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Task-modulated neural activation patterns in chronic stroke patients with aphasia

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Background: Neuroimaging research on language recovery in patients with aphasia due to left hemisphere damage has generated some intriguing results. However, it is still not clear what role the right hemisphere plays in supporting recovered language functions in the chronic phase for patients with different site and size of lesion when different tasks are used.
Aims: The present study aimed at exploring the role of perilesional, ipsilesional, and contralesional activation in participants with aphasia with different site and size of lesion using two different language tasks. All participants were in the chronic stage with well-recovered or significant improvements in language functions.
Methods & Procedures: Functional magnetic resonance imaging (fMRI) was used to characterise brain activations in eight stroke patients and eight age/gender-matched controls during semantic judgement and oral picture naming. An event-related design using jittered interstimulus intervals (ISIs) was employed to present the stimuli.
Outcomes & Results: The fMRI scans of both language tasks in patients revealed differences in activation pattern relative to the normal control participants. The nature of this difference was task specific. During the semantic judgement task patients without lesions involving the left frontal region activated the left inferior frontal gyrus similar to observations in the normal control participants. Participants with left frontal lesions activated contralesional regions in addition to perilesional left frontal regions. During the picture-naming task all participants activated bilateral brain regions irrespective of the site or size of lesion, consistent with other published studies utilising this task. Subsequent regions of interest analysis and laterality index analysis revealed that patients with large lesions produced greater right hemisphere activation than patients with small lesions.

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Conclusions: The results of this study demonstrate that recovery is task, lesion site, and size specific. Further, the results also indicate a role for both activation of homologous contralesional cortex and activity of left hemisphere regions (perilesional and ipsilesional) as efficient mechanisms for supporting language functions in chronic stroke patients.

Keywords: fMRI; Aphasia; Language recovery

Recent fMRI studies in participants with aphasia have primarily focused on whether patients compensate for their neurological and functional loss by increasing the level of language-related brain activation in the left or the right hemisphere. An in-depth examination of the literature indicates that the recovery of language functions in aphasia is a more complex process than transferring language functions as a whole to the right hemisphere or exclusive recruitment of left perilesional and other language areas. Several functional imaging studies have demonstrated that language recovery is associated with activation in contralateral homologous areas (Abo et al., 2004; Blank, Bird, Turkheimer, & Wise, 2003; Blasi et al., 2002; Ohyama et al., 1996; Weiller et al., 1995; Xu et al., 2004). In contrast, other studies have emphasised that good recovery of language functions in aphasia is accompanied by greater perilesional than right hemisphere reorganisation, whereas poor recovery of language functions is accompanied by greater right hemisphere than perilesional reorganisation (Fridriksson, Bonilha, Baker, Moser, & Rorden, 2010; Heiss, Kessler, Thiel, Ghaemi, & Karbe, 1999; Karbe et al., 1998; Perani et al., 2003; Postman-Caucheteux et al., 2010; Rosen et al., 2000). This lack of consistency in findings in the neuroimaging literature could be attributed to a number of factors, including time post onset, lesion size/site, language tasks, and single-participant versus group analysis.

The first factor that contributes to the discrepancies in the literature is the time post stroke onset that the patients are scanned. Hillis (2005) suggests that recovery of language function after stroke occurs in three overlapping phases, each with a unique set of underlying neural mechanisms. The initial phase is called the acute phase and lasts for about 2 weeks after the onset of the lesion. The second phase is the subacute phase and this usually lasts up to 6 months post onset. Finally, the chronic phase begins months to years after a stroke and may continue for the remainder of the person's life. Recent fMRI studies have come to some consensus regarding the time course of the relationship between right hemisphere activation and time post onset (Saur et al., 2006, Winhuisen et al., 2007). In Saur et al. (2006) increased right hemisphere activation was observed within 2 weeks after stroke and returned to baseline levels after 1 year, whereas left hemispheric activity increased gradually from acute to chronic stage. In addition, transcranial magnetic stimulation (TMS) of the right inferior frontal gyrus (RIFG) can hamper speech in participants with aphasia in the subacute phase, while having no effect in some of these patients during follow-up in the chronic phase (Winhuisen et al., 2007). This suggests that the RIFG is active during the early phase post-stroke but is absent or more modest at chronic phase. However, some studies found right hemisphere activation in chronic aphasic patients many years after stroke onset suggesting that right hemisphere along with left hemisphere supports language recovery in the chronic stage, particularly in patients with large left hemisphere lesions (Blasi et al., 2002; Cao, Vikingstad, George, Johnson, & Welch, 1999).

Another factor that determines the nature of ipsilesional or right hemisphere activation is the size/site of lesion. Increased activity in the right hemisphere is more frequently observed in patients with large ischaemic lesions and poor recovery, while

patients with small lesions display better outcomes in association with recruitment of primarily left language areas (Crosson, 2007). Further, Abo et al. (2004) and Xu et al. (2004) have suggested that, for speech production tasks, the site of right hemisphere activation depends on the site of the lesion. Abo et al. (2004) observed right frontal activation during auditory repetition in a patient with left frontal damage, but not in control participants or a patient with left temporoparietal damage. On the other hand, their patient with left temporoparietal damage showed right inferior parietal activation that was not observed in control participants or the patient with left frontal lesion. Likewise, Xu et al. (2004) observed right inferior frontal activation during covert word generation in a patient with left frontal damage but not in two patients with left temporoparietal damage. These studies imply that the nature of right or left hemisphere activation is dependent on the site of lesion even though these studies differ in the nature of language tasks implemented to study left or right hemisphere activation.

Consequently, the language paradigm that is selected for experiments also determines the degree of contribution of the left versus right hemisphere. It is clear that the effect of stroke on the language system may involve an extensive range of linguistic deficits. As a result, studies have employed a wide variety of tasks in order to evaluate the mechanisms underlying language recovery following stroke. The tasks that are typically used in neuroimaging experiments to investigate language recovery include: lexical decision (e.g., Zahn et al., 2004), word repetition (e.g., Abo et al., 2004; Karbe et al., 1998), word generation (e.g., Miura et al., 1999; Weiller et al., 1995), semantic judgement (e.g., Fernandez et al., 2004), sentence comprehension (e.g., Thulborn, Carpenter, & Just, 1999), and picture naming (e.g., Fridriksson et al., 2010; Postman-Caucheteux et al., 2010). Different tasks place different demands on the language-processing system and, when taken together with different sites and sizes of lesions, likely result in a complex pattern of activation that is individual and task specific.

The goal of the present study was to systematically tease apart this potential interaction. In the present study we selected two tasks (picture naming and semantic judgement) that have been widely used in behavioural and fMRI studies of language processing and language processing in response to disease or injury (e.g., Binder et al., 1997; Chee et al., 2000; Fernandez et al., 2004; Sonty et al., 2007; Thompson-Schill, 2003). Furthermore, there is an extensive literature regarding the underlying cognitive-linguistic framework and its associated functional anatomy for both the tasks (for reviews see Binder & Price, 2001; Hagoort, 2005; Levelt, 2001; Noppenney, Phillips, & Price, 2004). The brain activation observed when participants retrieve the name of a visually presented stimulus reflects complex cognitive processes involving visual perceptual processing, semantic processing, lexical retrieval, and speech production. Oral picture naming typically activates a large network in the perisylvian and extrasylvian cortex including bilateral superior and middle temporal lobe, left angular gyrus, left inferior frontal lobe, and bilateral occipital lobe (Abrahams et al., 2003; DeLeon et al., 2007; Grabowski, Damasio, Eichhorn, & Tranel, 2003; Harrington, Buonocore, & Farias, 2006; Martin et al., 2005; Price, Devlin, Moore, Morton, & Laird, 2005; Saccuman et al., 2006). A semantic judgement/selection task, on the other hand, requires visual/perceptual processing and semantic processing but does not require phonological processing. Neuroimaging studies have implicated the left prefrontal cortex as a consistent region activated during semantic processing tasks. Specifically, the left inferior frontal gyrus (LIFG) is commonly recruited when an explicit semantic judgement task, requiring semantic information about single words to be explicitly

selected is used (Badre & Wagner, 2002; Fiez, 1997; Kapur et al., 1994; Thompson-Schill, D'Esposito, Aguirre, & Farah, 1997; Wagner, Pare-Blagoev, Clark, & Poldrack, 2001).

A few studies have investigated the role of the type of task in language recovery in participants with aphasia. For example, Rosen et al. (2000) examined the verbal performance of six patients with infarcts centred in the LIFG using a word stem completion task and a simpler reading task, using fMRI. Results revealed increased activation in the RIFG during the word stem completion task but not during the word-reading task. However, the level of activation in the RIFG did not correlate with verbal performance. In addition, perilesional responses were found in two patients who gave the best performance in the word stem completion task. The results provide evidence that intact perilesional tissue in stroke patients will have an important influence on recovery from aphasia. However, Rosen et al. (2000) included only patients with lesions restricted to left inferior frontal gyrus. So it is not clear whether there would be a similar pattern of activation for lesions in the posterior region.

In a recent study, van Oers et al. (2010) examined the neural correlates of language recovery in 13 patients using three language tasks (picture–word matching, semantic decision, and verb generation) at two different stages of recovery: 2 months after stroke and after at least 1 year. The authors also correlated recovery of naming ability and scores on the Token Test with data from fMRI in the chronic phase. The results of this study indicated that in the chronic stage after stroke LIFG activity was associated with improvement of picture naming and sentence comprehension, whereas activity in the RIFG may reflect up-regulation of non-linguistic cognitive processing. One main limitation of this study was that the tasks used were not designed to activate the temporal region. So limited information was obtained regarding the contribution of the temporal region in language recovery. Further, the authors used group averaging instead of single-participant analysis in patients with aphasia. However, information about perilesional patterns of activation can be lost through averaging of patient brain images (Crosson, 2007). In addition, when the activation of right hemisphere homologues of language cortex depends on the degree of damage to their specific left hemisphere counterparts, the boundaries of the left hemisphere lesion may affect which right hemisphere structures are active as well. Thus it is essential to analyse images from patients with aphasia at the individual participant level.

In summary, the association between the site of lesion, size of lesion, time post onset, and type of task, in relation to the involvement of the right hemisphere regions in language recovery remains largely unclear. Therefore the present study was designed to systematically examine the contribution of left and right hemisphere regions in language recovery in patients with different sites and sizes of lesions using a semantic judgement task and an oral picture-naming task. All patients in the present study were in the chronic stage and had achieved high levels of recovery. We analysed images from patients with aphasia at the individual participant level because information about individual patterns of activation can be lost through averaging of patient brain images (Crosson, 2007).

We hypothesised that during the semantic judgement task normal control participants and patients without left frontal lesions would recruit the LIFG. Patients with left frontal lesions would recruit perilesional regions in the frontal lobe and ipsilesional temporal and/or contralesional right hemisphere regions. During the picture naming task, we hypothesised that normal control participants would activate a broad bilateral network (more left than right) including frontal, temporal, and occipital

regions. Participants with aphasia were expected to recruit similar regions including perilesional and contralesional regions.

METHOD AND MATERIALS

Participants

Eight monolingual, right-handed, English-speaking participants with aphasia were involved in the experiment (age range 40–79 years). All patients had suffered an ischaemic stroke with the exception of P4 who had suffered a cerebral haemorrhage. Strokes were generally in the distribution of the left middle cerebral artery and affected primarily posterior and/or anterior cortical areas, although P8 had evidence for some subcortical involvement. All participants were at least 24 months post onset (mean 48.25 MPO). Localisation of lesion was determined by an experienced neuroradiologist based on each individual participant's T-1-weighted MRI slices (see Figure 1). At the time of testing, six patients were classified as anomic and two patients were classified as non-aphasic based on the results of the Western Aphasia Battery (Kertesz, 1982). Please see Table 1 for details of participant information.

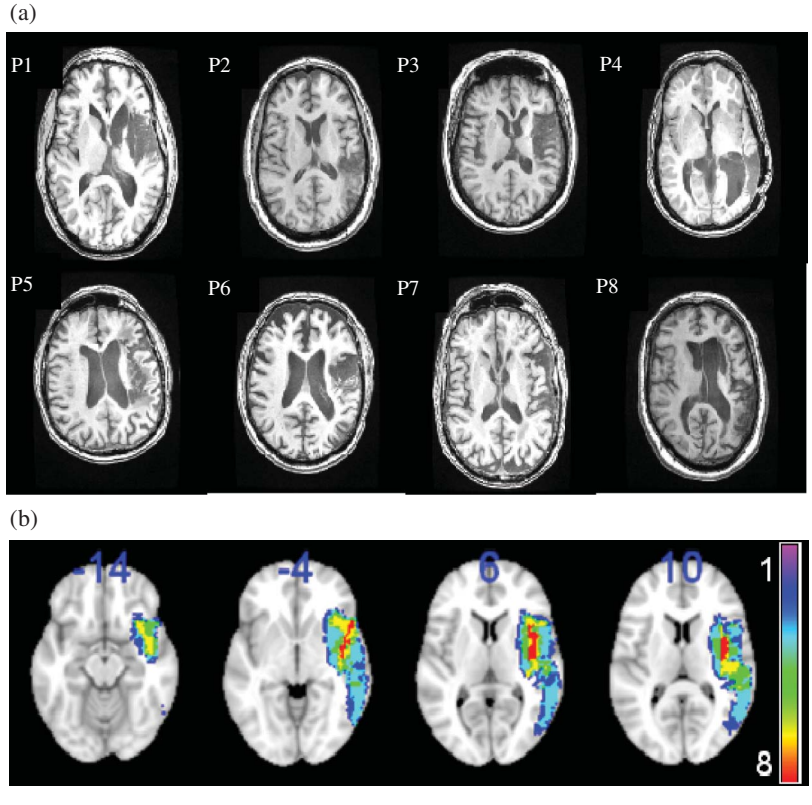

Figure 1. (a) T1 axial images for the eight patients in their native space; (b) lesion overlap maps for the eight patients. Lesion overlaps for the eight patients are displayed on the MNI template brain. Images are in radiological orientation with the right side of the brain to the left and the left side to the right.

TABLE 1
Demographic data, lesion site, lesion volume, and test scores for the patients

Participant	*Age*	*Sex*	*Gender*	*Education*	*MPO*	*Site of Lesion*	*Lesion volume(mm^3)*	*WAB AQ*	*WAB AC*	*WAB Fluency*	*WAB Repetition*	*BNT*	*PAPT*
P1	M	62	M	J.D.	52	Left frontal (pars opercularis of Broca's area and primary motor cortex), insula extending into the white matter	37330.84	96.2	10	10	9.8	58	51
P2	M	57	M	High School	36	Left temporo-parietal region	31886.7	97.8	10	10	9.6	59	52
P3	F	60	F	2 years college	78	Left motor cortex, temporal and insular region	37813.4	91	10	9	8.6	46	52
P4	F	40	F	Bachelor's Degree	30	Left temporo-parietal region	23487.56	93.2	10	9	9.2	35	50
P5	M	70	M	High School	36	Left motor cortex, temporoparietal extending into the white matter	43383.5	78.4	8	8	7.5	13	49
P6	M	51	M	Master's Degree	38	Left frontal including the motor cortex and part of the pars opercularis of Broca's area, SMA, insula extending into the white matter	42126.98	84.8	9.4	8	7.6	42	49
P7	M	79	M	J.D.	56	Left temporal and insula	28837.31	91.1	9.25	9	8.8	40	49
P8	F	60	F	High School	60	Left temporo-parietal, insula, lateral occipital cortex, and left putamen	45203.06	74	8.75	8	8	13	47

MPO = Months Post Onset, WAB AQ = Western Aphasia Battery Aphasia Quotient; WAB AC = Western Aphasia Battery Auditory comprehension; WAB Fluency = Western Aphasia Battery Fluency; WAB repetition = Western Aphasia Battery Repetition; BNT = Boston Naming Test; PAPT = Pyramids and Palm Trees.

Eight older adults were also recruited for the experiment (age range 40–82 years). All control participants were matched for age (± 3 years), gender, and education. The normal control participants had normal hearing and either normal or corrected to normal vision. Exclusionary criteria included neurological disorders such as stroke, transient ischaemic attacks, Parkinson's disease, Alzheimer's disease, psychological illness, learning disability, seizures, and attention deficit disorders. All individuals were right-handed as determined by the handedness and language inventory (Oldfield, 1971). The *Mini Mental Status Exam* (MMSE) (Folstein, Folstein, & McHugh, 1975) was administered to the normal control participants in order to ensure that they did not have any cognitive impairment. All participants scored a 30/30 on the MMSE. Participants gave informed consent according to the University of Texas at Austin Human Subjects Protocol. Participants in the fMRI tasks also completed screening forms to verify eligibility to participate in the scanner.

The experiment consisted of three sessions. The first session involved collecting patient medical history and administering the language tests. The tests include the *Western Aphasia Battery* (WAB) (Kertesz, 1982), *Boston Naming Test* (BNT) (Kaplan, Goodglass, & Weintraub, 1983), portions of the *Psycholinguistic Assessment of Language Processing in Aphasia* (PALPA) (Kay, Lesser, & Coltheart, 1992), the *Pyramids and Palm Trees* (PAPT) (Howard & Patterson, 1992), and the *Cognitive-Linguistic Quick Test* (CLQT, Helm-Estabrooks, 2001). For the normal control participants, the *Mini Mental Status Exam* was administered. The second session consisted of practice session outside the scanner (only for participants with aphasia) and the third session consisted of the fMRI experiment inside the scanner.

Stimulus and task

The experiment consisted of two tasks: a semantic judgement task and an oral picture-naming task. The order of presentation of the tasks was counterbalanced across participants in order to minimize the effect of task. The picture-naming task consisted of 60 grey-scaled pictures taken from the international picture-naming project database (Bates et al., 2003). Photos sized 4 × 6 inches were selected for each target example. The control condition consisted of viewing grey-scaled scrambled pictures and saying "pass". The scrambled pictures were derived by pixellating photographs from the naming task using Adobe PhotoShop7.0. This control task has now been examined in several studies investigating word retrieval (e.g., Meltzer, Postman-Caucheteux, McArdle, & Braun, 2009; Wierenga et al., 2008). In the semantic judgement task word triplets were presented on the screen. The stimuli for this task were taken from the Pyramids and Palm Tree test (Howard & Patterson, 1992). The experimental design is similar to that utilised in Chee et al. (2000) and Kurland et al. (2004). Participants had to match one item closer in meaning (presented on top of the screen) to one of the two items presented at the bottom of the screen. There were 48 word triplets. For the semantic judgement task the control condition consisted of symbol triplets. One of the items was 8% smaller than the sample item presented on top and the other one was 16% larger than the sample item. Participants had to choose the item that was closer in size to the sample item presented on top.

An event-related design using jittered interstimulus intervals (ISIs) was employed. The control condition was presented during the ISI. For the picture-naming task the ISI consisted of passively viewing the scrambled pictures and saying "pass". For the semantic judgement task, the ISI consisted of the size judgement task. The timing and

order of stimulus presentation was optimised for estimation efficiency using Optseq2 (Greve, 2002). In the picture-naming task each stimulus was presented for 5 seconds. In the semantic judgement task each stimulus was presented for 4 seconds. The ISI varied from 2 to 6 seconds. Both the tasks were divided into two runs. For the picture-naming task each run consisted of 30 items. For the semantic judgement task each run consisted of 24 items.

All stimuli were concrete nouns controlled for syllable length, frequency of occurrence (Frances & Kucera, 1983), imageability (Gilhooly & Logie, 1980), familiarity (Gilhooly & Logie, 1980; Toglia & Battig, 1978) and concreteness (Gilhooly & Logie, 1980). The stimuli were presented with EPrime (Psychology Software Tools, Inc.) using an InVivo system that presents images on a screen fitted to the head coil in the MRI scanner. Corrective optical lenses were used to correct visual acuity. The picture-naming task required the participant to orally name the picture stimuli. Microphone output from the scanner room was run through the penetration panel and connected to a Dell Inspirion Laptop Computer in the scanner control room. The Audacity™ software on the computer recorded verbal responses from each scanning run. These responses were scored for accuracy and reaction time off-line. Scanner noise cancellation software was used to remove the scanner noise from each participant's response. For the semantic judgement task participants responded by pressing the middle finger of their left hand if they matched the stimulus on the left and the index finger if they matched the stimulus on the right. Before all the runs began a baseline fixation condition was presented for 8 seconds to ensure that the scans had reached equilibrium.

Magnetic resonance images were acquired on a 3 Tesla GE MRI scanner. Once participants were physically aligned in the scanner, the magnet was shimmed to achieve maximum homogeneity. Scout images (4s) were obtained to determine the proper angle for subsequent structural and fMRI data acquisitions. This was followed by one high-resolution T1 SPGR scan lasting 5 minutes and 44 seconds (128 1 mm sagittal slices, FOV 240 × 240 mm, flip angle = 20, bandwidth = 31.25, phase encoding = A-P, TR = 9.5 ms, TE = 6.1 ms). Blood-oxygen-level-dependent (BOLD) sensitive functional images were collected using a gradient echo-planar pulse sequence (TR = 2000 ms, TE = 35 ms, 64 × 64 matrix, 24 × 24cm FOV, flip angle 90, 31 oblique slices covering the whole brain, 3-mm thick, 0.3-mm interslice gap).

Data analysis

Behavioural. The data were analysed in terms of accuracy and reaction times for both the tasks. Naming latencies were measured from recorded sound files as the duration between the onset of the stimulus and the onset of the participant's response. For the semantic judgement task the latency and accuracy of responses were recorded based on the button press. Only correct responses were entered into the reaction time analysis.

Imaging. All fMRI data were analysed using the Oxford Centre for Functional MRI of the Brain (FMRIB)—FMRIB's software library (FSL) version 5.9 (Smith et al. 2004; Woolrich et al., 2009). Image pre-processing was performed to remove non-brain tissues and correct for image intensity fluctuations and RF inhomogeneities. The following pre-statistics processing were applied: motion correction (Jenkinson, Bannister, Brady, & Smith, 2002), non-brain removal (Smith, 2002), spatial smoothing using a Gaussian kernel of FWHM 5 mm, mean-based intensity normalisation of all

volumes by the same factor, and highpass temporal filtering. After pre-processing, statistical analyses were performed at the individual level (for both control participants and patients) within FSL (FEAT, FMRI Expert Analysis Tool). The task timing was convolved with the standard gamma variate function implemented in FSL (lag, 6 s; width, 3 s), and the fMRI signal was then linearly modelled on a voxel-by-voxel basis using a general linear model (GLM) approach, with local autocorrelation correction (Woolrich, Ripley, Brady, & Smith, 2001). Only correct responses were included in the data analysis.

For the picture-naming task contrasts examined differences in activation between picture naming versus scrambled picture viewing and between scrambled picture viewing versus picture naming. For the semantic judgement task contrasts examined differences in activation between semantic judgements versus size judgements and between size judgements versus semantic judgements.

Registration of participants' fMRI images to the MNI standard space was carried out using a linear image registration tool included in FSL. Functional images were first aligned to the T1-weighted SPGR and, then the T1-SPGR to the standard MNI Avg152, T1 $2 \times 2 \times 2$ mm. All transformations were carried out by using 12 degrees of freedom affine transforms (Jenkinson & Smith, 2001). For patients, the cost function masking method of normalisation was employed (Brett, Leff, Rorden, & Ashburner, 2001), in which a hand-drawn stroke mask, derived from the T1 MRI scan, prevents the normalisation algorithm from interpreting the infarct's edge as part of the brain surface. T1-weighted images from each patient were also normalised into MNI space using the cost function masking method found in FLIRT (Jenkinson & Smith, 2001). Higher-level analysis (analysis across runs for the same subject) was carried out using fixed effects. Z (Gaussianised T/F) statistic images were thresholded using clusters determined by $Z > 3.5$ and a (corrected) cluster significance threshold of $p = .05$ (Worsley, 2001). Group analysis was carried out only for the control participants. In order to further understand the difference in activation between the patient group and control group for both the tasks, a comparison analysis was carried out using FMRIB's Local Analysis of Mixed Effects (Beckmann, Jenkinson, & Smith, 2003; Woolrich, Behrens, Beckmann, Jenkinson, & Smith, 2004). This analysis was carried out to determine whether patient's activated additional compensatory brain regions compared to that observed in the normal control participants. In this analysis each patient's statistical activation map was directly compared to that of the normal control groups mean activation.

Regions of interest analysis and lesion volume analysis

Regions of interest (ROI) analysis were done in order to examine the patterns of activation in regions that are typically activated by language tasks (for reviews see Binder, Desai, Graves, & Conant, 2009; Indefrey & Levelt, 2004). This included the anterior perisylvian regions and posterior perisylvian regions. The anterior perisylvian regions included the left inferior frontal gyrus (LIFG) (pars opercularis and pars triangularis) and the posterior perisylvian regions (PPR) included the Wernicke's area (the posterior part of the superior temporal gyrus), posterior part of the middle temporal gyrus, angular gyrus, and supramarginal gyrus. Homologous areas on the right side were chosen as ROIs in the right hemisphere. The mean intensity of signal change associated with each task in these four main regions of interest—left inferior frontal gyrus (LIFG), right inferior frontal gyrus (RIFG), left posterior

perisylvian regions (LPPR), and right posterior perisylvian regions (RIFG)—was extracted. The anatomical mask for each ROI was created using fslmaths (part of FSL) and the Harvard–Oxford cortical structural atlas was used as a guide for defining anatomical landmarks. In patients with lesions affecting the regions of interest we developed ROI maps from the perilesional regions not more than 5 mm from the lesion in three axes (Bonakdarpour, Parrish, & Thompson, 2007). The mean activation within each region associated with each task for each participant was obtained using the Featquery tool, which is part of FSL (FMRIB's Software Library, www.fmrib.ox.ac.uk/fsl). Lesion volumes were calculated for each patient in order to determine whether there was any relationship between lesion volumes and BOLD signal change in the four ROIs. Using the T_1 MRI scans the location and extent of each lesion was drawn by the first author and verified by the neuroradiologist. Lesion volumes and the number of damaged voxels were obtained using fslmaths, which is part of FSL. We used MRICRON software for qualitative display of lesion overlap maps (MRIcron: http://www.sph.sc.edu/comd/rorden/mricron/). See Figure 1 for lesion overlay maps.

Laterality index

The laterality index reflects the degree of activation in a left hemisphere ROI in relation to its right hemisphere ROI. To determine to what extent particular brain regions were involved in both the tasks, the intensity, spatial extent, and number of activations were obtained to compute an intensity-weighted area of activation. For each of the significant activation foci (i.e., activation above a threshold of $p < .05$ corrected) an intensity-weighted area of activation was calculated, which is defined as the integral of intensity over that significantly activated region and which thus includes the combined effects of intensity and spatial extent for that region. These intensity-weighted volumes could then be combined to calculate the lateralisation index (LI). The intensity-weighted volumes of the significant activations were calculated for the following ROIs: inferior frontal gyrus, superior temporal gyrus, middle temporal gyrus, angular gyrus, and supramarginal gyrus for both left and right hemispheres.

The LI was computed for each individual participant from the five ROIs by the following equation (Binder et al., 1995; Desmond et al., 1995; Xiong, Rao, Gao, Woldorff, & Fox, 1998): $LI = (\sum sl(i) - \sum sr(i)) \; / \; (\sum sl(i) + \sum sr(i))$ where sl(i) and sr(i) refer to the intensity-weighted areas of activations in the ith left and right side ROIs. The value of the LI can range from +1 to –1; a negative value indicates right-hemispheric dominance; a positive value indicates left-hemispheric dominance; and a value near zero indicates no dominant hemisphere (or indeterminant).

RESULTS

Behavioural results

The mean reaction times and accuracy for each individual participant are shown in Figure 2. Participants with aphasia were significantly less accurate than the normal control participants for the semantic judgement task, $t(14) = 3.66$, $p = .002$, and the picture-naming task, $t(14) = 3.22$, $p = .006$. Further, participants with aphasia were significantly slower than the normal control participants for the semantic judgement task, $t(14) = –3.56$, $p = .003$, and the picture naming task, $t(14) = –3.44$, $p = .003$.

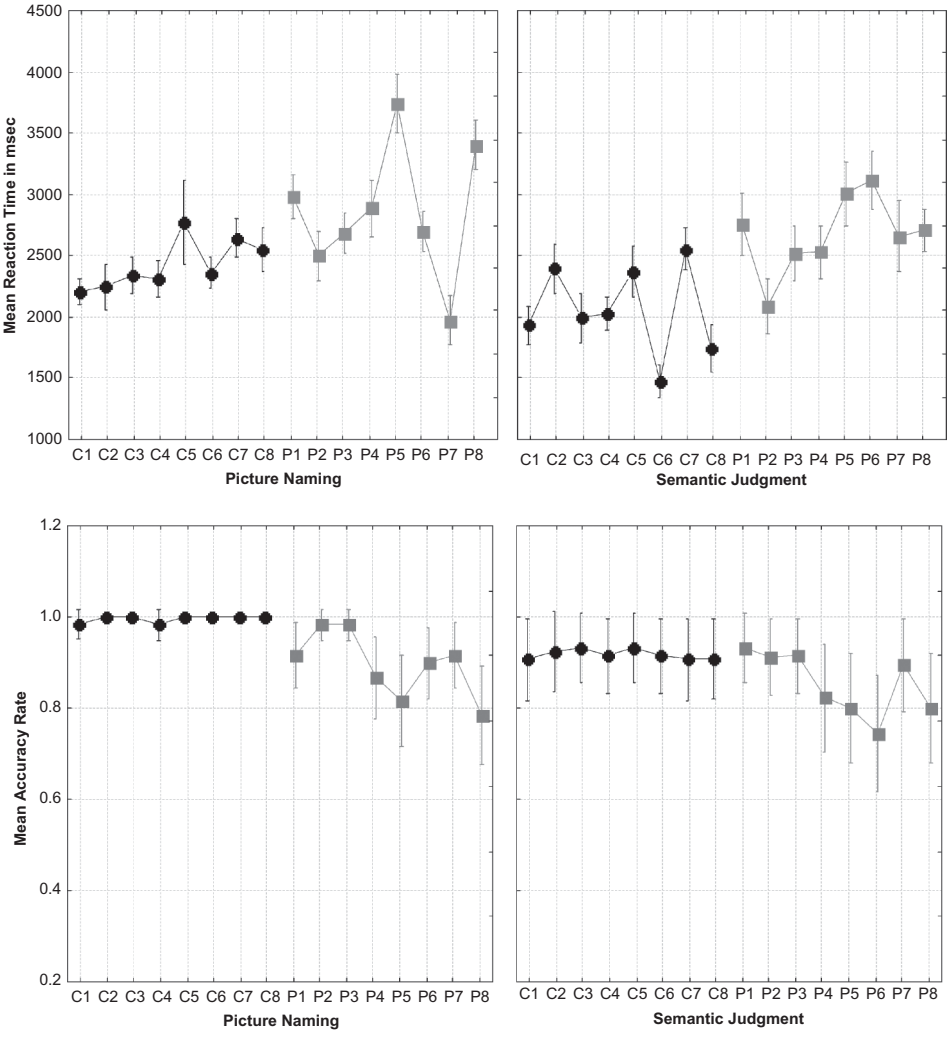

Figure 2. (a) Mean reaction time for the normal control participants and the patients, (b) mean accuracy rate for the normal control participants and the patients. "Black" represents normal controls and "grey" represents patients.

Imaging results

Normal control participants. The mean brain activation maps for the semantic judgement task and the picture-naming task are shown in Figure 3, and activation coordinates (in MNI standard space) are shown in Table 2. For the semantic judgement task, robust activation was observed in the left inferior frontal gyrus (BA 44, 45) for all participants. In addition, activation was also present in the left middle temporal gyrus (BA 21) and right lingual gyrus (BA 18). For the picture-naming task, activation was observed in the bilateral superior and middle temporal lobe (BA 22 and BA 21 respectively), left inferior frontal gyrus (BA 44, 45), bilateral supramarginal gyrus (BA 40), left precentral gyrus (BA 4), and bilateral occipital lobe (BA 17, 18).

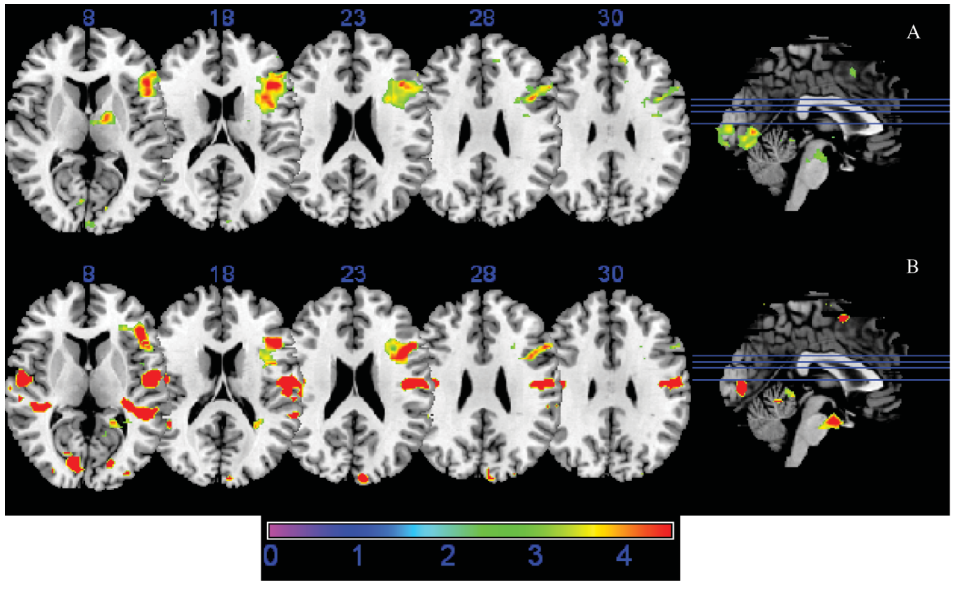

Figure 3. Mean activation maps for the normal control participants for (a) semantic judgement task determined by the contrast of semantic and size judgement conditions and (b) picture-naming task determined by the contrast of picture naming and scrambled picture viewing. Statistical maps are thresholded by using clusters determined by Z>3.5 and a (corrected) cluster significance threshold of $p = .05$. Images are in radiological orientation with the right side of the brain to the left and the left side to the right.

TABLE 2
MNI activation coordinates and significance (Z statistics) for the normal control participants

Region	*Z*	*x*	*y*	*z*
Semantic judgement versus Size judgement				
Left inferior frontal gyrus, BA 45	5.9	−44	48	18
Left inferior frontal gyrus, BA 44	4.2	−40	16	18
Left middle temporal gyrus, BA 21	3.6	−56	−38	−10
Right lingual gyrus, BA 18	3.5	6	−78	4
Picture naming versus Scrambled viewing				
Left inferior frontal gyrus, BA 44/45	4.1	−52	28	24
Left precentral gyrus, BA 4	3.5	−50	2	26
Left superior temporal gyrus, BA 22	5.8	−50	−36	6
Left middle temporal gyrus, BA 21	5.3	−54	−46	6
Left occipital gyrus, BA 17	3.5	−26	−80	24
Left supramarginal gyrus, BA 40	4.1	−56	−44	12
Right supramarginal gyrus, BA 40	4.4	50	−36	12
Right precentral gyrus, BA 4	3.6	60	0	12
Right superior temporal gyrus, BA 22	4.7	64	−22	4
Right middle temporal gyrus, BA 21	3.5	52	−36	−2
Right occipital gyrus, BA 17	3.6	44	−80	−2

Participants with aphasia. The list of activation coordinates (in MNI standard space) and activation significance (Z statistics) for the semantic judgement task and the picture-naming task are shown in Table 3. Activation maps for participants with aphasia are shown in Figure 4. The direct comparison between each patient's activation and the control groups' mean activation revealed several interesting findings. For the semantic judgement task only patients P1 and P6 had significantly greater activation than the control groups' mean activation. P1 had significantly greater activation in the right inferior frontal gyrus (BA 44, 45) and left superior frontal gyrus (BA 8). P6 had significantly greater activation in the right inferior frontal gyrus (BA 44). For the picture-naming task most patients had significantly greater activation than the control groups' mean activation in the left inferior frontal gyrus (P1, P2, P3, P4, and P7). Increased activation was also noted in the right frontal cortex (P5) and/or right superior/middle temporal gyrus (P6 and P8). The activation coordinates for the direct comparison between each patient's activation and the control groups' mean activation are shown in Table 4.

TABLE 3
MNI activation coordinates and significance (Z statistics) for the patients

	Semantic judgement				*Picture naming*			
Region	*Z*	*x*	*y*	*z*	*Z*	*x*	*y*	*z*
Participant 1								
Left middle frontal gyrus, BA 46	5.8	−28	52	8				
Left inferior frontal gyrus, pars triangularis, BA 45	3.6	−42	36	6	4.9	−44	36	0
Left postcentral gyrus, BA 3					5.2	−54	−18	40
Left superior temporal gyrus, BA 22	6.0	−64	−22	−6	6.2	−60	−22	−6
Left middle temporal gyrus, BA 21	3.9	−54	−42	−6	5.3	−58	−52	4
Left inferior parietal lobe, BA 39/ 40	4.5	−54	−48	22	6.2	−54	−48	20
Right inferior frontal gyrus, BA 44/45	4.0	42	16	22				
Right superior temporal gyrus, BA 22					4.9	60	−22	2
Right middle temporal gyrus, BA 21					4.8	58	−42	2
Participant 2								
Left inferior frontal gyrus, BA 44/45	6.2	−50	26	18	6.7	−44	22	2
Left middle frontal gyrus, BA 46	5.7	−54	22	26				
Left precentral gyrus, BA 4	6.0	−48	−8	58	5.3	−54	−4	18
Left middle temporal gyrus, BA 21					5.3	50	−32	−10
Left postcentral gyrus, BA 3					4.3	−54	−6	16
Right superior temporal gyrus, BA 22					4.1	52	−20	−4
Right middle temporal gyrus, BA 21					4.3	50	−32	−10
Right lingual gyrus, BA 18	4.0	18	96	−2	4.0	16	98	−2
Participant 3								
Left inferior frontal gyrus, BA 44/ 45	5.7	−40	22	18	5.3	−46	34	2
Left middle frontal gyrus, BA 46	5.6	−46	6	46				
Left middle temporal gyrus, BA 21					4.2	−58	−20	−8
Left supramarginal gyrus, BA 40					4.5	−56	−42	12
Left middle occipital gyrus, BA 18	3.8	−8	−94	20				
Right precentral gyrus, BA 4					5.2	48	−4	42
Right superior temporal gyrus, BA 22					4.2	62	−28	−2
Right middle occipital gyrus, BA 18					4.0	32	−88	8

TABLE 3
(Continued)

	Semantic judgement				*Picture naming*			
Region	*Z*	*x*	*y*	*z*	*Z*	*x*	*y*	*z*
Participant 4								
Left inferior frontal gyrus, BA 44/45	6.2	−40	22	18	6.7	−50	14	24
Left middle frontal gyrus, BA 46					3.5	−42	22	38
Left precentral gyrus, BA 4	6.0	−46	0	40	6.5	−64	0	24
Left postcentral gyrus, BA 3					3.5	−60	−20	24
Left middle occipital gyrus, BA 18					3.5	−44	−90	8
Right inferior frontal gyrus, BA 44/45					3.5	56	20	28
Right precentral gyrus, BA 4					4.2	62	−4	22
Right middle occipital gyrus, BA 18					4.1	44	−82	−8
Participant 5								
Left inferior frontal gyrus, BA 44/45	5.9	−52	22	16	4.2	−46	18	18
Left middle frontal gyrus, BA 46	4.0	−34	50	14	4.1	−36	38	16
Left superior frontal gyrus, BA 8					3.6	−22	54	18
Left superior occipital gyrus, BA 19	4.7	−30	−56	32				
Left anterior cingulate gyrus, BA 24					3.5	−16	42	8
Right inferior frontal gyrus, BA 45					3.5	46	20	6
Right precentral gyrus, BA 4					3.6	52	10	8
Right postcentral gyrus, BA 3					3.5	48	−22	38
Right supramarginal gyrus, BA 40					3.5	54	−20	26
Right anterior cingulate gyrus, BA 24					3.6	16	40	12
Participant 6								
Left inferior frontal gyrus, pars triangularis, BA 45	5.7	−48	22	20	5.5	−46	28	12
Left superior frontal gyrus, BA 8	3.5	−16	58	16				
Left superior temporal gyrus, BA 22	4.0	−58	−52	20	4.9	−46	−32	−4
Left supramarginal gyrus, BA 40					4.3	−60	−34	30
Left inferior occipital gyrus, BA 17					6.7	−22	−96	−4
Right inferior frontal gyrus, BA 44	3.5	40	30	8				
Right superior temporal gyrus, BA 22					6.1	54	−14	6
Right middle temporal gyrus, BA 21					4.1	50	−34	−4
Right inferior occipital gyrus, BA 17					6.1	30	−90	−18
Participant 7								
Left inferior frontal gyrus, BA 44/45	5.8	−44	20	10	4.9	−48	30	0
Left middle frontal gyrus, BA 46					4.0	−34	44	18
Left superior frontal gyrus, BA 8					3.9	−14	52	18
Left precentral gyrus, BA 4	3.6	−58	0	6				
Left middle temporal gyrus, BA 21					3.6	−64	−22	−6
Left superior occipital gyrus, BA 19	3.5	−32	−76	24	3.8	−20	−82	28
Right superior temporal gyrus, BA 22					4.5	64	−30	14
Right postcentral gyrus, BA 3					4.5	54	−14	28
Right superior occipital gyrus, BA 19					5.9	30	−78	28
Participant 8								
Left inferior frontal gyrus, BA 44/45	5.4	−46	16	12	3.5	−48	30	8
Left middle frontal gyrus, BA 46	4.3	−46	8	42	4.2	−40	52	8
Left cingulate gyrus, BA 24					3.5	−12	18	42
Right inferior frontal gyrus, BA 45					3.9	48	34	0
Right superior temporal gyrus, BA 22					6.8	64	−26	0
Right middle temporal gyrus, BA 21					4.0	54	−18	−16
Parahippocampal gyrus, BA 32					3.8	38	−36	−16
Right middle occipital gyrus, BA 18					3.5	44	−78	6
Right superior occipital gyrus, BA 19					3.5	32	−88	36

TABLE 4
MNI activation coordinates for the direct comparison between each patient's activation and the control groups' mean activation

Region	*Z*	*x*	*y*	*z*
	Semantic judgement task			
Participant 1				
Right inferior frontal gyrus, BA 44/45	3.6	34	14	26
Right occipital gyrus, BA 18	3.5	32	−80	8
Left postcentral gyrus, BA 3	3.5	−44	−16	48
Participant 6				
Right inferior frontal gyrus, BA 44	3.7	58	28	10
Left middle occipital gyrus, BA 19	3.5	−34	−86	10
	Picture-naming task			
Participant 1				
Left inferior frontal gyrus, BA 45	3.6	−42	40	2
Right frontal pole	3.5	24	42	−14
Participant 2				
Left inferior frontal gyrus, BA 44/45	3.8	−42	22	8
Left postcentral gyrus, BA 3	3.5	−46	−20	44
Left Heschl's gyrus, BA 41	3.5	−42	−30	18
Right postcentral gyrus, BA 3	3.5	44	14	32
Participant 3				
Left inferior frontal gyrus, BA 44/45	3.6	−44	20	10
Right precentral gyrus, BA 4	3.81	48	−6	42
Participant 4				
Left inferior frontal gyrus, BA 44/45	3.7	−48	6	20
Left precentral gyrus, BA 4	3.5	−58	4	14
Right middle occipital gyrus, BA 18	3.5	16	−88	30
Participant 5				
Right inferior frontal gyrus, BA 45	3.6	44	24	8
Left cingulate gyrus, BA 24	3.8	−10	28	24
Right cingulate gyrus, BA 24	4.0	10	38	16
Participant 6				
Right postcentral gyrus, BA 3	3.5	58	−16	24
Right superior temporal gyrus, BA 22	3.6	64	−26	−2
Participant 7				
Left inferior frontal gyrus, BA 45	3.5	−46	40	−4
Left frontal pole	3.5	−16	62	−4
Participant 8				
Left superior frontal gyrus, BA 8	3.2	−28	56	−10
Left cingulate gyrus, BA 24	3.5	−8	40	6
Right cingulate gyrus, BA 24	3.3	8	30	16
Right middle temporal gyrus, BA 22	3.7	62	−24	−4

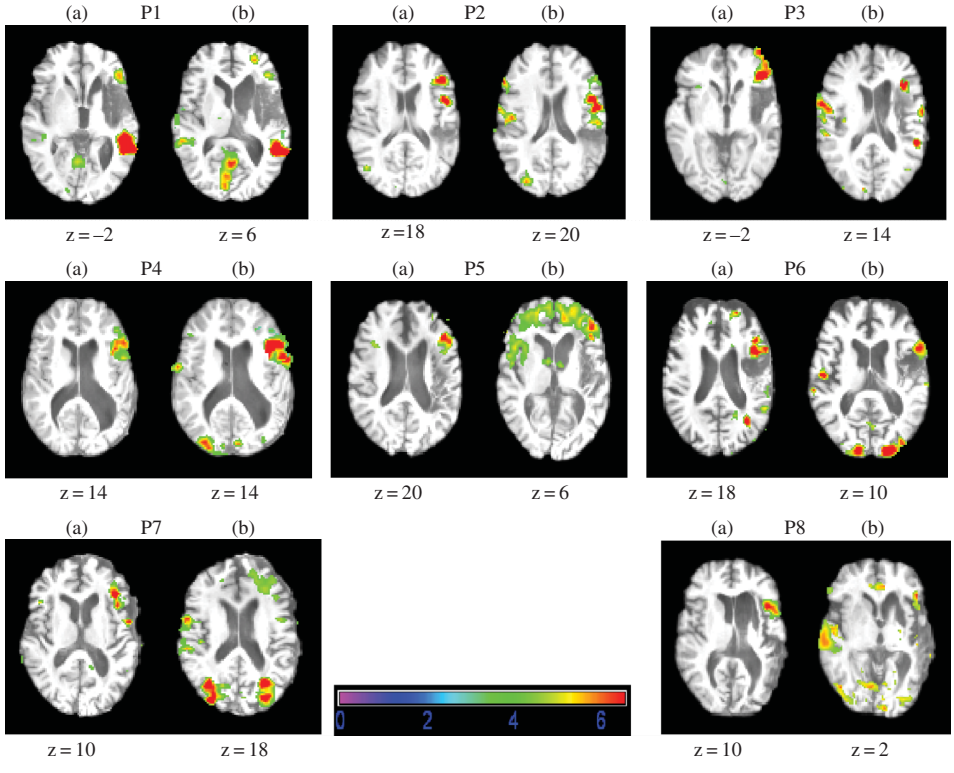

Figure 4. Activation maps for the patients for (a) semantic judgement task determined by the contrast of semantic and size judgement conditions and (b) picture-naming task determined by the contrast of picture naming and scrambled picture viewing. Statistical maps are thresholded by using clusters determined by $Z > 3.5$ and a (corrected) cluster significance threshold of $p = .05$. Images are in radiological orientation with the right side of the brain to the left and the left side to the right.

Regions of interest analysis

The results of the ROI analysis are presented in Figure 5 and are compared statistically using non-parametric Wilcoxon paired sample test. The mean percent BOLD signal change was similar for the normal control participants in the LIFG for both the tasks ($Z = 1.06$, $p = .09$). Patients also showed similar patterns of activation in the LIFG for both the tasks ($Z = 0.56$, $p = .57$). Nevertheless, inspection of the individual participant data revealed that some patients (P1, P2, P3, P4, and P7) showed greater BOLD signal change in the LIFG for the picture-naming task compared to that for the semantic judgement task. While examining the mean percent BOLD signal change in the LPPR, the normal control participants showed significantly more activation for the picture-naming task compared to that for the semantic judgement task ($Z = 2.52$, $p = .01$). Most patients did not show activation in the LPPR for either task, with the exception of P1 and P6. Nevertheless, as a group patients showed significantly more activation for the picture-naming task compared to that for the semantic judgement task ($Z = 2.52$, $p = .01$). For the normal control participants there was no significant difference in the mean percent BOLD signal change for picture-naming and semantic judgement tasks in the RIFG. Again, with the exception of P1 and P6 (who

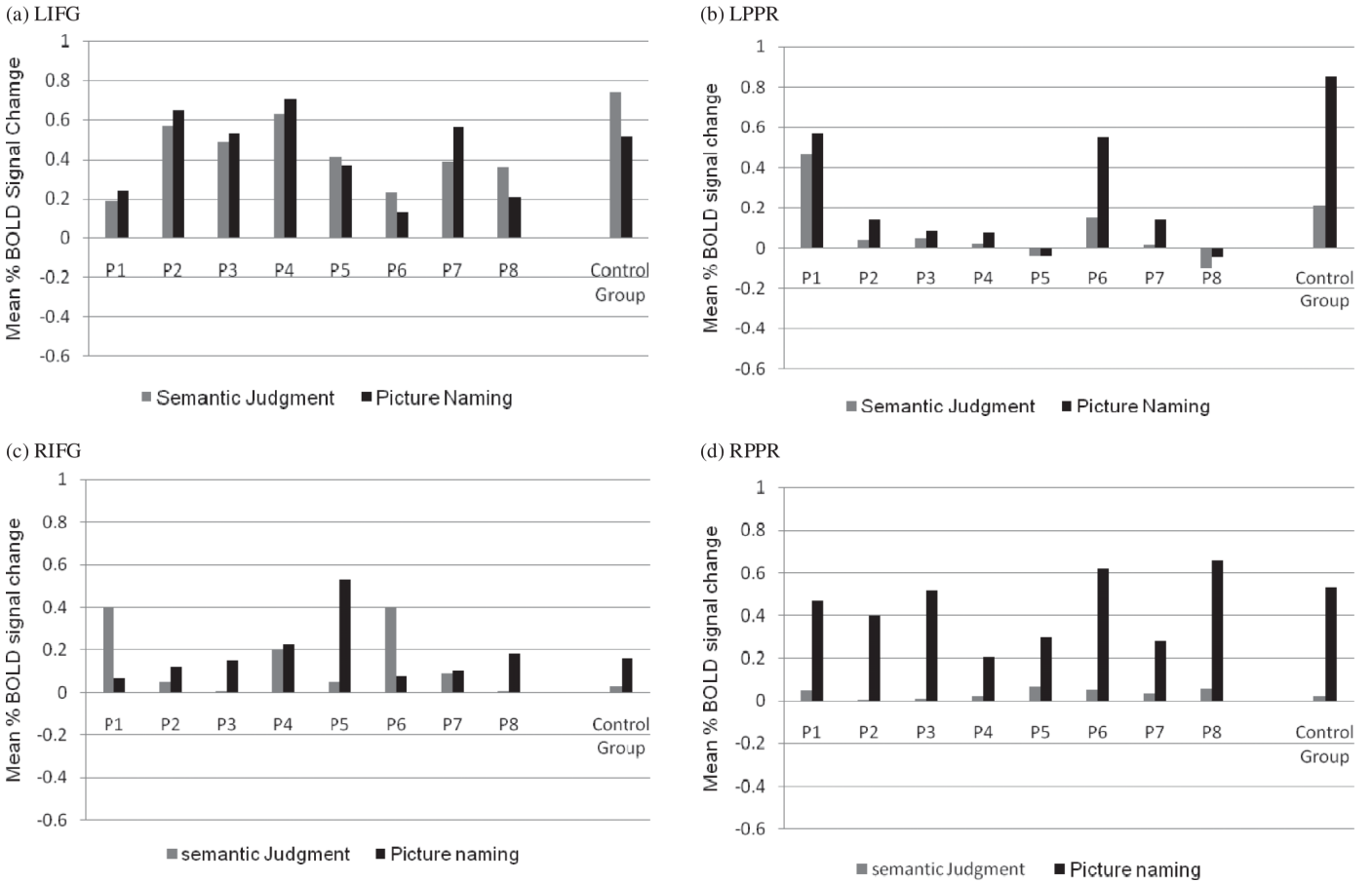

Figure 5. Mean percent BOLD signal change for the patients and the normal control group for the (a) left inferior frontal gyrus (LIFG), (b) left posterior perisylvian region (LPPR), (c) right inferior frontal gyrus (RIFG), and (d) right posterior perisylvian region (RPPR).

showed more activation in the RIFG for semantic judgement than picture naming) and P5 and P8 (who showed more activation in the RIFG for picture naming than semantic judgement), all other participants showed patterns of activation similar to that observed in the normal control participants. Finally, while examining the mean percent BOLD signal change in the RPPR, all the control participants and patients showed more activation in this region for the picture-naming task compared to that for the semantic judgement task: controls ($Z = 2.52$, $p = .01$), patients ($Z = 2.38$, $p = .01$).

To examine the relationship between lesion size and mean BOLD signal change in the different ROIs, a Spearman rank correlation analysis was carried out. This analysis enabled us to examine the relationship between lesion volumes and the mean BOLD signal changes in the four regions of interest: LIFG, RIFG, LPPR, and RPPR. For the picture-naming task there was a significant positive correlation between BOLD signal change in the RPPR and lesion volume ($r = .74$, $p = .03$) indicating that patients with larger lesions had greater percent BOLD signal change in the RPPR than patients with smaller lesions. No other significant correlations were found.

Laterality index

The results of the laterality index analysis are presented in Figure 6. For the normal control participants the mean laterality index for the semantic judgement task was 0.99 ± 0.007 and 0.55 ± 0.17 for the picture-naming task. The semantic judgement task was significantly more left lateralised than the picture-naming task ($Z = 2.52$, $p = .01$). For participants with aphasia the mean laterality index for the semantic judgement task was 0.83 ± 0.17 and 0.32 ± 0.35 for the picture-naming task. The semantic judgement task was significantly more left lateralised than the picture-naming task ($Z = 2.24$, $p = .02$). Additionally, two participants with aphasia (P5 and P8) had negative laterality index for the picture-naming task. To understand the relationship between lesion volume and laterality index for each task a Spearman rank correlation analysis was carried out. The results revealed a significant negative correlation between laterality index and lesion volume ($r = -.55$, $p = .002$) for the picture-naming task, indicating that patients with larger lesion volumes were significantly more right lateralised than patients with smaller lesion volumes.

DISCUSSION

The present study was aimed at investigating the neural correlates of language functions in eight chronic participants with aphasia with different sites and sizes of lesions. To this end, we utilised two tasks that have been successfully demonstrated to activate specific neuroanatomical networks in normal and brain-injured individuals. As predicted, in the control group both tasks induced activation in language areas that are commonly activated during picture naming and semantic judgement (Binder et al., 2009; Indefrey & Levelt, 2004). Activated volumes and regions were larger for the picture-naming task compared to the semantic judgement task for the control participants. Consistent with the whole brain analysis, the ROI analysis demonstrated greater BOLD signal change in the bilateral posterior perisylvian regions for the picture-naming task compared to the semantic judgement task. In addition, the laterality index indicated that the task with increased cognitive demands (picture naming) is less left lateralised than the task with reduced cognitive demands (semantic judgement),

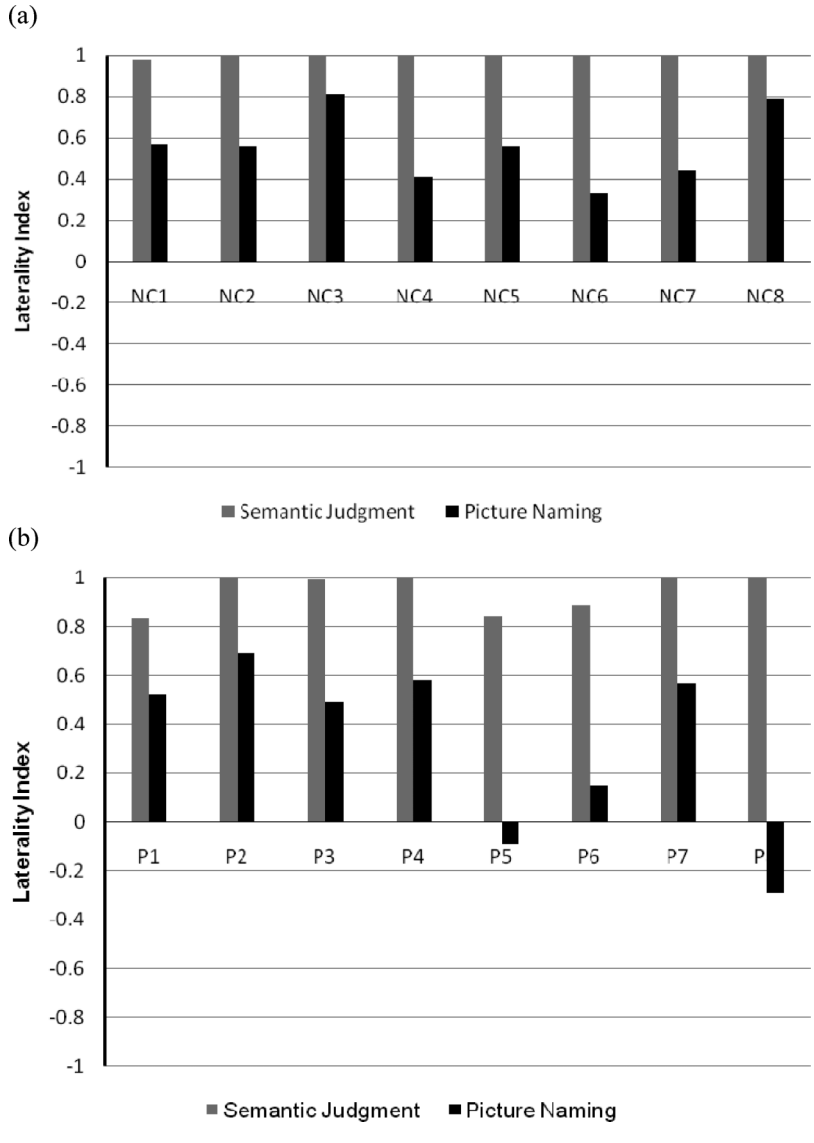

Figure 6. Laterality index for (a) normal control participants and (b) patients.

confirming previous studies reporting that even normal control participants activate both hemispheres during certain language tasks (e.g., Indefrey & Levelt, 2004).

The imaging data in participants with aphasia revealed an interaction between lesion site, lesion size, and task difference. For the semantic judgement task a direct comparison analysis between each patient's activation to that of the control group's activation indicated that all patients without lesions involving the left inferior frontal gyrus activated the left inferior frontal gyrus (LIFG). Further, greater BOLD signal change was observed in the LIFG for all patients with the exception of P1 and P6 during the semantic judgement task. This finding indicates that the LIFG is crucial for the selection of responses from competing lexical information. More

specifically, the results indicate that, when the LIFG is not damaged, patients were able to inhibit competing lexical items and successfully complete the semantic judgement task, similar to the performance observed in the normal control participants. This corresponds with previous studies that have implicated the LIFG in semantic processing (e.g., Bookheimer, 2002; Cai, Kochiyama, Osaka, & Wu, 2007; Hirshorn & Thompson-Schill, 2006; Poldrack, et al., 1999).

Previous neuroimaging studies have emphasised that good recovery of language function in aphasia is associated with perilesional activity (Cao et al., 1999; Perani et al., 2003; Postman-Caucheteux et al., 2010; Warburton, Price, Swinburn, & Wise, 1999). The data from the semantic judgement and picture-naming tasks support the premise that perilesional activity in chronic participants with aphasia is important for neural recovery. We found perilesional BOLD signal change in the LIFG for patients with left frontal lesions (P1 and P6) during both the tasks. Likewise, we found perilesional BOLD signal change in the posterior perisylvian regions for the picture-naming task for patients with left temporal and/or parietal lesions (P2, P3, P4, and P7).

In addition to the importance of perilesional activity in neural recovery, the data also support the premise that right hemisphere regions are involved in language recovery. During the semantic judgement task P1 and P6, who sustained lesions involving the LIFG, showed increased activity in the right inferior frontal gyrus (RIFG). Increased activity in the right hemisphere regions has usually been linked to a less favourable outcome in most studies and seems to be related to large lesions (Heiss et al., 1997), error processing (Postman-Caucheteux et al., 2010) or recovery level (Cao et al., 1999; Dombovy, 2009; Heiss & Thiel, 2006; Winhuisen et al., 2007). The observed right frontal activation for P1 and P6 cannot be attributed to error-related processing or recovery level, as only correct responses were included in the analysis and both patients had achieved high levels of recovery (please see Table 1 for standardised language test scores). Further, the increased activity observed in the RIFG cannot be attributed to lesion size, as there was no correlation between lesion volume and BOLD signal change in the RIFG. Since the left frontal cortex is critical for normal performance of semantic judgement, the present finding implies that activity in right frontal cortex likely represents an efficient compensatory strategy when part of the left inferior frontal gyrus is damaged.

The direct comparison analysis for the picture-naming task further indicated that participants with aphasia recruit regions similar to that observed in normal control participants, although to a larger extent in the non-lesioned regions. For the picture-naming task the direct comparison between each patient's activation to that of the mean control group's activation (see Table 4) revealed greater mean cortical activation in the left inferior frontal gyrus, pars triangularis, for patients P1, P2, P3, P4, and P7. The left pars triangularis was spared in all patients, suggesting that the anterior part of Broca's area may be the strategic centre for developing a new, functionally reorganised, linguistic network able to control most aspects of language. Additionally, there is growing recent evidence that supports the idea that Broca's area and, more generally, the LIFG plays an important role in unification processes (Hagoort, 2005) and is able to organise not only linguistic functions but also hierarchically structured behaviours (Koechlin & Jubault, 2006).

In addition, there was no significant difference in activity in the right frontal or the right temporal region between each patient and the control group with the exception of P5, P6, and P8 (see Table 4). This lack of difference in right hemisphere activation suggests that recovered participants with aphasia utilise neural regions similar to those of control participants, even for complex tasks. In contrast, analyses of the

three patients with large left hemisphere lesions (see Table 1) showed increased right frontal activity (noted for P5) and right temporal activity (noted for P6 and P8). This activation pattern may indicate compensatory function due to a large left hemisphere lesion.

Increased activity in the anterior cingulate cortex was observed for two patients with large lesions (P5 and P8). The anterior cingulate cortex has been recruited by tasks that engage selective attention, response selection, monitoring of conflicting responses, error detection, and initiation of action (Barch et al., 2000; Botvinick et al., 1999; Carter et al., 1998; Fu et al., 2002; Kiehl, Liddle, & Hopfinger, 2000; MacDonald, Cohen, Stenger, & Carter, 2000). To name a picture, the intended word must be selected from a competing set of other words. This may induce a degree of response conflict and place a demand on response selection, leading to activation of the anterior cingulate cortex. Both P5 and P8 had relatively greater difficulty in retrieving words compared to the other patients as revealed during standardised testing (both patients scored 13/60 on the BNT, see Table 1). This indicates an increased likelihood of response conflict and higher demands on response selection prior to overt articulation. Thus the recruitment of this area during successful picture naming is most likely secondary to increased attentional demands. Reaction time data provide further support for this argument as both patients had longer reaction times compared to the other patients (see Figure 2).

The LI results provided further support regarding the interaction between size of lesion and type of task. Interestingly, lesion size did not play a role in determining the activation patterns for the semantic judgement task. Unlike the semantic judgement task, during the picture-naming task participants with aphasia showed less left lateralisation and two patients (P5 and P8) showed predominant right lateralisation, indicating that patients with large lesions in the left hemisphere recruited more right hemisphere regions. This explanation is further supported by the correlation analysis between the laterality index and lesion volumes, which indicated that as lesion size increased, the laterality index changed from positive to negative. These findings are in line with that of Blasi et al. (2002) and Cao et al. (1999) who found right hemisphere activation in chronic participants with aphasia with large left hemisphere lesions many years after stroke onset, suggesting that right hemisphere along with left hemisphere supports language recovery in the chronic stage.

In summary, the results of this study highlight that recruitment of language regions after a stroke is task specific. The findings of the present study indicate a role for both homologous contralesional cortex and perilesional and ipsilesional regions as efficient mechanisms for supporting language functions in chronic stroke patients. Recent studies of motor and speech recovery have suggested that some of the activations (particularly in the hemisphere contralateral to the lesion) observed in post-stroke recovery may not reflect activity that is important to the task, but rather "maladaptive" activation that is unrelated to functional performance (Naeser et al., 2005). In fact, inhibition of right hemisphere areas with repetitive TMS can result in task improvement (Winhuisen et al., 2007). However, the results of our study appear to support the view that the right hemisphere plays an important role in reorganisation. The right hemisphere activation patterns in our patients were task and lesion site/size dependent. Results from motor recovery studies also support the role of contralesional hemisphere for recovery. Nair et al. (2007) studied motor representation in well-recovered stroke patients using two tasks: unimanual index finger movement (abduction–adduction) and wrist movement (flexion–extension) using their recovered and non-affected hand. Imaging results suggested that good recovery utilises both

ipsilesional and contralesional resources, although results differ for wrist and index finger movements. Wrist movements of the recovered arm resulted in significantly greater activation of the contralateral (lesional) and ipsilateral (contralesional) primary sensorimotor cortex (SM1), while recovered index finger movements recruited a larger motor network, including the contralateral SM1, supplementary motor area (SMA), and cerebellum. This further supports our finding that task differences can lead to differences in recruitment of right and left hemisphere regions.

The use of two different tasks with different cognitive demands helped clarify the role of right hemisphere in aphasia recovery. Had our investigation utilised only one task (e.g., semantic judgement task), we might have concluded that non-lesioned tissue within the left hemisphere contributed to neural activation in chronic recovered stroke patients. However, to investigate function in other areas we included the picture-naming task, designed to place greater processing demand bilaterally, and by doing so we were able to elicit activation in the right superior/middle temporal gyrus for both patients and control participants. With regard to task demands, if we had used a less-demanding task (e.g., lexical decision) as compared to semantic judgement, then non-lesioned tissue in the left hemisphere might have been adequate for all patients to perform the task. Ongoing research in our lab supports this premise that when task demand is low, the spared tissue in the left hemisphere is adequate for task performance irrespective of the site or size of the lesion. However, further research is needed to address this issue in detail.

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