Spatiotemporal patterns of language-specific brain activity in patients with chronic aphasia after stroke using magnetoencephalography

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Six participants with chronic aphasia secondary to first-ever ischemic stroke within the middle cerebral artery (MCA) distribution of the left hemisphere and six neurologically intact controls of similar age were given a running recognition memory task for words while the magnetic flux normal to the scalp surface was measured with a whole-head neuromagnetometer. This task had been previously shown to be valid for the localization and lateralization of brain activity specific to receptive language function. As expected, patients exhibited relatively decreased activation in areas known to be involved in receptive language function, including superior temporal gyrus (STG) in the left hemisphere, as well as increased activation of areas outside of the left STG that might potentially support language function. Decreased activation within left STG was associated with a reduction in receptive language in patients, as was increased activation outside of left STG. Results support hypotheses suggesting that peri-lesional areas outside premorbid language areas may assume receptive language function after aphasia secondary to stroke, but that better recovery occurs when putative premorbid language areas are able to normalize.

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Introduction

While the natural history and pattern of functional recovery in aphasia after stroke have been well described (e.g., Kertesz, 1984, 1988, 1996), the brain mechanisms underlying this recovery are less well understood. Hypotheses regarding these mechanisms include (1) restoration of activity in premorbid language areas; (2) expansion to peri-lesional areas within the left hemisphere that may be able to support language (map expansion); and (3) reorganization in homotopic areas of the right hemisphere (Karbe et al., 1998b; Kertesz, 1989; Knopman et al., 1984; Thompson, 2000; Weiller et al., 1995; Welch et al., 2000).

Until relatively recently evidence for these hypotheses was derived primarily from structural data obtained from magnetic resonance imaging (MRI) or postmortem studies; however, with the advent of noninvasive functional imaging methodology, it has become possible to characterize the change in physiological markers of neuronal function after stroke and correlate these with behavioral measures. Studies using either functional magnetic resonance imaging (fMRI) or positron emission tomography (PET) often indicate that normalization of hemodynamic response or metabolic activity in or around putative premorbid language areas of the left hemisphere, specifically superior temporal gyrus and sulcus, is associated with a better outcome than increased right hemisphere activation in homologous areas, with bilateral activation associated with intermediate behavioral outcome (e.g., Cao et al., 1999; Heiss et al., 1997, 1999; Karbe et al., 1998b; Warburton et al., 1999; Welch et al., 2000). However, there are some reports suggesting a significant role for the right hemisphere in recovery of language after stroke (e.g., Musso et al., 1999; Thulborn et al., 1999).

As the specific mechanisms underlying recovery in an individual patient are likely to be dependent on several stroke, demographic, and anatomical factors, vary with time, and have differential degrees of efficacy, elucidation of the timing and relative efficacy of mechanisms for recovery of language, as well as the potential mitigating factors, has significant import for planning of both pharmacological and behavioral interventions. In the current study, we used magnetoencephalography (MEG) to provide initial data regarding the spatiotemporal pattern of activation associated with receptive language function in patients...
with chronic aphasia secondary to first-time unilateral stroke in the left middle cerebral artery (MCA) distribution. MEG, the newest of the functional imaging modalities, directly reflects sources of neuronal activity generated by large neuronal aggregates (Papanicolaou, 1995; Papanicolaou and Tarkka, 1996). MEG combines excellent spatial and temporal resolution to provide the unique opportunity to characterize the spatiotemporal properties of cortical activation associated with sensory (e.g., (Nakasato et al., 1995; Papanicolaou, 1995; Papanicolaou et al., 1990; Zouridakis et al., 1998) and cognitive (e.g., Breier et al., 1998, 1999a, 2000, 2001; Eulitz et al., 1994; Papanicolaou et al., 1999; Salmelin et al., 1994; Simos et al., 2002) function. Therefore, MEG provides an important complement to modalities that image neuronal function indirectly, such as fMRI and PET, and may have a particular advantage over modalities that image changes in hemodynamic response in patients with vascular disease.

The methods used in the current study were developed and validated in a programmatic series of experiments in neurologically intact controls and patients with chronic seizure disorder that demonstrated that (1) the task employed (identifying which words in a list were previously presented in either auditory or visual modalities) can activate receptive language-specific cortex; (2) this language-specific activation is reflected in the late components (after the resolution of the N1m) of the event-related fields (ERFs) to the words, whether target or foil; (3) the mathematical model for estimating the sources of those components (i.e., identifying the activated brain areas) is sufficiently valid; and (4) the number of sources thus identified is a valid index of the relative degree of engagement of a particular brain area (Breier et al., 1999b, 2000, 2001; Papanicolaou et al., 1999, 2004; Simos et al., 1999, 2002; Zouridakis et al., 1998).

In the current study, the spatiotemporal parameters of MEG activation obtained by applying the methods developed in the above-referenced studies to patients with chronic aphasia were used to test several hypotheses. We expected that patients with chronic aphasia, relative to age-matched neurologically intact controls, would exhibit (1) a decrease in the degree of late (after the resolution of the N1m) activation of left superior temporal gyrus (STG) as well as abnormalities in the timing of this activation; (2) an increase in activation of areas within the left hemisphere outside of STG; and (3) an increase in activation in homologous areas of the right hemisphere, including STG. We also evaluated the relation between receptive language function in these patients and the degree of engagement of left STG, areas outside of STG in the left hemisphere, and homologous areas within the right hemisphere, expecting poorer language performance to be associated with increased spatiotemporal abnormality in language-specific MEG activity in left STG.

**Methods**

**Participants**

Patients were six right-handed individuals (two females) recruited at the Texas Institute for Rehabilitation and Research in Houston, TX, ranging in age from 46 to 69 (M = 54.3, SD = 8.5). All six patients had a history of first-ever ischemic stroke in the territory of the left MCA, were at least 10 months post-stroke, and were right-handed premorbidity as assessed with the Edinburgh Handedness Inventory (Oldfield, 1971). Six participants (three females) with no history of stroke or other neurological disorder, ranging in age from 40 to 57 (M = 49.3, SD = 7.2), served as controls. All patients were administered the Western Aphasia Battery (WAB) (Kertesz, 1982), the Boston Naming Test (BNT) (Kaplan et al., 2000), and the Token and Controlled Oral Word Association (COWA) tests from the Multilingual Aphasia Examination (Benton et al., 1994). Patient demographics and scores on language tests are presented in Table 1. There were no statistical differences in age or gender makeup of the two groups. Areas affected by stroke as appreciated on MRI are presented in Table 2.

**Stimuli and tasks**

Participants were given a recognition memory task for spoken words and event-related fields (ERFs) were recorded to each word stimulus. The word list consisted of 90 abstract English nouns with scores of 3.0 or lower on the Paivio Concreteness scale (Paivio et al., 1968). Word frequency ranged from “very frequent” (AA) to nine occurrences per million for some words (Thorndike and Lorge, 1944). A native speaker of English with a flat intonation produced the auditory stimuli (duration between 300 and 750 ms, mean: 450 ms), which were digitized with a sampling rate of 22,000 Hz and 16-bit resolution, stored on a portable computer, and delivered binaurally via two 5-m-long plastic tubes terminating in ear inserts. Intensity was 80 dB SPL at the patient’s outer ear.

Thirty words from each list were used as targets and the remaining 60 as distractors forming six blocks of trials. There were no significant differences between the target and distractor lists in either word concreteness or frequency. The target stimuli were repeated in every block (in a different random order each time).

### Table 1

<table>
<thead>
<tr>
<th>Patient #</th>
<th>Age</th>
<th>Time post-stroke</th>
<th>WAB AQ</th>
<th>WAB comprehension index</th>
<th>BNT (raw score)</th>
<th>COWA (raw score)</th>
<th>Token test (raw score)</th>
<th>Paraphasic production</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>54</td>
<td>10 months</td>
<td>53.0</td>
<td>8.8</td>
<td>22</td>
<td>1</td>
<td>8</td>
<td>yes</td>
</tr>
<tr>
<td>2</td>
<td>48</td>
<td>2 years 9 months</td>
<td>27.8</td>
<td>6.2</td>
<td>1</td>
<td>1</td>
<td>11</td>
<td>yes</td>
</tr>
<tr>
<td>3</td>
<td>50</td>
<td>1 year 9 months</td>
<td>88.4</td>
<td>10.0</td>
<td>50</td>
<td>7</td>
<td>38</td>
<td>yes</td>
</tr>
<tr>
<td>4</td>
<td>46</td>
<td>1 year 2 months</td>
<td>69.1</td>
<td>7.5</td>
<td>9</td>
<td>4</td>
<td>10</td>
<td>yes</td>
</tr>
<tr>
<td>5</td>
<td>59</td>
<td>1 year 7 months</td>
<td>75.8</td>
<td>8.4</td>
<td>22</td>
<td>5</td>
<td>25</td>
<td>yes</td>
</tr>
<tr>
<td>6</td>
<td>69</td>
<td>1 year</td>
<td>76.1</td>
<td>8.1</td>
<td>21</td>
<td>26</td>
<td>24</td>
<td>yes</td>
</tr>
</tbody>
</table>

WAB = Western Aphasia Battery; AQ = Aphasia quotient from the Western Aphasia Battery; BNT = Boston Naming Test; COWA = controlled oral word association (FAS); MAE = Multilingual Aphasia Examination.
lateral eye movements with magnetic deflections caused by brain artifacts were defined as magnetic flux deflections in excess typically present in MEG recordings. The next step involved visual to minimize the amount of low frequency magnetic noise that is subjected to an adaptive filtering procedure that is part of the 4D sampling rate) including a 150-ms prestimulus period, and pass between 0.1 and 20 Hz, digitized for 950 ms (254-Hz approximately 15 min. The signal was filtered online with a band that can interfere with the accurate detection of task-related brain activity, the surface distribution of magnetic flux associated with these deflections was frequently taken into account.

A minimum of 80 artifact-free ERF epochs were used to calculate the averaged waveform. Averaged ERF data were then inspected to verify that they were of sufficient quality using the following criteria: (1) mean prestimulus root mean square (RMS; an estimate of “noise” or task-independent magnetic flux in the recordings) < 25 fT, (2) RMS ratio of “signal” (i.e., magnetic flux associated with a given computed source) to “noise” (i.e., mean magnetic flux during the prestimulus time interval) > 2:1.

The intracranial generators of the observed ERFs (activity sources) were modeled as single equivalent current dipoles and fitted at successive 4-ms intervals by using the nonlinear Levenberg–Marquardt algorithm (Sarvas, 1987). For a given point in time, the source fitting algorithm was applied to the magnetic flux measurements obtained from a group of 34–38 sensors, always including both magnetic flux extremes. While the source computation was generally restricted to latency periods during which a single pair of magnetic flux extremes dominated the left or the right half of the head surface, multiple dipoles were fit within the same hemisphere during the same time period if the data warranted it. The algorithm used in this study searched for the source that was most likely to have produced the observed magnetic field distribution at a given point in time. Source solutions were considered satisfactory if they were associated with a correlation coefficient of at least 0.9 between the observed and the “best” predicted magnetic field distribution.

To determine anatomical regions corresponding to each activity source, source locations, which were initially computed in reference to the MEG Cartesian coordinate system mentioned above, were co-registered on T1-weighted, magnetic resonance (MR) images (TR 13.6 ms; TE 4.8 ms; recording matrix 256 × 256 pixels, one excitation, 240 mm field of view, and 1.4 mm slice thickness) obtained from each participant. Transformation of the MEG coordinate system into MRI-defined space was achieved with the aid of three lipid capsules inserted into the ear canals and attached to the nasion, which could be easily visualized on the MRIs, using the MR Overlay tool, which is part of the 4D Neuroimaging software. A standard MRI atlas of the human brain (Damasio, 1995) served as a reference for the identification of the cerebral structures where sources were localized. Satisfactory source solutions can be described from four complementary measures: (a) location (i.e., spatial coordinates on the MEG Cartesian coordinate system defined by the ear canals and the nasion), (b) estimated current moment of the net neuronal population response (in nA m), (c) global field power (RMS) of the measured magnetic flux used to calculate each activity source (in fT), and (d) latency or delay after stimulus onset at which point a given source is estimated (in ms). In our previous studies with healthy volunteers and patients, the metric that produced the most conclusive results as an index of the degree of regional activation was the total number of successive activity sources occurring after the resolution of the N1m (approximately 200 ms post-stimulus onset) in a particular area or group of areas (e.g., Breier et al., 1998, 1999b, 2000, 2001; Papanicolaou et al., 1999; Simos et al., 2002).

**Results**

As in previous studies using the English and Spanish versions of this task (Breier et al., 1999a,b, 2001; Maestú et al., 2002;
Papanicolaou et al., 1999), all control participants exhibited activation of the superior temporal gyrus, often extending into the superior temporal sulcus, predominantly within the left hemisphere. Less frequently, sources were found in the supramarginal, middle, and inferior temporal gyri as well as mesial temporal and inferior frontal areas, including insula. Occasionally, activity sources were also found in perirolandic areas. As is common in studies using a variety of functional imaging modalities (e.g., Binder, 1997; Breier et al., 2000; 2001; Heiss et al., 1999; Karbe et al., 1998a; Papathanassiou et al., 2000; Warburton et al., 1999; Weiller et al., 1995), MEG activity sources were often found bilaterally in these areas in controls.

Co-registered MEG-MRI scans for the six control participants are presented in Figs. 1a and b, while scans for each of the six patients are presented in Figs. 2a and b. Activation sources extending over the width of 1.5 cm are projected onto the same sagittal image. Recent imaging evidence suggests that anterior perisylvian areas may play a role in receptive language function in both neurologically intact adults (e.g., Binder, 2000; Binder et al., 1997; Booth et al., 2002) and in patients with both acute and chronic lesions (e.g., Heiss et al., 1999; Lazar et al., 1997). Therefore, we included inferior frontal gyrus and insula along with more posterior areas outside of STG, including middle and inferior temporal, supramarginal, and angular gyri, as potential candidates for language reorganization. Activity in mesial temporal, motor, and somatosensory areas is not included.

In the control participants, left hemisphere activation is generally predominantly within STG and well organized, while in the right hemisphere, activation within STG is relatively reduced and more dispersed. Patients generally exhibit decreased activation in left STG compared to controls, with many exhibiting peri-lesional activation within left hemisphere areas outside STG. Increased activation within the right as compared to the left hemisphere is also evident in some patients.

To examine group differences in the temporal unfolding of late, language-specific MEG activation, sources in STG were placed in consecutive 50-ms epochs (i.e., 200–250, 251–300, . . ., 951–1000 ms). The mean number of MEG activation sources within each epoch within each hemisphere is shown for controls and patients in Figs. 3a and b, respectively. Activation occurring during the early component of the recorded epoch (N1m: between approximately 80 and 200 ms), which is generally located in primary auditory cortex (Breier et al., 2001; Nakasato et al., 1995; Papanicolaou, 1995; Zouridakis et al., 1998), is included for comparison purposes. While there is little interhemispheric asymmetry in activation during this early component, controls exhibited the expected left hemisphere predominance of activation in left STG after the resolution of N1m. In the patients, however, the opposite profile was evident, with greater right as compared to left hemisphere activation in this area during the later portion of the recorded epoch.

Trends for the later portion of the recorded epoch (after the resolution of the N1m) were evaluated using repeated measures ANOVA with epoch and hemisphere as the within-subjects factors and group (patient, control) as the between-subjects factor. The hemisphere by group interaction was significant, $F(1,10) = 8.48$, $P < 0.016$, indicating a significant difference in the degree of engagement of left and right STG between groups across epochs. Follow-up analyses evaluated interhemispheric asymmetries in activation within group as well as group effects on the degree of activation within each hemisphere. While there was greater activation of left than right STG in the control group, $F(1,5) = 16.7, P < 0.01$, patients, as a group, did not exhibit a hemispheric asymmetry in the degree of activation of left and right STG ($P > 0.35$). Comparing the degree of activation within hemisphere for the two groups, there was a marginal group effect for the left hemisphere.
hemisphere, $F(1,10) = 3.42, P < 0.09$, while the effect for the right hemisphere was not significant, $F(1,10) = 0.85, P < 0.35$. The latter results suggest that a relative reduction in left hemisphere activation, rather than an increase in right hemisphere activation, accounts for much of the attenuation of interhemispheric asymmetry in activation observed in the patient group.

The effects of stroke on the spatial profile of language-specific MEG activation

To test hypotheses regarding the neural bases for recovery of language function we first determined the total late activation within (1) left STG; (2) middle and inferior temporal, supramarginal, and angular gyri as well as inferior frontal gyrus and insula (primary motor and sensory and mesial temporal areas were not included); and (3) homologous areas within the right hemisphere, including STG. Each of these measures was then normalized to the total observed late MEG activation after the resolution of the N1m, forming, and activity index (AI) for each area. Group means on these indices are depicted in Fig. 4.

These trends were evaluated using separate one-way ANOVAs with group (patient, control) as the independent variable. The only
significant group effect was for the degree of engagement of left STG, $F(1,10) = 6.95, P < 0.025$. As can be seen in Fig. 4, patients tended to exhibit significantly less activation of left STG than controls. There was also a trend for patients to exhibit greater activation in areas within the left hemisphere outside of STG, although this trend did not reach significance ($P > 0.19$). There was little difference between the groups in degree of engagement of right hemispheres in areas that might potentially support language ($P > 0.9$). There was no difference between groups in total brain activation ($P > 0.5$).

The effects of stroke on the temporal profile of activation within primary sensory cortices and STG in left and right hemispheres

Group means for the timing of the onset as well as peak RMS for both the early and later (after the resolution of the N1m) portions of the recorded epoch within left and right hemispheres are presented in Table 3. These trends were evaluated in separate one-way ANOVAs with group as the independent variable.

For the early component (N1m), there was a trend toward a slight delay (about 10–15 ms) in the onset within the left hemisphere for patients, $F(1,10) = 3.33, P < 0.09$, but no group differences in timing of peak RMS ($P > 0.2$) for this component. There were no significant effects for the right hemisphere ($P > 0.2$).

For the later component, there was a significant group effect for latency of onset, $F(1,10) = 5.25, P < 0.05$, and a trend for timing of peak RMS, $F(1,10) = 3.33, P < 0.09$, in the left hemisphere only. There were no significant findings within the right hemisphere. As can be seen in Table 2, both the onset and latency of peak RMS for the later portion of the recorded epoch were delayed significantly (>100 ms) in the patient group in the left hemisphere, with essentially no group differences in these temporal parameters of MEG activation in the right hemisphere. There were no significant group differences in the peak RMS for the later portion of the recorded epoch for either hemisphere ($P > 0.6$).

The relation between speech comprehension and activation of areas within the left and right hemisphere

The relation between receptive language function as measured by the receptive language index of the WAB and each of the three

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>N1m</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Onset (SD)</td>
<td>92 (10)</td>
<td>107 (16)</td>
</tr>
<tr>
<td>Peak (SD)</td>
<td>124 (11)</td>
<td>133 (16)</td>
</tr>
<tr>
<td>STG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Onset (SD)</td>
<td>219 (46)*</td>
<td>367 (152)</td>
</tr>
<tr>
<td>Peak (SD)</td>
<td>314 (109)</td>
<td>491 (212)</td>
</tr>
<tr>
<td>Right hemisphere N1m</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Onset (SD)</td>
<td>87 (10)</td>
<td>97 (13)</td>
</tr>
<tr>
<td>Peak (SD)</td>
<td>126 (12)</td>
<td>126 (16)</td>
</tr>
<tr>
<td>STG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Onset (SD)</td>
<td>287 (75)</td>
<td>270 (104)</td>
</tr>
<tr>
<td>Peak (SD)</td>
<td>379 (131)</td>
<td>365 (181)</td>
</tr>
</tbody>
</table>

* $P < 0.05$.

indices derived above for patients was evaluated using Pearson correlation coefficients.

For the WAB comprehension index, there were strong correlations between the degree of activity within ($r = 0.69, P < 0.13$) and outside left STG ($r = -0.61, P < 0.19$), although neither reached significance within this small group. The relation between the WAB comprehension index and degree of activation of areas within the right hemisphere was markedly smaller ($r = 0.16, P < 0.76$). The relation between the comprehension index of the WAB and degree of engagement of left STG and areas outside STG within the left hemisphere is presented in Figs. 5a and b, respectively. As can be seen, greater activation of left STG is associated with better comprehension while the reverse is true of greater activation of areas outside of STG within the left hemisphere that might support language function.

Performance on the WAB comprehension index was also correlated with the timing of the latencies of the peak and onset of activation within left and right STG. While there were no relationships within the right hemisphere, there was a significant correlation between receptive language function and the latency of onset of activation within left STG ($r = -0.95, P < 0.004$). The WAB comprehension index is plotted as a function of latency of onset of left STG activation in Fig. 5c. Longer latency of activation was associated with reduced performance.
There were no significant relations between performance on the Token test and spatiotemporal parameters of MEG activation.

Discussion

The current study provides initial data regarding the spatiotemporal parameters of receptive language function in patients with chronic aphasia secondary to ischemic stroke in the distribution of the left MCA and some degree of support for specific hypotheses regarding the spatial pattern of reorganization of receptive language function in this group. As expected, there was no interhemispheric asymmetry in degree of activation of primary auditory cortex that occurred during the early portion (generally before 200 ms post-stimulus onset) of the recorded epoch in either patients or controls. Consistent with previous studies utilizing a similar protocol (Breier et al., 1999b, 2000; Papanicolaou et al., 1999; Simos et al., 1998, 1999), neurologically intact adults of similar age to patients exhibited consistent activation in STG bilaterally, with an overall left hemisphere predominance of activity. In contrast, patients exhibited a more bilateral spatial profile of activation in this area known to be involved in receptive language function, with evidence for significantly reduced activation in left STG and increased activity in areas outside of STG that might support language function. Timing of activation within left STG was also affected in patients, with significant delays in the onset and peak of late, language-specific MEG activity, but not in activation of primary auditory cortex. In addition, receptive language function was correlated with the spatiotemporal parameters of MEG activation within left STG as well as areas outside of STG within the left hemisphere that might support language function. Generally, a greater degree of abnormality in the spatiotemporal parameters of late MEG activation within left STG was associated with reduced speech comprehension. Increased activation within left hemisphere areas outside of STG was also associated with poorer performance.

It has long been thought that portions of STG and STS in the left hemisphere are involved in speech perception (Hillis et al., 2001; Kreisler et al., 2000; Martin, 2003; Wernicke, 1874), and that restoration of functional activity in these areas after stroke is crucial to recovery of language function (Heiss et al., 1999; Karbe et al., 1989; Metter et al., 1990). Consistent with this hypothesis, aphasics, as a group, exhibited relatively decreased activation within left STG. However, receptive language is most likely subserved by a distributed network within the left hemisphere, including areas within superior, middle, and inferior temporal gyri, supramarginal and angular gyri in the parietal lobe (Binder, 2000; Binder et al., 1997; Burton et al., 2001; Martin, 2003). These areas, along with more anterior perisylvian areas that had been previously implicated in speech comprehension in normal and patient groups, were therefore considered as potential candidates for reorganization of language function after stroke in this study. Consistent with hypotheses suggesting a role for perilesional areas in the recovery of language function (Warburton et al., 1999; Weiller et al., 1995), patients exhibited a greater degree of activation in these areas outside of left STG and this activation often impinged upon damaged cortex.

A role for the right hemisphere in the recovery of receptive language function has also been suggested (Calvert et al., 2000; Cappa et al., 1997; Gainotti, 1993; Mimura et al., 1998). However, current results did not provide strong support for this hypothesis as applied to patients in the chronic stage of recovery. While there was evidence for a relative increase in activity in right STG and perisylvian areas in some patients compared to controls, group trends did not reach significance, and much of the attenuation in interhemispheric asymmetry observed in this group was attributable to relative reduction in left hemisphere activation. As the ability of the right hemisphere to participate in language function both before and after stroke may vary across individuals (Thompson, 2000), this mode of reorganization may require a larger study sample to detect.

As expected, speech comprehension was related to abnormalities in the temporal parameters of activation within the left STG. Performance on the speech comprehension index of the WAB decreased with increasing delay in the onset of language-specific MEG activity in the left STG. In addition, while the correlations between comprehension and activation within and outside left STG did not reach significance, the correlations were large (\( r > 0.6 \)) (Cohen, 1988), suggesting that in a larger study sample a significant relation would be found. Greater activation within the left STG was associated with better performance while the reverse was true for greater activation outside of this area within the left hemisphere. Both of these findings are consistent with previous reports of improved recovery with restitution of activity within left STG and relatively less improvement when left STG cannot be reactivated and peri-lesional and other areas outside of left STG must be relied on to subserve language function (e.g., Cao et al., 1999; Gainotti, 1993; Heiss et al., 1997, 1999; Hillis et al., 2001; Karbe et al., 1998a,b; Metter et al., 1990).

There were no significant relations between comprehension and the spatiotemporal parameters of right hemisphere activation. Again, the role of the right hemisphere in recovery might be too variable to detect in a small study sample, although a lack of correlation between changes in right hemisphere activation and behavioral measures in individuals with aphasia after stroke has been previously reported (Metter et al., 1990).

While Token Test scores did not replicate the findings of the WAB comprehension index, the trends were generally in the same direction. The stimuli in the Token Test likely put a load on working memory, as subjects have to remember increasingly longer phrases like “put the large black square on the small red circle” to respond accurately. Therefore, given the imaging evidence implicating dorsolateral prefrontal cortex in working memory (e.g., Curtis and D'Esposito, 2003; Drummond et al., 2003; Nyberg et al., 2003; Rypma et al., 2002; Wagner et al., 2001), the lack of strong correlation between performance on this task and activation in temporal areas is perhaps not surprising.

The task used in the current study included a memory component, and mesial temporal activation was observed in many patients. However, we did not include this activation as a candidate for language reorganization. While there is some possibility that activation elsewhere in the brain, including perisylvian areas, was due to the memory requirement, data to address this issue are not available. The possibility that the finger response requirement affected findings would appear to be minimal as areas in motor and premotor cortex were not included in the study, the response was identical for all participants, and the methodology used had been previously validated for the purpose of mapping receptive language cortex in a large series of studies in patients and neurologically intact controls (Breier et al., 1999a, b, 2001; Papanicolaou et al., 1999, in press; Simos et al., 1999).
This is a small study, and patients had a mixture of language deficits as well as lesions of differing sizes and locations, making generalization of findings difficult. However, consistent with hypotheses regarding the potential mechanisms underlying recovery of language function after aphasia secondary to stroke, there was evidence for a disruption in the spatiotemporal profile of language-specific MEG activation within left STG, as well as for increased activation in areas within the left hemisphere outside of STG, including peri-lesional and other areas that have been implicated in receptive language function. Relations between spatiotemporal parameters of MEG language maps and behavioral function were also consistent with previous reports suggesting an association between better recovery from aphasia and a greater degree of activation of left STG. Further research is necessary to confirm the current findings, determine to what extent they generalize to patients during the subacute stages of stroke, and assess the effects of stroke, demographic, and interventional factors that might potentially mitigate them.

References


