Evidence for cortical reorganization of language in patients with hippocampal sclerosis

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Naming is mediated by perisylvian cortex in the left (language-dominant) hemisphere, and thus, left anterior temporal lobe resection for pharmacologically intractable temporal lobe epilepsy (TLE) carries risk for post-operative naming decline. Interestingly, this risk is lower in patients with hippocampal sclerosis (HS) relative to those without HS (non-HS). Although the hippocampus has traditionally been considered a critical structure for memory, without contribution to naming, this pattern might implicate direct hippocampal naming involvement. On the other hand, critical naming sites have been found in anterior, lateral temporal (i.e. extra-hippocampal) neocortex, the region typically removed with ‘standard’ TLE resection. We, therefore, speculated that the relative preservation of naming in post-operative HS patients might reflect cortical reorganization of language to areas outside this region. Using pre-resection electrical stimulation mapping, we compared the topography of auditory and visual naming sites in 12 patients with HS and 12 patients without structural brain pathology. Consistent with previous work, non-HS patients exhibited post-operative naming decline, whereas HS patients did not. As hypothesized, HS patients had proportionally fewer overall naming sites in anterior temporal cortex, the region typically removed with standard anterior temporal resection, whereas non-HS patients exhibited a more even distribution of naming sites in anterior and posterior temporal regions ($P = 0.03$). Although both groups exhibited the previously reported pattern of auditory naming sites anterior to visual naming sites, auditory naming sites had a significantly more posterior distribution in HS patients ($P = 0.02$). Additionally, non-HS patients exhibited a greater proportion of visual naming sites above the superior temporal sulcus, whereas visual naming sites in HS patients were scattered across superior and inferior temporal cortex. Results suggest that preserved naming ability in HS patients following anterior temporal resection might be attributable, at least in part, to intrahemispheric reorganization of language in response to the likely, early development of sclerosis in the medial temporal region. Furthermore, their more posterior distribution of naming sites is consistent with the more anterior propagation of EEG discharges in TLE. These results hold theoretical implications regarding the role of the dominant hippocampus in determining the cortical representation of semantic and lexical information, and raise questions regarding the specific roles of medial and lateral temporal cortex in targeted word retrieval. The different patterns of naming areas identified in patients with and without HS may also carry clinical implications, potentially improving efficiency during the time-constrained process of stimulation mapping.

Keywords: language mapping; cortical stimulation; cortical reorganization

Abbreviations: TLE = temporal lobe epilepsy; HS = hippocampal sclerosis


It is well established that naming is mediated by perisylvian cortex in the left (language-dominant) hemisphere. This is based on results from lesion studies (Brust et al., 1976; Mazzocchi and Vignolo, 1979), direct cortical stimulation (Penfield and Roberts, 1959), and more recently, functional imaging (Tomaszewki-Farias et al., 2005). Accordingly, anterior temporal lobe resection for treatment of pharmacologically intractable temporal lobe epilepsy (TLE) involving the language dominant hemisphere carries the risk of post-operative naming decline.
Interestingly, the risk of naming decline is lower in TLE patients with hippocampal sclerosis (HS) relative to those without HS (non-HS) (Davies et al., 1998). Although this pattern might suggest direct hippocampal involvement in naming, essential naming areas have been found in anterior, lateral temporal (extra-hippocampal) neocortex, the region typically removed with standard TLE resection (Ojemann et al., 1989). Thus, it is possible that the relative preservation of naming in HS patients following anterior temporal resection might reflect cortical reorganization of language to areas outside the anterior temporal region. Early injury to the language-dominant hemisphere, such as head trauma or stroke, can elicit partial or complete hemispheric transfer of language (Duchowny et al., 1996; Liegeois et al., 2004). HS, which is assumed to occur early in development (Hesdorffer et al., 2005), might induce more subtle, intra-hemispheric neural reorganization of language, in that cortical sites essential for naming might shift away from the region of seizure onset (Saykin et al., 1995). Consequently, naming sites would less likely be included within the boundaries of most ‘standard’ anterior temporal resections, and thus naming would more likely remain stable post-operatively. To our knowledge, however, the topography of naming sites has not been directly compared in patients with and without HS.

Although intracarotid amobarbital testing and functional imaging techniques have been useful in studying hemispheric lateralization of language, electrical stimulation mapping remains the gold standard for intrahemispheric identification of language cortex. The goal of stimulation mapping is to identify ‘essential’ language cortex, and spare these sites from resection with the objective of preserving post-operative language function (Ojemann and Dodrill, 1981; Hamberger et al., 2005). Using this technique, patients are requested to perform various language tasks, traditionally visual object naming, during brief periods of electrical stimulation applied to discrete cortical sites. Positive sites are identified when task performance is disrupted during stimulation, yet normal upon cessation of stimulation. Results of studies utilizing stimulation mapping have shown considerable variability among patients with respect to the particular location of cortical naming sites (Ojemann et al., 1989). Using visual object naming, positive sites have generally been found in the mid to posterior portion of the lateral temporal region. However, utilization of auditory description naming (e.g. ‘what a king wears on his head’) together with visual naming, has shown auditory naming sites in the anterior temporal region, typically <5 cm from the temporal pole, with visual or ‘dual’ naming sites (i.e. supporting both visual and auditory naming) in the mid to posterior temporal region (Malow et al., 1996; Hamberger et al., 2001).

Given that TLE patients with HS tend to show less post-operative naming decline relative to patients without HS, together with the fact that temporal lobe resection typically encompasses the anterior 3.5–4.5 cm of lateral temporal cortex, we hypothesized that patients with HS would have proportionally fewer naming sites in anterior than posterior temporal cortex. On the other hand, patients without HS would have a more even distribution of naming sites across the lateral temporal region. Additionally, given that auditory naming sites have been found primarily in the anterior temporal region, we also hypothesized that either: (a) HS patients would exhibit fewer auditory naming sites overall, or that (b) auditory naming sites in HS patients would be located more posteriorly relative to those in non-HS patients.

Pre-resection, stimulation mapping provided the opportunity to address these hypotheses. Specifically, we compared (1) the proportionate distribution (anterior/posterior) of auditory and visual naming sites, and (2) the number and topographical distribution of auditory naming sites in left (dominant) TLE patients with and without HS. Historically, naming sites have been identified using visual object naming, exclusively. Thus, for purposes of both brevity and consistency with previous literature, sites at which stimulation disrupted visual naming, regardless of auditory naming performance, will be referred to as ‘visual’ naming sites.

**Methods**

**Subjects**

Twenty-four consecutive, right-handed patients (14 women, 10 men) who underwent stimulation-based cortical language mapping before left temporal surgical resection and met inclusion criteria were included in this study. All patients were required to be left hemisphere language dominant, as determined by intracarotid amobarbital (Wada) testing, and to be native English speakers or to have learned English prior to age 5 years. Naming was tested in all patients using the Boston Naming Test (Kaplan et al., 1983) and Auditory and Visual Naming Tests (Hamberger and Seidel, 2003) within 4 months preceding surgery, and approximately 1 year post-operatively (HS mean: 12.1, SD = 4.2, non-HS mean: 14.5, SD = 7.8; P = 0.45). Twelve patients had HS confirmed on post-operative histology, and 12 patients showed no evidence of HS or any other abnormalities on MRI, and no medial temporal abnormalities on post-operative histology. Thus, to the best of our knowledge, all patients in the non-HS group were lesion free.

Sixteen patients (7 HS, 9 non-HS) underwent language mapping extra-operatively via subdural electrodes, 10 at Columbia University Medical Center and six at New York University Medical Center. In the seven HS patients who underwent subdural monitoring, both the scalp EEG and seizure semiology were not clearly consistent with medial temporal onset. Given the possibility of dual pathology (Fauser and Schulze-Bonhage, 2006), these patients were implanted to most accurately identify the region of seizure onset and maximize the likelihood of post-operative seizure freedom. Eight by eight grids were tailored as necessary on a case by case basis to cover the desired area based on pre-operative prediction of the epileptogenic zone. Eight patients (five HS, three non-HS) at Columbia University Medical Center.
Medical Center underwent intra-operative language mapping before resection. Results of Fisher’s exact test indicated no significant difference in the number of patients who underwent extra- versus intra-operative mapping between HS and non-HS patients ($P=0.67$).

Demographic and clinical information are presented in Table 1. This study was approved by both the Columbia University Medical Center and New York University Medical Center institutional review boards. All patients signed informed consent prior to participation.

**Table 1** Demographic data, IQ and Naming test scores

<table>
<thead>
<tr>
<th></th>
<th>HS</th>
<th>Non-HS</th>
<th>$P$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>38.1 (9.1)</td>
<td>30.7 (10.1)</td>
<td>0.07</td>
</tr>
<tr>
<td><strong>Seizure onset (years)</strong></td>
<td>18.3 (12.1)</td>
<td>16.3 (10.8)</td>
<td>0.69</td>
</tr>
<tr>
<td><strong>IQ</strong></td>
<td>100.2 (12.1)*</td>
<td>91.1 (14.2)</td>
<td>0.10</td>
</tr>
<tr>
<td><strong>Education (years)</strong></td>
<td>15.0 (3.1)</td>
<td>14.1 (3.0)</td>
<td>0.89</td>
</tr>
</tbody>
</table>

*IQ was available for 10 HS patients.

**Note:** Mean (SD); Abbreviations: IQ = WAIS-III Full Scale IQ.

Electrodes

For the 16 patients who underwent extra-operative mapping, an eight by eight (i.e. 64 contact) grid array, with 5 mm diameter electrodes embedded in silastic with centre-to-centre inter-electrode distances of 1 cm (Ad-Tech, Racine, Wisconsin), was positioned over the frontal-parietal-temporal region (trimmed as needed to conform to the covered area). The exposed cortical surface and grid position were documented by digital photography and schematic diagrams. Initial schematics were drawn by the surgeon intra-operatively, while looking directly at the brain surface. Digital photos were then used post-operatively to refine the diagrams and subdural electrode positions were verified by skull X-rays, post-operatively. In addition to skull X-rays, electrode location was confirmed with post-operative MRI and/or CT neuroimaging. Post-operative volumetric studies were loaded into a frameless stereotactic workstation and a 3D model was rendered. Electrode location was verified in comparison to the intra-operative digital photographs. From 16 to 38 sites (mean = 24.7, SD = 6.4) were tested in each patient. For the eight patients evaluated intra-operatively, 9–23 sites (mean = 15.3, SD = 4.1) along the superior, middle and inferior temporal gyri and the posterior perisylvian cortex were stimulated using a bipolar stimulator with 2 mm diameter ball contacts separated by 5 mm (Ojemann Cortical Stimulator, Radionics Inc.). The sites were chosen based on gyral/vascular anatomy and spaced less than 10 mm apart. Electrode positions were documented using digital photography and schematic diagrams.

**Mapping procedures**

Stimulation mapping was conducted using both visual and auditory naming tasks. As noted, all naming stimuli were administered to patients within 4 months pre-operatively, to assess baseline naming ability. Only items which patients successfully completed at baseline were administered during cortical mapping (i.e. items associated with naming errors at baseline could not be used to identify stimulation-related errors during mapping). For all patients, mapping was conducted while antiepileptic drug levels were in the therapeutic range, to minimize after-discharges and seizure activity.

Extra-operative language mapping was conducted following intracranial video/EEG monitoring to identify the seizure onset zone. Testing was conducted during electrical stimulation applied to two adjacent electrodes. When results were positive, each electrode was studied individually, referenced to a remote electrode in ‘silent cortex’. All available sites along lateral temporal cortex, as well as parietal sites in the perisylvian area were stimulated.

Patients who underwent intra-operative mapping were initially anaesthetized with propofol. Language mapping began following craniotomy/dural opening, electrocorticography and stimulation to determine the threshold for after-discharges. Several practice trials were conducted to ensure an adequate level of patient responsiveness. Stimulation sites were primarily in the vicinity of the anticipated resection. Sites were tested with a bipolar stimulator (see earlier).

Stimulation mapping followed well-established methods (Ojemann, 1983; Ojemann et al, 1993). For both intra- and extra-operative mapping at Columbia University Medical Center, a constant current stimulator (Ojemann Cortical Stimulator, Radionics Inc.) delivered a biphasic square waveform at a frequency of 60 Hz with a 2 ms pulse duration and amperage ranging from 3 to 15 mA during extra-operative mapping and 2–12 mA during intra-operative mapping. Mapping at NYU Medical Center was conducted using a Grass Instruments S-12 Cortical Stimulator with a biphasic square waveform at a frequency 50 Hz with a 0.3-ms pulse duration, with amperage ranging from 3 to 15 mA. At both centres, after-discharge levels were determined by increasing amperage until an after-discharge was elicited, with an upper limit of 15 mA. Amperage for stimulation was set at 0.5 to 1 mA below that which elicited an after-discharge (or 15 mA). Results reported here are from trials during which no after-discharges were elicited.

At least two trials of both visual and auditory naming were conducted at each site. If results were ambiguous or the patient was temporarily inattentive, additional trials were administered.

For visual naming, patients were shown line drawings of common items (e.g. bench, helicopter), and for auditory naming, patients heard oral descriptions of common items (e.g. ‘what a king wears on his head’). For visual naming, patients began with the carrier phrase, ‘This is a’ to enable differentiation between motor speech arrest and anomia, whereas, for auditory naming, patients were instructed to name the target item. Sites at which stimulation elicited speech arrest were not considered ‘naming’ sites. As visual naming was tested at all sites, differentiation between speech arrest and naming impairment was straightforward. Auditory naming stimuli were limited to those that contained a maximum of eight words and could be presented clearly in less than 4 s. Additionally, the requirement for patients during visual naming to articulate the carrier phrase before naming the pictured object balanced the stimulus presentation and stimulation duration times between tasks.

Electrical stimulation began immediately before presentation of pictured objects and auditory descriptions, and lasted for a maximum of 10 s, but terminated immediately upon the patient’s production of a correct response. Patients were instructed to respond as quickly as possible. When one of two trials was performed inaccurately, another two trials were administered. Sites were considered critical for task performance only when
responses to both of these latter two trials were incorrect (i.e. 75% incorrect). Sites at which this further testing resulted in ≥50% accuracy were not considered critical for task performance, and responses recorded at these sites were not included in data analyses. The number of sites tested per patient was comparable between groups (HS: mean = 20.3, SD = 7.1; non-HS mean: 22.9, SD = 7.4, P = 0.39).

Although mapping is typically more extensive extra-operatively, several factors suggest that the HS and non-HS groups underwent comparable mapping procedures, as critical aspects of the protocol are standardized in the two settings: (1) as noted earlier, the number of patients who underwent intra- and extra-operative mapping, and the number of sites tested per patient in HS and non-HS groups were comparable, (2) patients were alert and attentive throughout both intra- and extra-operative procedures, (3) in both settings, stimulation was conducted 1 mA below after-discharge thresholds with a maximum of 15 mA, (4) all patients underwent at least two trials of both auditory and visual naming, (5) in both settings, only trials free of after-discharge activity were considered valid and (6) the superior (STG), middle (MTG) and inferior temporal (ITG) gyri as well as mid to posterior suprasylvian cortex within 1 cm above the sylvian fissure were reliably mapped in all patients. This was determined empirically by segmenting the STG, MTG, ITG and suprasylvian region into centimetre-wide sections from the temporal pole, and comparing the number of sites tested within each section between groups. Results of independent samples T-tests with Bonferroni’s corrections indicated that these regions from the temporal pole to approximately 9 cm from the temporal pole were comparably mapped between the HS and non-HS groups.

**Data analysis**

Both auditory and visual naming sites from each patient were plotted on a schematic of the temporal region. Separate schematics were created for HS and non-HS patients. The number of auditory naming sites, visual naming sites and total naming sites (regardless of modality) per patient were compared between HS and non-HS patients via independent sample T-tests. To assess potential topographical differences between groups, the anterior temporal region was defined as <5 cm from the temporal pole, and the posterior temporal region as ≥5 cm from the temporal pole. The measurement of 5 cm was selected given the typical resection boundary, with a margin of ~1 cm. Although the functional neuroanatomy of naming, as determined by traditional visual naming measures, might implicate posterior to ~4 cm from the temporal pole (Ojemann, 1983), we used the resection parameters to operationally define anterior and posterior temporal cortex given the impetus for the study (i.e. to understand post-operative naming differences following resection). The proportion of auditory and visual naming sites in the anterior and posterior temporal regions was compared in HS versus non-HS patients via Fisher’s exact tests. Topographical differences in the superior/ inferior distribution of naming sites were tested similarly, with superior sites defined as those located above the superior temporal sulcus, and inferior sites defined as those located below the superior temporal sulcus (middle and inferior temporal gyri). Demographic and clinical data and were compared between HS and non-HS patients with independent sample T-tests. Comparisons between pre- and post-operative naming scores were performed via paired sample T-tests for both HS and non-HS patients. T-tests were used rather than repeated measures ANOVA due to the small sample size of eight non-HS patients who met criteria for inclusion in this analysis (see later, ‘Results’ section).

**Table 2: Pre- and post-operative naming performance in HS and non-HS patients**

<table>
<thead>
<tr>
<th>Naming test</th>
<th>Pre-operative performance</th>
<th>Post-operative performance</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BNT</td>
<td>46.9 (78)</td>
<td>44.8 (79)</td>
<td>0.30</td>
</tr>
<tr>
<td>ANT</td>
<td>44.8 (5.5)</td>
<td>45.7 (4.1)</td>
<td>0.43</td>
</tr>
<tr>
<td>VNT</td>
<td>490 (1.2)</td>
<td>492 (1.1)</td>
<td>0.73</td>
</tr>
<tr>
<td><strong>Non-HS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BNT</td>
<td>44.8 (8.6)</td>
<td>378 (8.3)</td>
<td>0.03</td>
</tr>
<tr>
<td>ANT</td>
<td>44.6 (4.1)</td>
<td>44.0 (4.2)</td>
<td>0.61</td>
</tr>
<tr>
<td>VNT</td>
<td>481 (2.3)</td>
<td>476 (2.5)</td>
<td>0.32</td>
</tr>
</tbody>
</table>

Note: Mean (SD); Abbreviations: BNT = Boston Naming Test, ANT = Auditory Naming Test, VNT = Visual Naming Test. BNT scores: number of items correct of possible 60; Auditory and Visual Naming Test scores: number of items correct of possible 50.

**Results**

**General group comparisons**

**Post-operative naming performance**

To maintain consistency with the Davies et al. (1998) study, together with our question regarding the role of the hippocampus in naming and/or language organization, we restricted analyses of post-operative naming change to patients who received hippocampectomy. Due to lateral temporal neocortical onset, the hippocampus was spared in four non-HS patients. Post-operative naming scores were available for 10 HS and 8 non-HS patients. Results of related sample T-tests are shown in Table 2, replicating the finding of significant BNT decline in non-HS patients, yet no significant BNT decline in patients with HS. No significant changes were evident on the Auditory Naming Test or the Visual Naming Test.

**Topography of naming sites**

The topographical distribution of auditory and visual naming sites in HS and non-HS patients is shown in Fig. 1A and B. At least one positive naming site was found in all 12 HS patients and in 10/12 non-HS patients. The mean number of naming sites identified per patient was higher among HS patients (3.7, SD = 2.1) than in non-HS patients (1.9, SD = 1.4, P = 0.03). Consistent with previous work, both HS (P = 0.01) and non-HS patients (P = 0.01) showed auditory naming sites generally anterior to visual naming sites (Hamberger et al., 2001). Also consistent
with previous findings, disruption of visual naming was generally accompanied by disruption in auditory naming (i.e. co-occurrence in 92% of visual naming sites in the current data) (Hamberger et al., 2001).

A priori hypotheses

Anterior versus posterior distribution

Results of Fisher’s exact test comparing the anterior/posterior distribution of naming sites between HS and non-HS patients indicated a significantly different pattern between the two groups (Table 3, \( P = 0.03 \)). As hypothesized, HS patients exhibited proportionally fewer naming sites in anterior temporal cortex (HS: 37.5%, non-HS: 56.5%). Separate analyses for auditory and visual naming sites revealed a significant group difference for auditory naming sites (Table 4, \( P = 0.01 \)), in that non-HS patients had no auditory naming sites in posterior temporal cortex, whereas auditory naming sites were more evenly distributed across anterior and posterior temporal cortex in the HS group. No significant group differences were found specific to visual naming sites with respect to anterior versus posterior temporal cortex (Table 5, \( P = 0.32 \)).

Number and location of auditory naming sites

Although we hypothesized that HS patients might have fewer auditory naming sites overall, there was no significant group difference in the number of auditory naming sites identified (HS mean = 1.6, SD = 1.1; non-HS mean = 0.83, SD = 1.1, \( P = 0.11 \)). However, consistent with our hypothesis regarding the location of auditory naming sites, these sites were located more posteriorly in HS than in non-HS patients (Table 6, \( P = 0.02 \)). No group differences were found for number (\( P = 0.13 \)) or location (\( P = 0.26 \)) of visual naming sites.

Superior versus inferior distribution of naming sites

Visual inspection of Fig. 1A and B suggested a potential group difference in the superior versus inferior distribution...
of naming sites. Specifically, naming sites in non-HS patients appeared to cluster more superiorly, whereas naming sites in HS patients were scattered across superior and inferior temporal cortex. Results of Fisher’s exact test assessing group differences in the overall number of naming sites identified above versus below the superior temporal sulcus approached significance \((P = 0.07)\). Analysis of visual naming sites indicated a significant group difference, with most visual naming sites in the non-HS group located above the superior temporal sulcus \((P = 0.01, \text{Table}\ 7)\). Similar analysis of auditory naming sites revealed no group difference \((P = 1.0)\).

### Location of seizure onset and naming site topography

Given the possibility that seizure onset location might influence the topography of naming sites, we sought to address this question empirically. However, all HS patients and all except four non-HS patients were found to have hippocampal seizure onset. Given the small sample of patients with lateral temporal onset, we were unable to statistically analyse the topography of naming sites in these two groups. Nonetheless, naming sites (both auditory and visual combined) appeared to be located at similar distances from the temporal pole for patients with hippocampal \((\text{mean: } 5.3 \text{ cm, SD } = 1.7)\) and lateral temporal seizure onset \((\text{mean: } 5.5 \text{ cm, SD } = 1.9)\). Insufficient data were available for meaningful calculations of auditory and visual naming site locations.

### Seizure outcome

All patients in the HS group achieved a seizure outcome rating of Engel’s class I or II (i.e. seizure free or only rare disabling seizures) \((\text{Engel et al., 1993})\), which is confirmatory for the diagnosis of TLE. One patient in the non-HS group with hippocampal seizure onset did not undergo surgical resection due to concerns of verbal memory decline. Ten non-HS patients had seizure outcome of Engel’s class I or II, and one patient was considered class IV (insignificant reduction). Although this patient may have had an additional epileptogenic zone that was missed with the resection, intracranial monitoring indicated temporal lobe seizure onset, as it did for all patients in the non-HS group.

### Discussion

The risk of naming decline following anterior temporal resection is lower in patients with HS relative to those with a structurally normal hippocampus \((\text{Davies et al., 1998})\). We speculated that differences in the cortical representation of naming between patients with and without HS might account for this difference in their susceptibility to postoperative naming decline. Consistent with our first hypothesis, HS patients had proportionally fewer overall naming sites in anterior temporal cortex, the region typically removed with ‘standard’ anterior temporal resection, whereas non-HS patients exhibited a more even distribution of naming sites in the anterior and posterior temporal region. With regard to modality specific naming sites, both groups exhibited the previously reported pattern of auditory naming sites anterior to visual naming sites \((\text{Hamberger et al., 2001})\); however, the location of auditory naming sites was significantly more posterior in HS than in non-HS patients, consistent with our second hypothesis. In fact, all auditory naming sites in the non-HS group were located within the anterior 5 cm from the temporal pole \((\text{i.e. anterior temporal cortex})\). Although we hypothesized the possibility of finding fewer auditory naming sites in patients with HS, the overall number of auditory naming sites was not significantly different between groups.

Although not hypothesized, we found group differences in the superior/inferior dimension, in that visual naming sites were represented more superiorly in non-HS patients, with most sites located above the superior temporal sulcus. In contrast, naming sites in HS patients were more equally distributed superiorly and inferiorly across lateral temporal lobe cortex.

The current results suggest that the relatively preserved naming ability in HS compared to non-HS TLE patients following anterior temporal resection might be attributable, at least in part, to intrahemispheric reorganization of language in response to the likely, early development of sclerosis in the medial temporal region. Specifically, it appears that additional naming sites develop in the posterior and inferior temporal region in HS patients, and that these sites might compensate functionally for those removed with anterior temporal resection. Additionally, the location of auditory naming sites, more often found in anterior than posterior temporal cortex, appears to be shifted more posteriorly in HS patients. These more posterior sites are less likely to be removed with standard anterior temporal resection. In comparisons of HS and non-HS patients, age of seizure onset is often a
confounding factor, as onset age is typically earlier in patients with HS (Bell and Davies, 1998). The comparable seizure onset age in the groups studied here suggests that this reorganization of naming sites might be more closely associated with the presence of HS than with the onset of recurrent seizures.

Another feasible position regarding the different patterns of post-operative naming in patients with and without HS is that the hippocampus itself holds a direct role in naming. Under this assumption, removal of a functional (non-HS) hippocampus results in naming decline due to loss of the normal hippocampal contribution to naming (Davies et al., 1998; Seidenberg et al., 2005). Although not evident in the present data, baseline naming has been reported to be poorer in HS relative to non-HS patients (Bell and Davies, 1998), supporting the notion that a damaged hippocampus compromises naming ability. Historically, the hippocampus has been considered the seat of learning and memory, with little, if any, implication for a significant role in naming (Squire and Alvarez, 1995). However, accumulating evidence from varied sources suggests a consistent relation between the integrity of the hippocampal region and naming. In addition to the pre- and post-operative association between hippocampal integrity and naming in TLE patients (Davies et al., 1998; Sawrie et al., 2000; Seidenberg et al., 2005), increased hippocampal activity has been reported during naming in studies of ‘online’ processing, including intracranial ERPs (Smith et al., 1986; Vannucci et al., 2003) and fMRI (Tomaszewki et al., 2005). In light of these findings, it has been proposed that direct hippocampal involvement in naming, rather than neocortical reorganization of language, underlies the significant naming decline in non-HS patients compared to the minimal decline in patients with HS (Seidenberg et al., 2005).

Considering the association between hippocampus and naming together with the current findings, which demonstrate significant and predictable differences in the topography of naming sites between patients with and without HS, one reasonable perspective might be that direct hippocampal involvement in naming and cortical reorganization of language are not mutually exclusive. Given the well-established role of the dominant hippocampus in verbal learning (Squire, 1992), the hippocampus likely plays an essential role in the initial acquisition of phonemic, lexical, and conceptual information, all of which comprise essential elements in the process of naming. It is possible that the early development of HS alters the neural connections that normally develop between the hippocampus and temporal cortex, which in turn, influences the particular cortical regions that ultimately support the semantic/lexical system, including, cortical sites that mediate naming. In line with this, a recent fMRI study in children found that language reorganization was more likely to occur when lesions involved the hippocampal region rather than ‘classic’ language regions such as Broca’s or Wernicke’s areas (Liegeois et al., 2004). Similarly, an fMRI study in adults with varied lesion locations found that patients with left hippocampal sclerosis were less likely to have clear left hemisphere language lateralization compared to patients with lesions in other locations (Weber et al., 2005). It is possible that although lateral temporal cortex ultimately assumes a greater role in semantic and lexical processing, the hippocampus might retain some role in targeted word retrieval. In this way, direct hippocampal involvement and cortical reorganization of language could be complimentary, rather than opposing theories.

Also notable is that despite the presence of recurrent seizures, the topography of naming sites in non-HS patients appears to resemble ‘normal’ language cortex, based on stroke data (Brust et al., 1976; Mazzocchi and Vignolo, 1979) and stimulation mapping findings in patients with space-occupying temporal lobe lesions (Hamberger et al., 2007). This also suggests that the overrepresentation of naming sites in posterior and possibly inferior temporal cortex associated with HS is an atypical pattern, likely resulting from degraded connectivity between the dominant hippocampus and lateral temporal cortex. As to why additional sites develop posteriorly and inferiorly is uncertain, yet, might reflect the particular subregions affected most by hippocampal sclerosis and their cortical connections, as well as patterns of EEG discharges propagating from the medial temporal region. Interictal discharges have been shown to more frequently propagate anteriorly than posteriorly (Emerson et al., 1995), and seizure activity in TLE is more likely to arise from anterior rather than posterior hippocampus (King et al., 1997), possibly displacing the development of naming sites to posterior temporal cortex. Additionally, the frequency of both seizures and interictal discharges from the medial temporal region to lateral temporal cortex has been shown to contribute to atypical language dominance (Janszky et al., 2003); perhaps, the presence of HS sets the stage for a spectrum of atypical language organization. Finally, the more anterior temporal distribution of auditory naming sites relative to visual naming sites (Hamberger et al., 2001), together with the higher frequency of anterior than posterior propagation of epileptiform discharges (Emerson et al., 1995), might explain why auditory naming sites in particular were more susceptible to posterior displacement than visual naming sites.

**Post-operative naming**

Consistent with the previous work, non-HS patients exhibited significant post-operative naming decline, whereas HS patients showed no such decline, as assessed by the BNT (Davies et al., 1998). No decline was evident on the other two naming tasks, which were published only recently, and thus, not utilized in the earlier study. In speculating why naming decline was not evident on these two tasks, it is important to note that unlike the
patients studied in Davies et al. (1998), the current patients underwent language mapping to reduce post-operative naming decline. Thus, it is possible that both greater BNT decline and decline on the other two naming measures may have been evident had mapping not been performed. Additionally, the BNT differs from the ANT and VNT in its inclusion of low-frequency items (e.g. abacus, sphinx). The ANT and VNT were developed specifically with the intention of excluding low-frequency items to avoid the potential confound of vocabulary level (Hamberger and Seidel, 2003). It is possible that lexical access to low-frequency items, which are typically acquired later in life, is more susceptible to decline following left ATL (Bell et al., 2000).

**Limitations**

Generalizations from the current findings are limited by the relatively small sample size. It should be noted, though, that patients with HS typically undergo standard temporal lobe resection without language mapping, and it is relatively uncommon that pharmacologically intractable TLE patients show no abnormalities on MRI or on post-operative histology. Thus, these mapping data are fairly unique, and therefore, potentially quite valuable. Nonetheless, the reliability of the topographical patterns reported here might be questionable without larger patient groups. Additionally, the absence of group differences in baseline naming between HS and non-HS patients is somewhat atypical, possibly limiting generalizability (Bell and Davies, 1998). However, the comparable naming ability between the two groups could also be advantageous, ruling out ability level as an explanation for the topographical differences between groups. Rather, the differences in cortical language representation might be considered more clearly attributable to the presence versus absence of HS.

Additionally, given the small sample size, we were unable to address the possibility that the location of seizure onset zones might be related to the topography of naming sites. As noted, all HS patients, and all except four of the non-HS patients had hippocampal seizure onset. Given the small sample of patients with lateral temporal onset, we were unable to assess the potential influence of seizure onset location on the topography of naming sites.

Despite potential limitations, the current findings hold theoretical implications regarding the role of the hippocampus in determining the cortical organization of semantic and lexical information, and raise questions regarding the specific roles of medial and lateral temporal cortex in targeted word retrieval. Our results also carry practical implications, providing some guidance for language mapping in MRI-normal, non-HS patients. Given the time constraints inherent in intra-operative mapping, it might be most efficient to begin testing in the superior temporal region, due to the lower probability of detecting positive naming sites below the superior temporal sulcus. Additionally, these results support the practice of performing most standard anterior temporal resections in HS patients without stimulation mapping, given the greater proportion of naming sites in the posterior temporal region.

On a speculative note, clinical lore dictates that we listen to our patients. Patients frequently present with complaints of memory difficulty, yet when queried, describe unequivocal word-finding difficulty (e.g. ‘I can’t remember the right word’). Perhaps, this subjective phenomenology provides a clue, that the hippocampus remains an integrated component of the semantic/lexical system, supported by both medial and lateral aspects of the dominant perisylvian region.

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**References**


