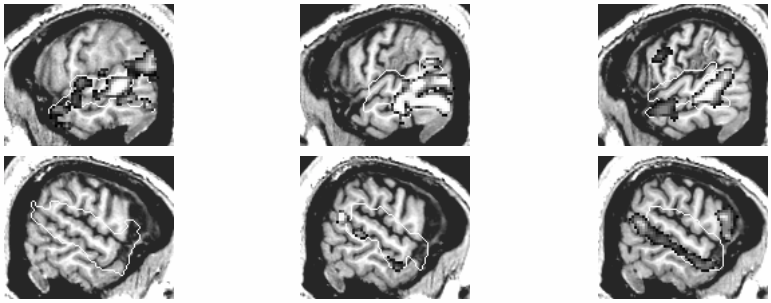


Figure 1. An illustrative case in which reperfusion of BA 37 was associated with an improvement of naming. Top, Day 1 DWI (left) and PWI (right) scans of a patient with impaired naming at day 1 of stroke. Bottom, DWI (left) and PWI (right) scans of the same patient on day 3, when naming had recovered. Dark green and blue areas on PWI are hypoperfused. Light green areas are normally perfused. The yellow arrow points to BA 37.

Hillis et al., 2006

But most improvements after 24 hours probably reflect functional reorganization.



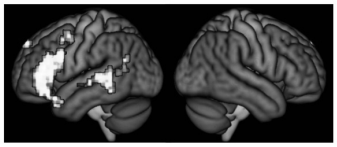
2 days post | 2 weeks post | 6 weeks post

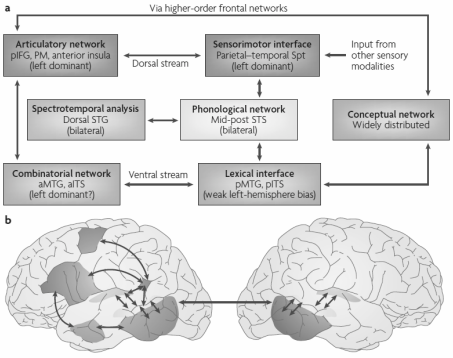
Wilson, unpublished data

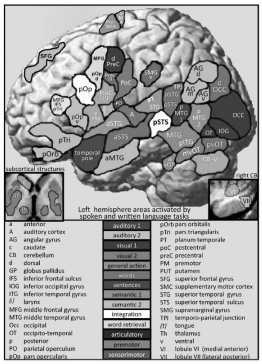
Normal brain organization of language is quite well understood.

Adaptive semantic vs perceptual matching

Healthy Controls ($n = 14$)

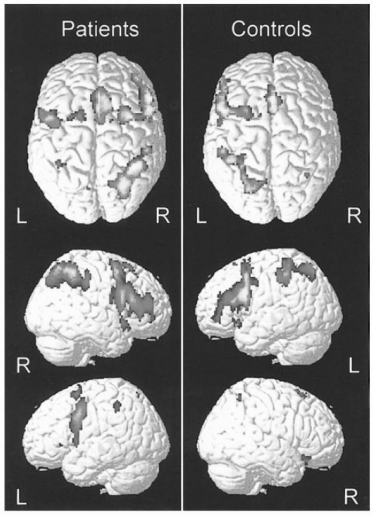






Wilson, unpublished data; Hickok and Poeppel, 2007; Price, 2012

Studies in children show that other brain regions can process language in principle.



Verb generation, 5 children with pre- or peri-natal lesions and R hemipareses

Staudt et al., 2002

Acquired aphasia is much harder to study, for many reasons.

- How do you study language processing when it is impaired?
- Confounds of difficulty, success, failure, etc., changing over time
- Group studies difficult to due individual differences in lesion location
- Test-retest reliability questionable for longitudinal studies
- Possible hemodynamic abnormalities, esp. in stroke
- Practical challenges, e.g. recruitment, other medical problems, MRI compatibility, mobility

Four papers

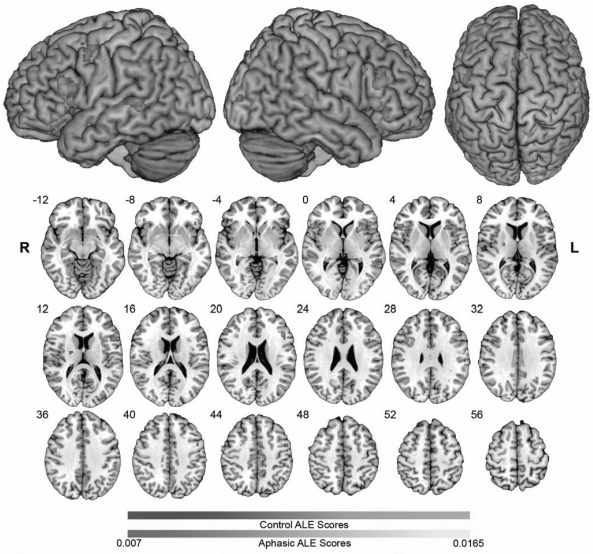
- Turkeltaub, P. E., Messing, S., Norise, C., & Hamilton, R. H. (2011). Are networks for residual language function and recovery consistent across aphasic patients? *Neurology, 76,* 1726–1734.
- Robson, H., Zahn, R., Keidel, J. L., Binney, R. J., Sage, K., & Ralph, M. A. L. (2014). The anterior temporal lobes support residual comprehension in Wernicke's aphasia. *Brain, 137,* 931–943.
- Geranmayeh, F., Brownsett, S. L. E., & Wise, R. J. S. (2014). Task-induced brain activity in aphasic stroke patients: what is driving recovery? *Brain, 137,* 2632–2648.
- Griffis, J. C., Nenert, R., Allendorfer, J. B., Vannest, J., Holland, S., Dietz, A., & Szaflarski, J. P. (2017). The canonical semantic network supports residual language function in chronic post-stroke aphasia. *Human Brain Mapping, 38,* 1636–1658.

Turkeltaub et al. (2011)

- An ALE meta-analysis of language activations in 105 patients with chronic post-stroke aphasia compared to 129 controls, derived from 12 fMRI or PET studies.
- Provides insight into nature of language reorganization, incorporating results from many studies that may individually have lacked power.
- Tasks included picture naming, lexical decision, word reading, word stem completion, speech discrimination, listening to stories, propositional speech production, verb and noun generation, semantic and phonemic fluency.
- Mostly low level baselines.

Turkeltaub et al., 2011

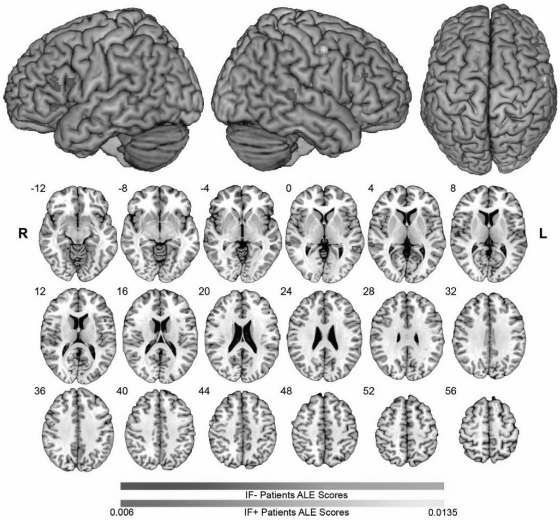
Patients and controls



Control ALE clusters are in blue-green scale, and show left hemisphere language and motor activity. ALE clusters for the group of all aphasic patients are in red-yellow scale. Significant areas in ALE maps represent locations at which peak activity is highly likely to occur in functional imaging experiments, not functional activity per se. ALE maps are overlaid on the standard Colin brain in Montreal Neurological Institute (MNI) space, using a false discovery rate q = 0.01 critical threshold, and minimum cluster size of 100 mm^3. Slices are in radiologic orientation, with the corresponding MNI *Z* coordinate.

Turkeltaub et al., 2011

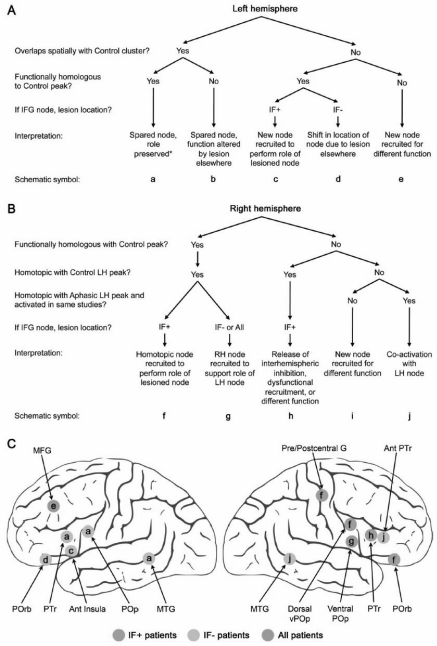
Patients with and without left inferior frontal damage ("Broca's area")



IF− ALE clusters are in blue-green scale. IF+ ALE clusters are in red-yellow scale. ALE maps are overlaid on the standard Colin brain in Montreal Neurological Institute (MNI) space, using a false discovery rate q = 0.01 critical threshold, and minimum cluster size of 100 mm^3. Slices are in radiologic orientation, with the corresponding MNI *Z* coordinate.

Turkeltaub et al., 2011

Interpretation of findings



Turkeltaub et al., 2011

Review

- Strengths:
  - large number of patients
  - basic evidence for reorganization
  - sophisticated interpretation
- Weaknesses:
  - no statistical comparisons between groups
  - diverse tasks of questionable validity

Turkeltaub et al., 2011

Four papers

- Turkeltaub, P. E., Messing, S., Norise, C., & Hamilton, R. H. (2011). Are networks for residual language function and recovery consistent across aphasic patients? *Neurology, 76,* 1726–1734.
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Robson et al. (2014)

- Language reorganization in Wernicke's aphasia (poor comprehension and repetition, fluent paraphasic speech)
- How does the semantic system reorganize when one if its crucial components is damaged?

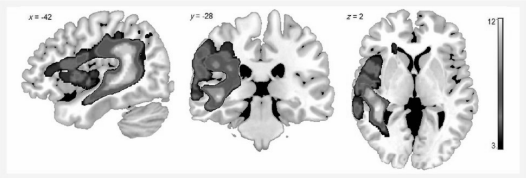
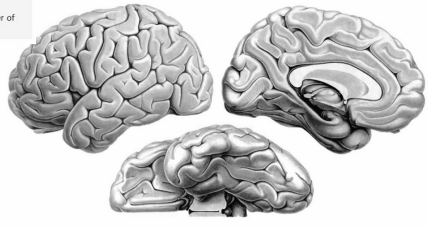


Figure 1 Lesion overlap map for the 12 participants with Wernicke's aphasia. The lesion distribution mirrors previous studies of Wernicke's aphasia, with lesions centred on posterior perisylvian cortical and subcortical regions. Colour bar indicates the number of participants with a lesion at each voxel (min = 3; max = 12).



Robson et al., 2014; Binder et al., 2009

Three tasks were used in a block design fMRI study.

- Task 1: judge if written words are animate or inanimate.
- Task 2: judge if pictures are animate or inanimate.
- Task 3: judgment if scrambled pictures are high or low on the screen.
- Each task was performed in a separate run, alternating with rest blocks.
- Tasks 1 and 2 were compared to task 3 as well as rest (?!)

		Pictures		Words		Scrambled pictures	
		d' (SD) Max 13.9	RT (SD)	d' (SD) Max 13.9	RT (SD)	d' (SD) Max 13.9	RT (SD)
	Wernicke's aphasia	4.9 (5.5)	1460 (422)	4.3 (5.6)	1583 (456)	6.5 (6.0)	1331 (568)
	Control	9.8 (4.8)	929 (187)	11.0 (5.3)	1123 (422)	11.7 (4.2)	749 (205)
t-test	*t*(22)	2.3	4	3	2.6	2.5	3.4
	P	0.03	0.001	0.006	0.018	0.02	0.003

Robson et al., 2014

Activation appeared to be shifted ventrally for patients, esp. in the left hemisphere.

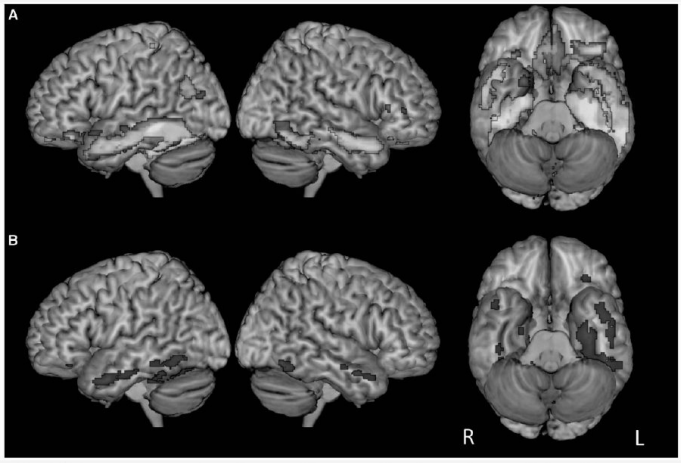
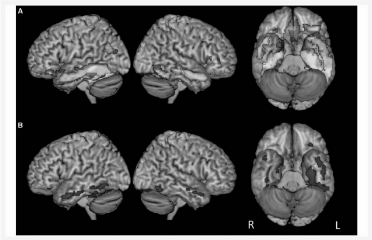


Figure 2 Whole-brain results for semantic condition versus dual baseline. (**A**) significant activation in the Wernicke's aphasia group for picture (red) and word (green) semantic judgement, overlapping regions in yellow. (**B**) Main effect of group. Regions significantly more active in Wernicke's aphasia than control group are shown in blue. No temporal lobe regions were more active in the control than Wernicke's aphasia group. Displayed activations significant at $P < 0.005$, uncorrected.

Robson et al., 2014

Review



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- Strengths:
  - homogenous patient group
  - tasks should tap damaged network
- Weaknesses:
  - patients found task more difficult, may explain more extensive activation
  - normal neural correlates of task not clear
  - results not corrected for multiple comparisons

Robson et al., 2014

Four papers

- Turkeltaub, P. E., Messing, S., Norise, C., & Hamilton, R. H. (2011). Are networks for residual language function and recovery consistent across aphasic patients? *Neurology, 76,* 1726–1734.
- Robson, H., Zahn, R., Keidel, J. L., Binney, R. J., Sage, K., & Ralph, M. A. L. (2014). The anterior temporal lobes support residual comprehension in Wernicke's aphasia. *Brain, 137,* 931–943.
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Domain-general cognitive control brain systems

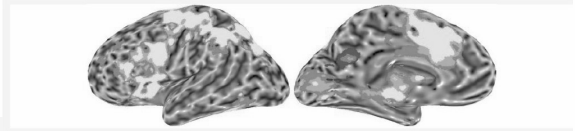


Figure 2 Regions showing a positive correlation between reaction times and activity during a lexical decision task from the study of Binder *et al*. (2005)

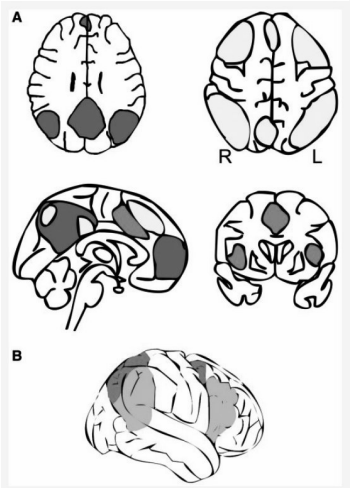


Figure 3 Schematic drawing of the typical spatial distribution of domain-general networks that may be engaged during neuroimaging of language tasks in healthy controls as well as aphasic patients. Many functional neuroimaging studies depict these networks as spatially overlapping. (**A**) The coloured networks are the Default Mode Network in blue, the fronto-parietal control network in yellow, and the cingulo-opercular network in red. The Default Mode Network is a 'task-negative' network that is deactivated during task performance on stimuli. Although they are functionally separable networks, the fronto-parietal control and cingulo-opercular networks often co-activate (see Fig. 2), and are considered to exert attention and executive control, and other processes involved in making a decision, selecting a response, and monitoring and correcting for errors. (**B**) Attentional networks can be divided into two broad systems; the dorsal attention network, in green, is thought to be a goal-driven 'top–down' attentional system, and is distributed symmetrically between the two hemispheres. The ventral attention network, in orange, is considered a stimulus-driven or 'bottom–up' attentional system, and largely lateralized to the right hemisphere.

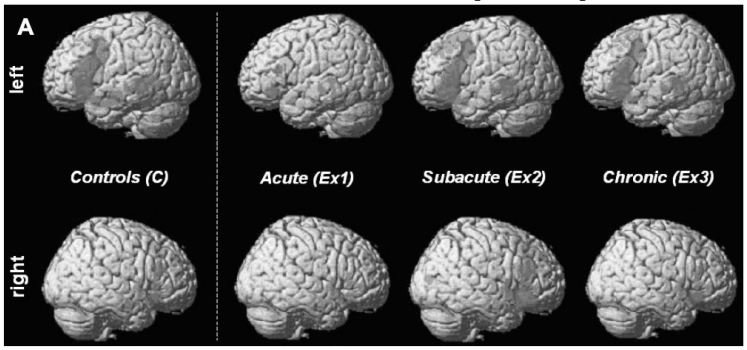
Geranmayeh et al., 2014

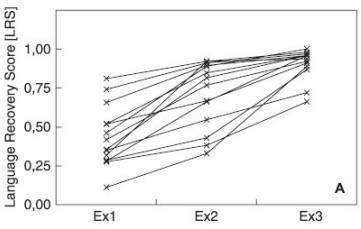
Thesis

- "Consideration is rarely given ... to the influence of intact domain-general networks on recovery, or the possibility that some of the 'abnormal' activity recorded in post-stroke aphasia is the result of the upregulation of normal activity within domain-general networks" (p. 2639)

Geranmayeh et al., 2014

For example, early right hemisphere recruitment in Saur et al. (2006)...





Patient	Task (0–100)		
	Ex1	Ex2	Ex3
01 HA	45	82	94
02 RD	10	89	95
03 RL	8	8	94
04 IK	10	80	95
05 PW	8	98	98
06 HS	5	88	94
07 MM	92	97	95
08 AK	94	97	97
09 TW	10	96	98
10 KO	10	83	98
11 BN	89	93	93
12 DR	10	76	94
13 PK	10	83	78
14 LJ	97	98	95
MEAN	36	83	94

Saur et al., 2006; Geranmayeh et al., 2014

Implications

- It is important to match language conditions with control conditions.
- It is also important to match difficulty between individuals with aphasia and healthy controls.
- The role of domain-general cognitive control systems in recovery is not just a confound; these functions may also be targets for rehabilitation.

Geranmayeh et al., 2014

Four papers

- Turkeltaub, P. E., Messing, S., Norise, C., & Hamilton, R. H. (2011). Are networks for residual language function and recovery consistent across aphasic patients? *Neurology, 76,* 1726–1734.
- Robson, H., Zahn, R., Keidel, J. L., Binney, R. J., Sage, K., & Ralph, M. A. L. (2014). The anterior temporal lobes support residual comprehension in Wernicke's aphasia. *Brain, 137,* 931–943.
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- Griffis, J. C., Nenert, R., Allendorfer, J. B., Vannest, J., Holland, S., Dietz, A., & Szaflarski, J. P. (2017). The canonical semantic network supports residual language function in chronic post-stroke aphasia. *Human Brain Mapping, 38,* 1636–1658.

Griffis et al. (2017)

- 43 patients with chronic aphasia and 43 matched controls.
- "[T]ested the prediction that longterm language outcomes depend on the preservation/restoration of language task-driven activation in canonical language networks." (p. 1638)
- Does right hemisphere activity depend on left hemisphere damage?

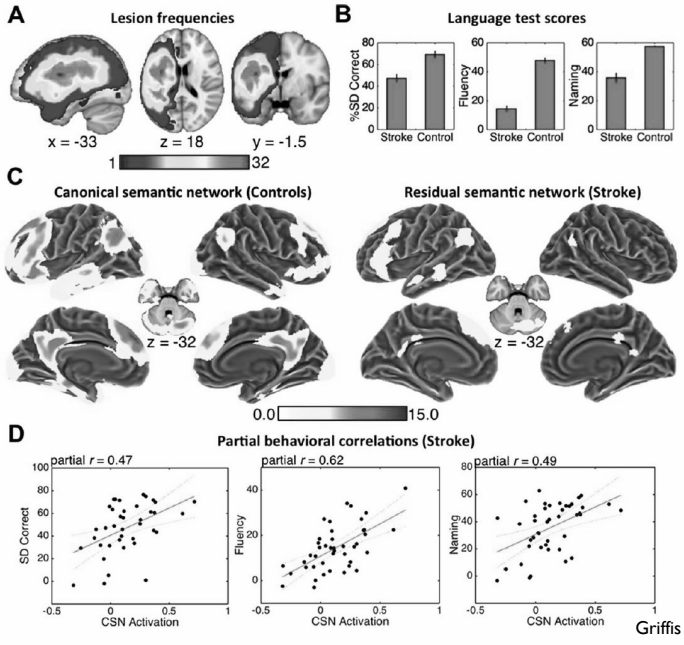
Griffis et al., 2017

Study design

- Semantic decision vs tone decision fMRI study (a well validated task that activates the semantic network)
- Language measures: BNT, semantic and phonemic fluency

Griffis et al., 2017

Results



Griffis et al., 2017

Preserved language function in aphasia reflects function of the normal network.

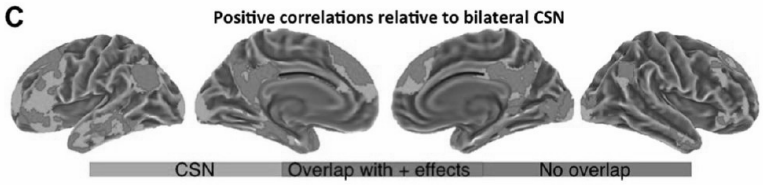
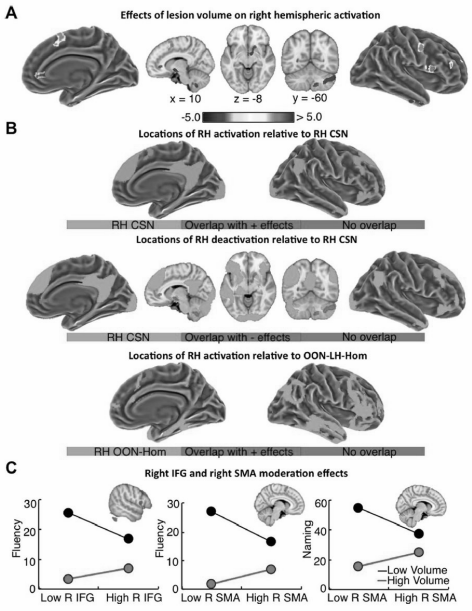


Figure 3.

The canonical network identified in controls is shown in green, regions within the CSN identified in healthy controls where SD activation was positively related to performance on any language measure in patients are shown in red, and regions outside of the CSN where SD activation was positively related to performance on any language measure in patients are shown in blue. Note that the overlays shown in (C) are qualitative illustrations of how the quantitatively identified behavioral relationships in patients relate to the canonical network identified in controls, and are intended to illustrate how activity supporting residual language task performance relates to the CSN. Each map is intensity thresholded at $P < 0.01$, uncorrected and cluster-corrected at $P < 0.01$ (126 voxels).

Griffis et al., 2017

Right hemisphere recruitment depends on lesion size.



Griffis et al., 2017

Review

- Strengths
  - very large sample size
  - fMRI task well characterized (in controls)
  - clear demonstration that normal language network critical for language function in aphasia
  - some evidence for right hemisphere recruitment
- Weaknesses
  - poor task performance in individuals with aphasia
  - limited language measures
  - addressed lesion size but not lesion location

Griffis et al., 2017

Conclusions

- Normal language regions comprise the most important neural substrate for preserved or recovered language function in aphasia.
- There is more limited evidence for recruitment of new regions in the left and right hemispheres.
- Domain-general cognitive control systems may explain many activations that have been attributed to reorganization.
- Recovery from aphasia may involve more neuroplasticity *within* the normal language network than outside it.