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Activity in Preserved Left Hemisphere Regions Predicts Anomia Severity in Aphasia

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Understanding the neural mechanism that supports preserved language processing in aphasia has implications for both basic and applied science. This study examined brain activation associated with correct picture naming in 15 patients with aphasia. We contrasted each patient's activation to the activation observed in a neurologically healthy control group, allowing us to identify regions with unusual activity patterns. The results revealed that increased activation in preserved left hemisphere areas is associated with better naming performance in aphasia. This relationship was linear in nature; progressively less cortical activation was associated with greater severity of anomia. These findings are consistent with others who suggests that residual language function following stroke relies on preserved cortical areas in the left hemisphere.

Keywords: brain plasticity, fMRI, neuroimaging, recovery, stroke

Introduction

Understanding brain plasticity following cortical damage is not only of theoretical importance but it also has enormous clinical implications. For example, 2 stroke patients who have suffered seemingly very similar brain damage may experience very different long-term recovery outcomes, even if both individuals receive identical medical management (Lazar and Antoniello 2008). Naturally, there are prognostic indicators, such as lesion location and extent of brain damage that may be related to outcome (Chapey 2001); however, these static measures tell us little about the dynamic reorganization that drives compensation.

The advent of neuroimaging has spurred increased study of functional reorganization of the cortex following brain damage—especially as a result of stroke. Much of this research has concentrated on where in the brain functional compensation takes place. Generally, the focus has been on 2 very broad areas of interest: surviving regions of the hemisphere that incurred the injury versus homologous regions of the intact contralesional hemisphere. Most likely because of practical issues related to neuroimaging techniques, the latter has received disproportionally greater attention than the former. That is, it is far less complex to examine group trends in brain activation in the intact hemisphere rather than attempting to generalize across different regions of the damaged hemisphere (where lesion location, size, and injury-induced spatial deformation vary across patients).

Aphasia is a common impairment associated with left hemisphere stroke. Several studies utilizing neuroimaging to investigate right hemisphere function in stroke-induced aphasia have yielded variable results. For example, damage to Broca's area has been associated with increased activity in its right hemisphere homologue, although this increase has not been specifically linked to patients' speech status (Naeser et al. 2004). In contrast, others have failed to show this relationship (Heiss et al. 1999). Greater activity in the right homologue of Broca's area has been associated with improved performance on language tasks (Fridriksson et al. 2009) and has demonstrated to be a strong predictor of behavioral language treatment success in aphasic patients (Richter et al. 2008). In addition, greater functional brain activity in the right temporal lobe has been related to better auditory comprehension, consistent with the notion that it plays a role in recovery or, at the very least, in maintaining function (Crinion and Leff 2007). Overall, these studies suggest that the right hemisphere plays a crucial role in aphasia recovery. On the other hand, it has also been suggested that left hemisphere recruitment is important for aphasia recovery (Heiss et al. 1999; Warburton et al. 1999). For example, evidence for left hemisphere involvement in aphasia recovery was provided by Fernandez et al. (2004), who found that improved language processing at one year poststroke was associated with increased left hemisphere brain activation in aphasic patients.

To shed further light on the role of the 2 hemispheres in language processing in aphasia, the current study examined brain activation as a predictor of anomia, a naming impairment, which is present in all types and severities of aphasia and is a reliable indicator of overall severity (Shewan and Kertesz 1980). More specifically, 15 patients underwent functional magnetic resonance imaging (fMRI) while they attempted to name colored pictures depicting common objects. Each aphasic patient was compared with a group of normal control participants on a case-by-case basis to better characterize stroke-related changes in brain activation. Thereby, the control group provided an average functional brain map—a gold standard—that was utilized to identify unusually high or low cortical activation among the aphasic patients.

Materials and Methods

Participants

All 15 patients (8 females; age range = 41–81 years; mean = 61.9) included in this research had aphasia secondary to a single-event left hemisphere ischemic stroke at least 6 months prior to study inclusion (mean = 29.7 months). The Western Aphasia Battery (WAB; Kertesz 1982) was administered to characterize overall language impairment. The composite score (aphasia quotient [AQ]) on the WAB is an indicator of aphasia severity where lower scores denote more severe aphasia and a score above 93.8 is considered within normal limits. The AQ range for the current patient sample was from 47.1 to 93.7 with a mean of 77.06 (Table 1). The patients also varied with regard to the location and extent of brain damage as well as with their performance

on specific subtests. Thus, for the purpose of predicting naming performance based on brain activity, our sample was ideal because it included a group of patients with a wide range of aphasia severities as well as lesion locations. For comparison of naming-related neural activity, 9 right-handed neurologically normal control participants were also included in this study (age range = 35–77 years; mean = 58.3 years). The difference in age between the aphasic and control groups was not significant, $P = 0.31$.

fMRI Protocol

During 20 min of fMRI scanning, participants completed a picture-naming task in which 80 colored pictures of high-frequency nouns (Snodgrass and Vanderwart 1980) were back projected on an MRI-compatible screen and seen via a mirror mounted on the scanner head coil. For the purpose of establishing a baseline for the fMRI data analysis, 40 colored abstract pictures were shown at random among the real picture presentations. Participants were instructed to try to name each target picture aloud but to say nothing for the abstract pictures. All naming attempts were recorded using a nonferrous microphone and were subsequently scored off-line, allowing for improved verification of naming accuracy compared with online scoring. To improve clarity of the audio recordings, as well as to minimize speech-related head motion, a sparse imaging sequence was utilized where a single full brain volume was collected every 10 s. Each volume acquisition lasted 2 s, allowing for 8 s of scanner silence until the next volume was collected; these 8 s of silence were utilized for stimulus presentation and response, in which a picture was shown for 2 s, and a naming attempt was recorded. To better model the hemodynamic response (HDR) in the fMRI data analysis, the interval between picture presentations was jittered (i.e., different time points following each stimulus presentation were sampled). To minimize the chance that participants would speak during fMRI data collection, pictures were always presented during the silent period between scans, appearing at least 3 s prior to acquisition of the subsequent scan.

All MRI data were collected on a 3T Siemens Trio system with a 12-element head coil. The fMRI (T_2^* echo planar imaging) sparse imaging sequence included the following parameters: 120 full brain volumes collected in 20 min; 90° flip angle; time repetition (TR) = 10 s; time acquisition = 2 s; time echo (TE) = 30 ms; in-plane resolution 3.25 × 3.25 mm; slice thickness = 3.25 mm (no gap); 32 axial slices collected in planes aligned parallel to the anterior commissure–posterior commissure line. To improve coregistration of images, all participants were scanned with a high-resolution T_2 MRI, which yielded a 1-mm isotropic image. This sequence utilized a SPACE (Sampling Perfection with Application optimized Contrasts by using different flip angle Evolutions) protocol with the following parameters: field of view (FOV) = 256 × 256 mm, 160 sagittal slices, variable degree flip angle, TR = 3200 ms, TE = 352 ms. For the purpose of lesion demarcation, all participants also underwent T_1 MRI using a turbo field echo sequence: FOV = 256 × 256 mm, 160 sagittal slices, 15° flip angle, TR = 9.5 ms, TE = 5.7 ms.

Table 1
Patients' biographical and diagnostic testing information

No.	Age	Postonset	Fluency	Auditory comprehension	AQ/aphasia type
1	63	101	4	5.85	47.1: Broca's
2	43	49	4	8.05	50.7: Broca's
3	52	56	7	9.30	85.2: Anomic
4	74	18	8	8.85	81.9: Anomic
5	71	10	8	8.95	83.9: Anomic
6	58	43	4	9.70	71.6: Broca's
7	71	18	8	9.50	89.4: Anomic
8	52	25	9	9.95	91.5: Anomic
9	41	39	6	8.00	74.4: Anomic
10	63	12	8	7.00	57.4: Conduction
11	59	9	9	8.70	79.6: Conduction
12	74	6	9	9.30	93.7: Anomic
13	70	38	9	9.40	92.0: Anomic
14	57	9	9	9.40	88.8: Anomic
15	81	13	7	7.25	68.7: Anomic

Note: Time postonset of stroke is measured in months. The maximum score for the Fluency and Auditory comprehension subtests from the WAB is 10, the maximum score for the AQ from the WAB is 100, and participant 13 was tested with the WAB-Revised.

fMRI Analysis

All fMRI data were analyzed using software designed and supported by the Oxford Centre for Functional MRI of the Brain (FMRIB)—FMRIB's software library (FSL) version 4.1 (Smith et al. 2004). For the analysis of individual participants' data, the following prestatistics processing was applied: motion correction, nonbrain removal, spatial smoothing using a Gaussian kernel of full width at half maximum 8.0 mm, grand mean intensity normalization of the entire 4D data set by a single multiplicative factor, and high-pass temporal filtering (Gaussian-weighted least squares straight-line fitting, with sigma = 60.0 s). The HDR was modeled using a Gamma function and a temporal derivative. A first-level statistical contrast of correctly named pictures versus viewing abstract pictures was computed using general linear modeling with local autocorrelation correction. Only those time points where participants correctly named pictures were contrasted with the baseline (viewing abstract pictures) in the analysis; accordingly, errors and nonresponses were excluded. Registration of individuals' fMRI images to standard space was carried out using a linear image registration tool included in FSL (aided by the inclusion of the patient's high-resolution T_2 image). For patients' fMRI images, lesion masking was utilized to improve the normalization (Brett et al. 2001).

To better understand brain activation associated with naming in aphasia, second-level analyses were performed on a case-by-case basis to compare the activation associated with correct naming in each patient to the naming-related activation observed in the control group. These comparisons utilized FMRIB's Local Analysis of Mixed Effects (FILM) and yielded a separate contrast of parameter estimates (COPE, a measure of the degree of "activation" for the statistical comparison) map for each patient, in which brain activity was characterized based on how much it deviated from naming-related activity in normal participants—the a priori defined gold standard. Thus, a significant increase or decrease in activation for a given patient compared with the group was thought to indicate stroke-related abnormality. This step in the analysis was only carried out to provide inputs for the third-level regression analysis described below. In other words, the third-level analysis was based on maps of effect size found when comparing neurological patients to healthy controls (rather than using the statistical maps, which are computed using the individual's effect size divided by error).

A third-level regression analysis including the 15 individual COPE maps generated in the second-level analyses was carried out to reveal what areas best predicted naming accuracy regardless of the overall mean activation. To emphasize, at the single voxel level, the inputs in this third-level analysis simply included the magnitude of activation difference between the control group and each of the 15 patients established in the second-level analysis. Participants' naming accuracy scores were utilized as a dependent factor to examine brain modulation associated with correct naming. This analysis relied on FILM with automatic outlier detection (Woolrich 2008) where the group mean was included as a cofactor of no interest. Z (Gaussianized T) statistical maps were initially thresholded at $Z > 2.0$ with the resulting clusters subsequently thresholded for $P < 0.05$ to correct for multiple comparisons.

Structural Analysis

Finally, an exploratory analysis was carried out to examine the relationship between localized brain damage and naming-related activation intensity established in the fMRI analysis described above. In short, this step examined whether intensity of activation, as compared with the control group in the third-level fMRI analysis, was associated with a specific lesion location. Thus, we attempted to appreciate whether patients with low (or high) naming-related activation also tended to have damage to specific cortical regions. For this purpose, we conducted a "lesion-activation intensity" mapping analysis using Non-parametric Mapping (Rorden et al. 2007), a part of the MRIcron software package. First, T_1-weighted images were normalized to 2-mm isotropic

stereotaxic space using the unified segmentation and normalization algorithms of SPM5 (Crinion and Leff 2007). Using the high-resolution T_1 MRI, the location and extent of each lesion was drawn by a neurologist (L.B.). Then, a voxelwise *t*-test identified voxels that predicted activation intensity established in the third-level analysis (Bates et al. 2003). Note that this lesion-intensity analysis was carried out using the same methods used in most lesion-behavior studies (Bates et al. 2003; Rorden et al. 2007, 2009; Karnath et al. 2009) with one exception: the dependent factor was not a measure of behavior but rather focused on naming-related activation intensity in areas related to naming identified in the third-level fMRI analysis.

Results

Control fMRI Results

For comparison, the mean statistical map representing naming-related brain activation in the normal control participants is shown in Figure 1. Not surprisingly, greatest activation was revealed in areas typically associated with speech and language processing: the bilateral superior and middle temporal lobe (Brodmann's area [BA] 22 and BA 37, respectively) as well as in Broca's area (BA 45). Bilateral activation in the occipital lobe (BA 18) was also noted (Table 2). To further demonstrate intersubject stability of naming-related cortical activation among the control group, the thresholded statistical map from each participant was overlaid on a standard template. This analysis revealed that all 9 participants had robust bilateral activation in areas typically associated with picture naming (e.g., Liljeström et al. 2008; Fridriksson et al. 2009; Meltzer et al. 2009; overlap map not pictured).

Patient fMRI Results

The mean number of correctly named pictures by the aphasic patients was 41.13 out of 80 (standard deviation [SD] = 15.29; range = 13–66), whereas the mean number of naming attempts was 66.33 (SD = 14.16; range = 26–79; Fig. 2). The number of correct and total naming attempts was correlated, $r_{15} = 0.68$, $P = 0.005$. Excluding one patient who only made phonological errors, all patients demonstrated both phonological and semantic naming errors, although the distribution of these errors varied. However, it should be noted that the results below only reflect brain activation associated with correct naming compared with the abstract baseline.

The third-level analysis revealed that the severity of anomia in the present study sample was related to the intensity of cortical activation in left hemisphere areas: the anterior cingulate gyrus (BA 32), the medial and middle frontal gyrus (BA 10 and BA 11/47), and the inferior occipital gyrus (BA 18; Table 2 and Fig. 3). This test did not detect any regions in the right hemisphere. The greatest lesion overlap was found in the left superior temporal lobe, specifically involving BA 22 (Montreal Neurological Institute coordinates [MNI]: 60, –28, 12). The third-level analysis did not show greater mean activation in the aphasic compared with the normal group. That is, as a group, the aphasic patients did not have greater overall activity in a single cortical region compared with their normal counterparts.

Therefore, the results shown in the red–yellow scale in Figure 3 indicate regions where increased activation in individuals with brain injury correlated with improved naming (where each individual's activity was contrasted to a group of neurologically healthy adults). This voxelwise map was

Table 2

The mean cortical activation map for naming in the control group (top) and the location of voxels with the highest *Z*-scores associated with the prediction of anomia in aphasia (bottom)

Mean activation map for the normal control participants

Z	*x*	*y*	*z*	Anatomy	BA
4.70	−62	−6	10	Precentral gyrus	L 22
4.69	26	−94	8	Middle occipital gyrus	R 18
4.66	−62	−14	10	Transverse temporal gyrus	L 42
4.63	44	−62	6	Middle temporal gyrus	R 37
4.60	2	−78	24	Cuneus	R 18
4.24	−46	−60	−8	Middle temporal gyrus	L 37
4.18	−44	28	6	Area triangularis	L 45
Areas that predict anomia severity in aphasia					
3.44	−8	40	2	Anterior cingulate gyrus	L 32
3.04	−2	62	2	Medial frontal gyrus	L 10
2.94	−42	40	−14	Middle frontal gyrus	L 11
2.93	−50	48	−10	Middle frontal gyrus	L 47
3.20	−34	−84	−2	Inferior occipital gyrus	L 18

Note: Anatomical locations were determined using the Talairach Daemon (http://www.talairach.org/). *Z*: intensity of activation measured in *Z*-scores; *x*, *y*, and *z*: MNI coordinates; L: left hemisphere locations; R: right hemisphere locations.

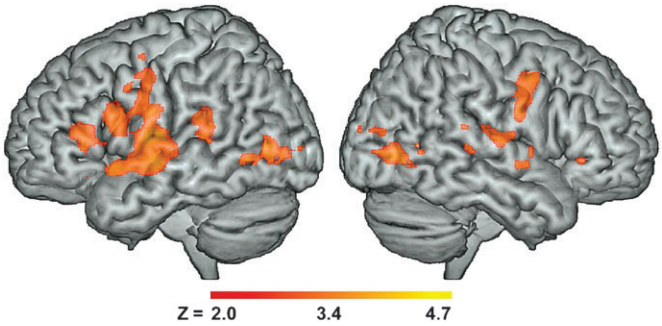

Figure 1. Brain activation associated with naming pictures in the neurologically healthy control group. The color scale represents *Z*-scores compared with baseline (viewing abstract pictures). The left hemisphere is shown on the left.

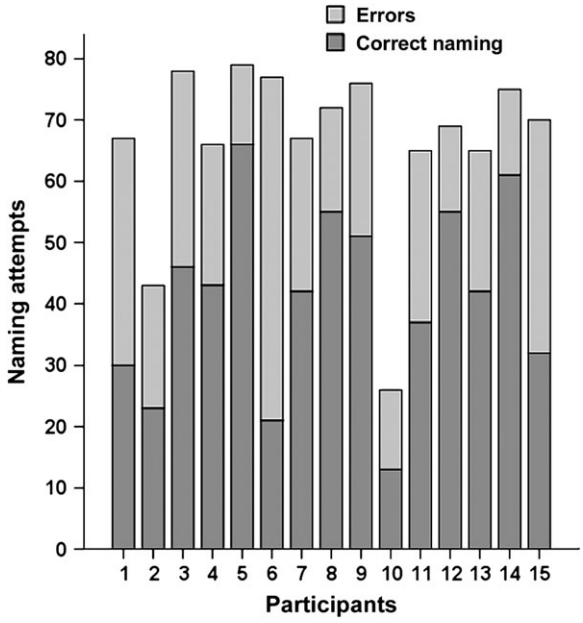

Figure 2. The number of total and correct naming attempts by each brain-injured participant. The height of each column denotes the number of naming attempts, whereas correct naming is shown in a darker shade of gray.

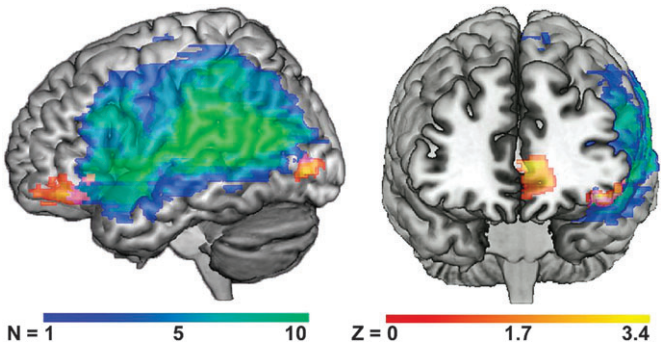

Figure 3. Cortical areas associated with naming task performance (red–yellow scale) in patients with aphasia. The lesion overlay map for all 15 patients is shown in the blue–green scale (note that the maximum range of the scale is set at 10, reflecting the highest degree of lesion overlap). The slight overlap between the activation and lesion maps (at the anterior–inferior and posterior edges of the lesion map) is shown in bright pink.

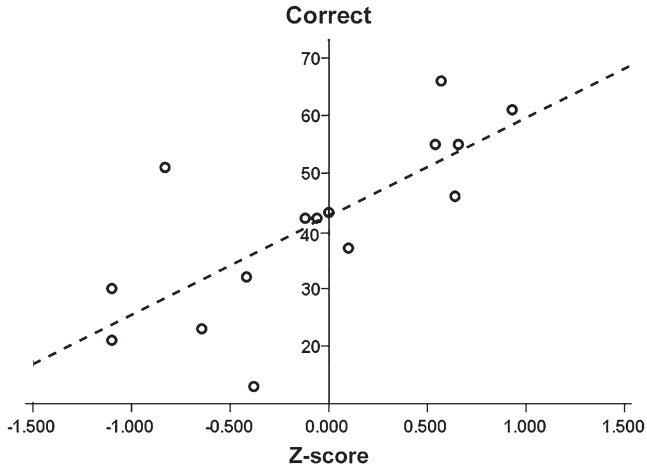

Figure 4. The relationship between intensity of activation (*x*-axis; measured in *Z*-scores compared with a group of normal control participants) and the number of correct naming attempts (*y*-axis; out of 80 pictures) during fMRI scanning. The dotted line represents a line of best fit.

computed without a priori assumptions (in theory, we could have identified regions anywhere in the brain) and survives statistical control for multiple comparisons. However, the nature of this finding is somewhat difficult to interpret. In theory, all patients may have shown reduced activation in these regions relative to controls (with individuals having the best performance showing brain activity most similar to controls). On the other hand, it is also possible that these regions show increased activation relative to controls across all patients (e.g., active compensation), with the best performing individuals showing the most difference relative to controls. To investigate this question, we conducted a speculative, posthoc volume of interest (VOI) analysis to better examine the relationship between brain activation in the aphasic patients and naming accuracy on the fMRI task. For this purpose, the activation map created in the third-level analysis was utilized as a VOI, and the mean activation (measured in *Z*-scores compared with the control group) in these areas was recorded for each aphasic patient. This analysis revealed that better naming performance was associated with greater activation compared with that seen in the control group, whereas lower than normal activity indicated more severe anomia (Fig. 4). It is important to note here that the normal group mean is represented as "0.000" on the *x*-axis in Figure 4. Thus, patients whose data points fall below this reference point would be considered to have less than normal activation in the VOI, whereas those above the mean would be considered to have higher than normal activation. Of the 15 aphasic patients, 4 had cortical activation roughly similar to the normal group, 6 had activation that was somewhat lower than normal, and the remaining 5 patients had activation that exceeded what was seen in their normal counterparts. The correlation between participants' mean *Z*-scores and naming accuracy was $r_{15} = 0.74$, $P = 0.002$ (2-tailed).

Patient Lesion-Deficit Mapping Results

The lesion-deficit analysis revealed that poor naming performance was predicted by damage to the left superior temporal lobe (BA 22; MNI: −52, −30, 10), with this effect surviving a 1% false discovery rate to control for multiple comparisons ($Z > 2.35$). However, this lesion location is in the center of middle cerebral artery territory, a region that is often damaged in large injuries (near the trunk) while spared in smaller injuries that occur in the branches. Thus, to rule out the possibility that the temporal lobe's association with anomia simply reflects a relationship between larger lesions and more severe anomia, the same analysis was rerun with overall lesion volume as a nuisance cofactor. This analysis did not yield significant results, perhaps due to insufficient statistical power. Therefore, with this small sample size, it is difficult to draw strong inferences regarding which lesion locations predict severe anomia.

Patient Lesion-Activation Mapping Results

A posthoc exploratory analysis was carried out to examine the relationship between lesion location and the intensity of activation found in the third-level fMRI analysis. More specifically, mean *Z*-scores (again, as compared with the control group) generated in the VOI analysis and shown in Figure 4 for each participant were utilized to determine whether intensity of activation was associated with a certain lesion location. The results suggest that lower *Z*-scores were related to damage in the posterior portion of Broca's area (BA 44; MNI: −44, 10, 26; Fig. 5). This means that patients whose data points fell to the left of the *y*-axis in Figure 4 were more likely to have Broca's area damage compared with those whose data points (i.e., higher *Z*-scores) fell to the right of the *y*-axis. Note that this analysis included lesion size as a covariate but was not corrected for multiple comparisons.

Discussion

Increased cortical activation in the left hemisphere, beyond what was seen in normal participants, was associated with improved picture naming by aphasic patients. More specifically, a positive linear relationship was revealed between intensity of activation in specific cortical areas in the left hemisphere and naming accuracy. This suggests that increased activation in these preserved cortical areas can compensate for damage to the cortical language network. That is, maintained function is supported by the damaged hemisphere and this compensation is mediated by preserved posterior and anterior cortical areas.

When the lateral cortical areas (BA's 11, 47, and 18) associated with naming accuracy are compared with the mean

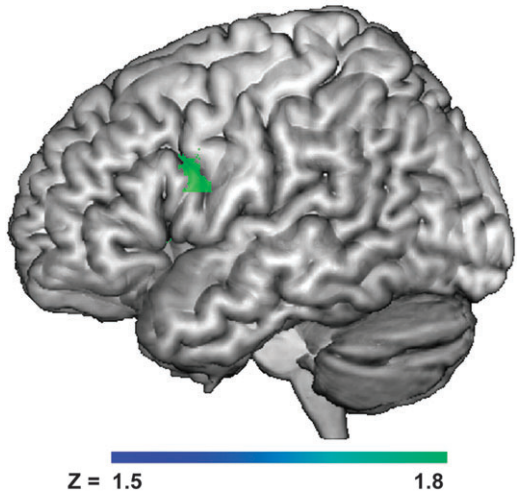

Figure 5. Critical brain damage associated with lower brain activation in the VOI generated in the third-level analysis. This analysis identifies regions where injury predicts lower *Z*-scores (as shown in the horizontal axis of Fig. 4). This analysis used overall lesion volume as a nuisance regressor. The resulting statistical map is shown uncorrected for multiple comparisons. Therefore, injury to Broca's area (shown here in green) predicted reduced brain activation in the brain areas shown as orange in Figure 3.

activation map for the control group, it seems straightforward to suggest that cortical map expansion (Grafman 2000) supported improved naming ability among those patients with less severe anomia. For example, modulation in the lateral occipital lobe (BA 18), an area immediately posterior to BA 37, was related to naming performance. A portion of this area was also activated in the normal control group; in fact, the cluster that partially included BA 37 extended into BA 18, although not as far caudally as that seen among the aphasic patients whose naming ability was relatively preserved. Accordingly, it is possible that recruitment of cortical regions (e.g., BA 18) proximal to areas crucial for naming (e.g., BA 37; Hillis et al. 2002, 2006; DeLeon et al. 2007) in normal participants supports improved or partially maintained naming ability in aphasic patients. Similarly, correct naming was associated with intensity of activation in BA 47—an area located ventral to Broca's area in the inferior frontal gyrus. Hence, increased reliance on BA 47 during picture naming may also represent cortical map expansion.

It is important to note that although the lateral cortical areas associated with improved naming were located at the edge of the group lesion map, not all the aphasic patients had incurred damage in the immediate vicinity of these areas. That is, not all patients had both anterior and posterior damage even though the distribution of lesions centered around the length of the Sylvian fissure, especially its posterior portion. Therefore, proposing that cortical compensation occurred in left hemisphere perilesional areas would only be accurate when the whole lesion map is considered. It is highly probable that recovery from anomia, or lack thereof, is related to different cortical areas in different patients. This issue is probably better examined in detail utilizing single case studies where activation in the perilesional rim can be explored separately in each patient (Postman-Caucheteux et al. 2009). Nevertheless, the current data suggest that naming ability in aphasia is related to the intensity of cortical activation in the left hemisphere.

As revealed in the exploratory lesion-activation intensity analysis, patients who were able to name more pictures also tended to have higher than normal activation in the specific left hemisphere areas shown in Figure 3. Conversely, those who had more severe anomia had less activation in these same cortical areas. Speculatively, the lesion-activation intensity analysis suggests that lower than normal neural recruitment during picture naming by aphasic patients is related to Broca's area damage. That is, patients whose Broca's area is damaged may have less activation in cortical areas important for anomia recovery. We emphasize that this relationship should be interpreted with caution because the lesion-activation intensity analysis did not yield statistically significant results when corrected for multiple comparisons. Clearly, more data are needed to examine whether specific lesion locations potentially affect cortical activation in other areas important for maintained or recovered language function in aphasia.

Several other studies have implicated the left hemisphere as supporting improved language processing in aphasia (Miura et al. 1999; Cornelissen et al. 2003; Breier et al. 2004; Crinion and Leff 2007; Crosson et al. 2007). Although the specific location of brain activation varies among these and the current study, it is probable that aphasia recovery relies, at least partially, on spared left hemisphere areas. It is also crucial to note that the kinds of fMRI tasks used in different studies of language-related cortical activation in aphasia vary greatly. Thus, it is perhaps unreasonable to expect that the same cortical areas will be recruited to support processing of these different tasks. Therefore, comparing results across different neuroimaging studies of aphasia is somewhat problematic. Moreover, the analysis of neuroimaging data also varies significantly among studies. For example, to examine language-related brain activation in a group of patients, some studies have utilized whole-brain analyses regardless of varying lesion sizes and locations among patients (Crinion and Leff 2007; Fridriksson et al. 2009). Such an approach has inherent limitations because statistical power will decrease in areas that are lesioned in one or more patients. Consequently, a specific area that supports recovery in some aphasic patients may not be detected in a whole-brain fMRI analysis because it is not intact in other individuals included in the group. Other studies have relied strictly on VOI analysis (Peck et al. 2004; Meinzer et al. 2008). This approach also has inherent problems because it may ignore important cortical activation not captured in the selected VOIs. As with whole-brain analyses, statistical power would also decrease when one or more patients have damage to areas included in VOIs. The current study relied on a whole-brain analysis to examine cortical activation and picture naming in aphasic patients. Then, the resulting statistical map was utilized as a VOI to better examine the relationship between brain activation and improved naming performance. Although this approach combines whole brain and VOI analyses, it may still fail to capture which cortical areas best predict anomia severity due to the previously mentioned problem of reduced statistical power in damaged brain regions. A more ideal approach might combine structural and fMRI data in the same statistical analysis, and therefore, it would allow for differential weighting for damaged cortical areas in the fMRI analysis. However, such an approach would require a large number of patients, thus making it less attractive from a practical standpoint given that most studies of aphasia only include a few patients.

It is worth noting that naming accuracy varied substantially among the aphasic group meaning that fewer trials were modeled in the first-level analysis for some patients compared with others (e.g., patient no. 5 vs. patient no. 10). Yet, the number of baseline trials was always the same across participants, and each participant showed robust activation in the first-level analysis. In spite of this fact, data from patients with lower accuracy should be viewed as being less reliable compared with those with less severe anomia.

Above we discussed how cortical map expansion, beyond areas traditionally associated with language processing (Broca's area and BA 37), may support improved naming in aphasia. It is unlikely, however, that this explanation would suffice with regard to recruitment of the left anterior cingulate gyrus. Rather than supporting language processing, the anterior cingulate gyrus is commonly associated with processing tasks that vary attentional load or require error detection (Corbetta 1998; Botvinick et al. 1999; Kiehl et al. 2000; MacDonald et al. 2000; Milham et al. 2001; Garavan et al. 2002). Impaired attentional processing in aphasia has been reported in several studies (Tseng et al. 1993; Murray et al. 1998; Murray 2000), suggesting that greater attentional demands contribute to decreased language task performance by aphasic patients. The current naming task requires sustained and selective attention due to long interstimulus intervals and intermittent scanner noise that needs to be suppressed. Accordingly, less than normal recruitment of the anterior cingulate gyrus may reflect poor naming task performance due to impaired attention allocation. With regard to error detection, patients with Wernicke's, transcortical sensory, or global aphasia were not included in this study. Therefore, the current study sample only included patients whose aphasia types are commonly associated with relatively intact error monitoring. However, it is likely that the ability to monitor errors varied among the study participants, although we did not explicitly test for this. Thus, greater anterior cingulate gyrus recruitment may have reflected improved error detection and, consequently, more successful picture naming.

The present results do not discount the role of the right hemisphere in aphasia recovery. For example, stimulation of the right frontal lobe has been shown to interrupt speech processing in some patients with aphasia (Winhuisen et al. 2007). Others have demonstrated that a right hemisphere stroke can induce further impairment of language processing in patients who already had aphasia associated with a prior left hemisphere stroke (Basso et al. 1989). However, it is crucial to note that the current study only examined picture naming; thus, comparisons to other studies that included different language tasks and modalities are somewhat difficult.

Although our findings can only be generalized to patients with aphasia, it is possible that a similar compensatory mechanism (i.e., increased reliance on preserved left hemisphere areas to support picture naming) is also involved in other stroke-induced disorders. For example, recovery of spatial neglect following right hemisphere stroke has been associated with increased functional activity in ipsilesional posterior cortical areas (Corbetta et al. 2005). Clearly, a better understanding of how and where functional compensations take place in the brain will allow for improved rehabilitation efforts. In that regard, we believe that this study provides significant support that preserved left hemisphere areas are important for anomia recovery in stroke patients with aphasia.

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Notes

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