Title

Temporal lobe regions essential for preserved picture naming after left temporal epilepsy surgery

Journal

Epilepsia, 61(9)

ISSN

0013-9580

Authors

Binder, Jeffrey R
Tong, Jia-Qing
Pillay, Sara B
et al.

Publication Date

2020-09-01

DOI

10.1111/epi.16643

Peer reviewed

HHS Public Access

Author manuscript

Epilepsia. Author manuscript; available in PMC 2020 December 08.

Published in final edited form as:

Epilepsia. 2020 September ; 61(9): 1939–1948. doi:10.1111/epi.16643.

Temporal Lobe Regions Essential for Preserved Picture Naming After Left Temporal Epilepsy Surgery

Jeffrey R. Binder[1], **Jia-Qing Tong**[1], **Sara B. Pillay**[1], **Lisa L. Conant**[1], **Colin J. Humphries**[1], **Manoj Raghavan**[1], **Wade M. Mueller**[2], **Robyn M. Busch**[3], **Linda Allen**[1], **William L. Gross**[1], **Christopher T. Anderson**[1], **Chad E. Carlson**[1], **Mark J. Lowe**[4], **John T. Langfitt**[5], **Madalina E. Tivarus**[6], **Daniel L. Drane**[7], **David W. Loring**[7], **Monica Jacobs**[8], **Victoria L. Morgan**[9], **Jane B. Allendorfer**[10], **Jerzy P. Szaflarski**[10], **Leonardo Bonilha**[11], **Susan Bookheimer**[12], **Thomas Grabowski**[13], **Jennifer Vannest**[14], **Sara J. Swanson**[1] **on behalf of FMRI in Anterior Temporal Epilepsy Surgery (FATES) study**

[1]Department of Neurology, Medical College of Wisconsin, Milwaukee, WI

[2]Department of Neurosurgery, Medical College of Wisconsin, Milwaukee, WI

[3]Department of Neurology, Cleveland Clinic Foundation, Cleveland, OH

[4]Department of Radiology, Cleveland Clinic Foundation, Cleveland, OH

[5]Department of Neurology, University of Rochester, Rochester, NY

[6]Department of Imaging Sciences, University of Rochester, Rochester, NY

[7]Department of Neurology and Pediatrics, Emory University, Atlanta, GA

[8]Department of Psychology, Vanderbilt University Medical Center, Nashville, TN

[9]Department of Radiology, Vanderbilt University Medical Center, Nashville, TN

[10]Department of Neurology, University of Alabama at Birmingham, Birmingham, AL

[11]Department of Neurology, Medical University of South Carolina, Charleston, SC

[12]Department of Neurology, University of California, Los Angeles, CA

[13]Department of Neurology, University of Washington, Seattle, WA

[14]Department of Neurology, University of Cincinnati, Cincinnati, OH

SUMMARY

Objective: To define left temporal lobe regions where surgical resection produces a persistent postoperative decline in naming visual objects.

Corresponding Author: Jeffrey R. Binder, MD, Department of Neurology, Medical College of Wisconsin, 8701 Watertown Plank Road, Milwaukee, WI 53226, Phone: 414-955-4662, jbinder@mcw.edu.

Disclosure of Conflicts of Interest

None of the authors has any conflict of interest to disclose.

Ethical Publication Statement

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

Methods: Pre- and postoperative brain MRI data and picture naming (Boston Naming Test) scores were obtained prospectively from 59 people with drug-resistant left temporal lobe epilepsy. All patients had left hemisphere language dominance at baseline and underwent surgical resection or ablation in the left temporal lobe. Postoperative naming assessment occurred approximately 7 months after surgery. Surgical lesions were mapped to a standard template, and the relationship between presence or absence of a lesion and the degree of naming decline was tested at each template voxel while controlling for effects of overall lesion size.

Results: Patients declined by an average of 15% in their naming score, with wide variation across individuals. Decline was significantly related to damage in a cluster of voxels in the ventral temporal lobe, located mainly in the fusiform gyrus approximately 4–6 cm posterior to the temporal tip. Extent of damage to this region explained roughly 50% of the variance in outcome. Picture naming decline was not related to hippocampal or temporal pole damage.

Significance: The results provide the first statistical map relating lesion location in left temporal lobe epilepsy surgery to picture naming decline, and they support previous observations of transient naming deficits from electrical stimulation in the basal temporal cortex. The critical lesion is relatively posterior and could be avoided in many patients undergoing left temporal lobe surgery for intractable epilepsy.

Keywords

Epilepsy; temporal lobe; anomia; lesion localization; fusiform gyrus

INTRODUCTION

Surgical removal or disruption of networks responsible for seizure generation is effective at reducing or eliminating seizures in many people with drug-resistant temporal lobe epilepsy (TLE) [1, 2]. Roughly 30–50% of people with TLE who undergo surgery in the left temporal lobe show decline in their ability to name pictures of objects [3, 4]. Predictors of greater decline include left language dominance on fMRI [5, 6], older age at onset of epilepsy [4, 7, 8], higher pre-operative naming scores [4], and absence of medial temporal sclerosis [9]. These factors, however, account for only a fraction of the wide variance in naming outcome observed in these studies, suggesting that other variables, such as the extent and location of the surgical lesion, also play a role.

Views regarding the location of “critical” temporal lobe zones for picture naming vary widely. Evidence from classic direct cortical stimulation mapping studies mainly implicated lateral temporal regions posterior to the standard anterior temporal lobe (ATL) resection zone [10, 11]. Later studies extending this technique to ventral temporal regions described a “basal temporal language area” in the ventral ATL where stimulation could produce a range of language impairments, including anomia [12]. Additional evidence for an important role of the ATL in naming comes from studies of people with the semantic variant of primary progressive aphasia, a condition featuring neural degeneration initially concentrated in the ATL bilaterally and presenting typically with anomia [13, 14]. Functional neuroimaging studies in healthy adults have variously implicated anterior and posterior regions of the ventral temporal and occipital lobes in picture naming [15], consistent with evidence from human and

nonhuman primate studies identifying this extensive region as a hierarchically-arranged network for visual object recognition [16–18]. Some authors have proposed a critical role for the hippocampus in picture naming, based largely on correlations between naming ability and hippocampal pathology [9, 19]. Recent evidence against this view comes from a study showing that focal laser ablation of the left hippocampus and amygdala does not substantially affect naming [20].

The aim of the current study was to clarify the critical regions supporting object picture naming ability in people with left TLE undergoing surgical treatments in the left temporal lobe. We used a method known as voxel-based lesion-symptom mapping (VLSM), which produces a statistical map of the relationship between the presence or absence of damage in a particular brain location and the degree of deficit on a cognitive measure across a cohort of patients [21]. To our knowledge, this method, which requires high-resolution images of each participant's lesion as well as standardized language outcome measures, has not previously been applied in an epilepsy surgery cohort. We restricted the analysis to people with preoperative left language dominance. One reason for doing so was to reduce heterogeneity in the sample, as language dominance likely modulates the extent of involvement of the left temporal lobe in naming. Another reason was to focus on people with the greatest risk for naming decline, in whom knowledge of critical language zones has the most clinical relevance. We hypothesized that picture naming decline would be related to damage in the ventral ATL and temporal pole, and to the overall volume of the surgical lesion, but not to hippocampal damage.

MATERIALS AND METHODS

Participants:

The participants were 59 adults (34 women, 25 men) who underwent resections in the left temporal lobe for drug-resistant focal epilepsy. Participants were enrolled prospectively in the Functional MRI in Anterior Temporal Epilepsy Surgery (FATES) study, a prospective, NINDS-funded, multi-center project aimed at identifying predictors of cognitive outcome after left temporal lobe epilepsy surgery. Prior to enrolling in the study, patients underwent inpatient video EEG, MRI, and neuropsychological testing as part of a comprehensive clinical work-up to determine their candidacy for surgery. Only patients who had left language dominance documented on subsequent research fMRI were included in the present analysis; patients with atypical (n = 24) or unclear (i.e., conflicting fMRI and clinical Wada data, n = 2) dominance were excluded. All participants were over the age of 17 and fluent speakers of English. All except 3 were right-handed. Written informed consent according to the Declaration of Helsinki was obtained from all participants prior to initiation of the research protocol. The demographic characteristics of the sample are presented in Table 1.

Picture Naming Test:

All participants completed the full Boston Naming Test (BNT) [22] prior to surgery and approximately 7 months after surgery. The BNT requires naming of 60 line drawings of common objects. The standard testing procedure was followed, in which the participant is allowed up to 20 seconds to provide a correct response. Although initial phoneme cues were

given when a correct response could not be provided, only responses made prior to the phoneme cue were included in the total score as per standard scoring procedure. All responses were recorded manually and rechecked by a board-certified neuropsychologist to assure scoring accuracy. All test administration and scoring were performed blind to post-operative MRI data. A BNT change score was computed by subtracting the preoperative from the postoperative score. No correlation was observed between BNT change and time from surgery to post-op testing ($r = .022$, $p = 0.868$).

MRI Acquisition:

All participants underwent 3T research MRI scanning prior to and at least 2 months after surgery. The scanner used varied by study site and was either a GE Excite (1 site), Siemens Tim Trio (4 sites), Siemens Allegra (1 site), or Philips Achieva (4 sites). The same scanner was used for pre- and postoperative scanning in all cases. High resolution T1-weighted anatomical imaging was performed using a magnetization-prepared rapid-acquisition gradient echo or spoiled-gradient-echo sequence, yielding high grey-white contrast and isotropic voxel size of approximately 1 mm^3. Two such images were acquired at each session and averaged to enhance signal-to-noise ratio. In the preoperative scanning session, participants also completed an fMRI language lateralization protocol consisting of alternating blocks of a semantic decision task and a tone decision task [23]. Lateralization was computed within a combined frontal-temporal-parietal mask consisting of voxels typically activated by this task contrast [24]. Language lateralization indexes derived with this protocol have been extensively validated using Wada testing [25], naming outcome prediction [5], and verbal memory outcome prediction [24]. Left language dominance was defined as a lateralization index $\geq .20$.

Surgical Lesions:

All resections/ablations were restricted to the left temporal lobe, but no other criteria regarding location or type of surgery were applied. Restricting the sample to a particular lesion location would defeat the purpose of the study, which was to understand the relative contribution of different lesion locations to naming decline. This can only be accomplished if locations vary across the sample. Fortunately, there was substantial variation in the treatment approach across and within the participating study centers, with some favoring standard ATL resections (although even these varied in posterior and superior extent), others favoring hippocampal laser ablations, and two favoring selective amygdalohippocampectomy using an anterior approach that removed the temporal pole, amygdala, and variable amounts of hippocampus. Also included were cases with focal temporal pole, ventral temporal, and/or lateral neocortical resections. Some example lesions are illustrated in Figure 1. Tailoring of resections based on language mapping with direct electrical stimulation was performed in 18 patients. The decision to use or not use electrical stimulation mapping was made by the treating clinical team.

Voxel-Based Lesion-Symptom Mapping:

Lesioned areas were labeled manually on the postoperative T1 structural scan by a single neuroimaging specialist/clinical neurologist (JRB) who was not involved in patient testing or clinical care and was blind to BNT change scores. Labeling was done in AFNI (https://

afni.nimh.nih.gov) using the DrawDataset plugin, which allows structures and labels to be simultaneously viewed in coronal, sagittal, and axial orientations. Lesion boundaries were first traced slice-by-slice in the coronal plane, then edited in the sagittal and axial planes to correct errors and maximize continuity. Each patient's anatomical image and associated lesion map were then morphed to a stereotaxic template ("Colin n27") using Advanced Normalization Tools Software (http://stnava.github.io/ANTs/) with a cost-function masking approach using the lesion volume as a mask, and resampling to a nominal 1×1×1 mm^3 voxel grid. This nonlinear registration process corrects for anatomical distortions that are common after focal brain damage, particularly local ventricular enlargement and tissue displacement into the resection cavity. See Figure 1 for examples of the morphing results. Normalized total lesion size (in template voxels) was obtained in each patient from the template-registered lesion map. Lesion volume averaged 21,737 template voxels (SD = 15,259) or 21.7 ml in normalized space.

VLSM uses lesion status at each voxel as a grouping variable, then compares the lesioned and non-lesioned groups on any given dependent measure, producing an effect size statistic for each voxel. A custom Matlab script was written in-house that implements VLSM as an analysis of covariance to account for within- and between-group variance of no interest (script available on request to the authors). Only voxels lesioned in at least five participants were included. The analysis of interest examined BNT percent change (%change) score as the dependent measure, calculated as 100 * (postop – preop)/(preop). Lesion volume was included as a covariate of no interest to minimize effects of covariance between lesion location and overall lesion volume. The resulting t-statistic map was thresholded at voxel-wise $p < .005$ and cluster-corrected at a family-wise error of $p < .05$ using a minimum cluster size criterion of 847 voxels, as determined by randomization testing with 10,000 permutations.

RESULTS

BNT Scores:

As a group, the participants declined significantly on the BNT (Table 2), though there was substantial variation across the cohort. About half of the patients (51%) showed a decline of 10% or more in their naming score, and 21 (36%) showed a decline of 20% or more. Fourteen patients (24%) showed severe declines of more than 30%. The change score was negatively correlated with lesion volume (Table 3), indicating greater declines with larger resections, and with age at surgery and age at onset of epilepsy. There was no difference in BNT change between the 18 patients who underwent surgery tailored with electrical stimulation language mapping (mean %change = −21.1) and the 30 patients (excluding laser ablation cases) who did not (mean %change = −17.7; two-sample t-test, two-tailed p = .532). These groups also did not differ in lesion volume (24,305 vs. 26,732 template voxels, respectively; two-sample t-test, two-tailed p = .566).

Effects of Resection Type:

As noted above, the anatomical location and size of resections varied considerably. Table 4 lists BNT outcomes by general type of resection. "Standard" ATL resections (n = 22)

included most of the temporal pole and amygdala; anterior portions of the hippocampus, parahippocampus, middle temporal (MTG), inferior temporal (ITG), and fusiform gyri; and variable portions of the anterior superior temporal gyrus (STG), hippocampal body, and mid-fusiform and mid-parahippocampal gyri. There was substantial variation in outcome even within this group. Ten (45%) of these patients had more than a 30% decline in naming, whereas 5 patients had less than a 10% decline. Resection volume was not correlated with BNT %change within this standard ATL resection group ($r = -.112$, $p = .396$).

Medial temporal lobe laser ablations (n = 11) were mostly confined to the hippocampus and immediately adjacent parahippocampus, with variable involvement of the amygdala. Focal neocortical resections (n = 8) included small lesions distributed throughout the lateral and ventral temporal lobe. Selective amygdalohippocampectomy (SAH) was carried out in most cases using an anterior approach (n = 6) that removed most of the temporal pole and amygdala and variable amounts of hippocampus and parahippocampus. Four patients had resections confined to the temporal pole, sparing the amygdala and variable amounts of the anterior STG. These more focal types of resections generally produced little or no decline: 20/29 patients (69%) showed little or no change, 6 patients (21%) had modest declines in the 10–25% range, and 3 patients (10%) improved by more than 10%.

Three ATL resections were limited to ventral regions, completely sparing MTG and the dorsal pole, but otherwise resembled the standard resection. Two surgeries involved a swath of cortex along the mid-portion of the ventral temporal lobe from ITG to hippocampus, sparing the pole and amygdala completely. One patient had what was otherwise a standard ATL surgery, but with ventromedial extension of the lesion posteriorly nearly to the occipital lobe. One patient had a lesion involving nearly all of the ventral and medial temporal lobe with sparing of the amygdala and pole. These ventral lesions with more posterior extension were associated with moderate to severe naming declines in all but one case. Finally, one patient underwent SAH via a trans-Sylvian approach and showed a moderate decline.

VLSM:

VLSM provides a precise method for identifying critical regions by comparing the performance of patients with vs. without a lesion at each voxel location. Figure 2A shows the lesion overlap map thresholded to show only voxels damaged in at least five participants. As shown in Figure 2B, decline on the BNT was associated with damage in a single region of the anterior ventral temporal lobe, centered on the fusiform gyrus and extending laterally into the inferior temporal gyrus. In standard stereotaxic space, the cluster extends from 4.1 cm posterior to the temporal tip (stereotaxic $y = -15$) to 6.1 cm posterior to the tip ($y = -35$). The implicated region notably spares the hippocampus as well as the temporal pole and lateral temporal cortex (middle and superior temporal gyri).

To assess further the relationship between hippocampal damage and naming decline, a follow-up analysis was conducted comparing BNT change scores in the 11 patients treated with hippocampal laser ablation, which produces a relatively focal lesion of the hippocampus (hippocampus-only group), and the 18 patients with lesions that overlapped at least 50% of the cluster identified in the VLSM analysis (basal temporal group). The groups differed significantly in outcome (two-sample t-test, two-tailed $p < .00001$), with the basal

temporal group showing a large decline (mean %change = −33.5; single-sample t-test, two-tailed p <.00001) and the hippocampus-only group showing a small, non-significant improvement (mean %change = +2.0).

Although patients did not decline after selective hippocampal ablation, it is possible that hippocampal damage adds to naming decline in patients with both basal temporal and hippocampal resection. We addressed this possibility using stepwise regression to test whether the extent of hippocampal damage (lesion volume measured in template voxels) accounted for any additional variance in naming outcome after considering the extent of damage to the basal temporal region. Basal temporal lesion volume alone accounted for 52.4% of the variance in outcome (adjusted R^2 = .516, p <.0001). Inclusion of hippocampal lesion volume increased the amount of variance explained by only 0.3% (adjusted R-squared = .511, p = .541), providing no evidence of an additive effect of hippocampal damage.

DISCUSSION

These results provide the first map of locations where lesions from left temporal lobe epilepsy surgery are statistically associated with picture naming decline. While functional neuroimaging and direct cortical electrical stimulation data show a degree of individual variability in the location of language areas [26, 27], group-level statistical methods like VLSM identify commonalities across individuals that provide a useful model of the “typical” brain. In the present case, knowing *a priori* which temporal lobe regions are most likely to support object naming ability in patients with drug-resistant left TLE should provide clinicians with useful information for decision making and surgical planning. Specifically, the left mid-fusiform gyrus and adjacent inferior temporal gyrus appear to be the most critical areas for maintaining visual object naming ability. The results add to prior evidence that picture naming decline is unrelated to hippocampus removal [20]. Somewhat surprisingly, picture naming decline was also unrelated to resection of the temporal pole, and unrelated to lesions in most of the lateral ATL neocortex.

Previous research on critical naming sites in people with TLE has mainly used electrical stimulation mapping. One recognized limitation of this method is incomplete coverage of the temporal lobe cortical surface, with classical studies using surface electrodes primarily limited to the lateral temporal convexity [10, 11]. The lack of sites sensitive to stimulation in the lateral ATL in early studies helped define the ATL as a relatively safe region to resect. Decades later, Lüders, Lesser, and colleagues [12, 28, 29] discovered that stimulation in the ventral temporal lobe often elicits language impairments. The clinical significance of these “basal temporal language area” (BTLA) sites became clearer with a report by Krauss et al. [30] of long-term language outcomes in patients undergoing left ATL resection following ventral temporal stimulation mapping. BTLA sites were observed in 80% of the patients in that study. Picture naming errors were the most frequent impairment encountered during stimulation, though a variety of other language deficits also occurred. The study is especially notable because the BTLA sites were removed in some patients but not in others. At 6-month follow-up, the 13 patients who had BTLA sites resected showed a decline in picture naming ability (mean 8.8% decline), whereas those who did not have BTLA resections improved slightly (mean 4.3% improvement), a difference that was statistically reliable and

could not be explained by differences in overall resection volume. Our data provide strong convergent evidence for the importance of this region, based on a very different but complementary method for measuring lesion-outcome correlations.

Precise localization of this critical region has been somewhat unclear, for several reasons. The stimulation mapping method is of limited spatial precision, and methods using surface electrodes can miss functional tissue buried within sulci. Short-term effects of stimulation may spread along axonal connections to nearby or even distant regions [31]. Maps produced in most basal temporal stimulation studies consisted of hand drawings of the visible ventral surface, which are inherently imprecise compared to high-resolution MRI data. In the largest of these early studies [30], BTLA sites were described as being mainly in the fusiform gyrus, “in a band ~1 cm lateral to the hippocampal sulcus and ~1 cm mesial to the lateral margin of the inferior temporal gyrus”, with fewer sites in the anterior parahippocampus and inferior temporal gyrus. Sites were observed as far posterior as 8–9 cm from the temporal pole and as far anterior as 1 cm posterior to the pole, with the largest concentration in the posterior half of this range. In a more recent stimulation mapping study that incorporated modern imaging localization tools, Forseth et al. also found the greatest concentration of picture naming disruption sites in the mid-fusiform gyrus, although positive sites were observed across a broad swath of the ventral temporal lobe [32]. Our results lend strong support to these findings, while adding further spatial precision regarding the region most critical for preserving naming ability, as well as validation with long-term outcome data. Specifically, they provide complementary new evidence for an essential ventral temporal naming area at the posterior end of the standard ATL resection zone.

Acceptance of the idea that there is a critical language zone in the left ventral temporal lobe has been slow, reflecting the fact that this region is far from perisylvian and lateral temporal networks classically implicated in core language processes like word comprehension and word retrieval. We propose that the function of this ventral ATL region can be understood in terms of the ventral visual object recognition pathway, a multi-stage network that proceeds hierarchically from primary visual cortex to anterior ventral temporal cortex, representing progressively more combinatorial and “conceptual” information [16–18]. At the highest levels of this hierarchy are neural ensembles that represent the viewpoint-invariant, schematic 3-dimensional forms of known object categories [33, 34]. We propose that this abstract visual representation is one component of a multimodal concept representation on which naming depends [35]. According to this view, lesions in the ventral ATL cortex disrupt naming by interfering with formation of an abstract visual object representation. A key point is that this abstract visual representation (pertaining mainly to visual shape) is only one component of a widely distributed concept representation, and therefore does not impair the ability to retrieve other knowledge about an object. Even so, this partial disruption has the effect of weakening overall activation of the object concept, in turn weakening the ability to retrieve its name.

Two implications of this account are worth noting. First, it predicts that basal temporal resection should impair visual naming to a greater degree than naming in response to a verbal description, since the latter task makes no use of visual input. Although data on this question are limited, one study that compared picture naming and auditory description

naming in patients undergoing standard left ATL surgery found that deficits on picture naming are much more prominent than deficits on description naming [36]. Electrical stimulation of the ventral temporal lobe also appears to impair picture naming more often than description naming [30, 32]. Forseth et al. observed electrocorticographic (broad-band gamma power) and fMRI activation responses in this region to both picture naming and auditory description naming tasks, concluding that it functions as a hub for accessing crossmodal semantic information [32]. Although the authors did not present a direct contrast between the two tasks, their figures suggest much stronger responses in this region for picture naming (see Figures 3 and 4 in Forseth et al., 2018). It is possible that the weak responses observed during description naming represent incidental activation of an abstract visual representation, as our model proposes. Future studies are needed to clarify whether damage to this zone significantly impairs auditory description naming.

Second, the account further highlights the idea that naming can be disrupted at multiple processing stages, and that naming is a complex task that depends on a network of brain regions rather than a localized “function” [32, 37]. Classical stimulation mapping studies, lesion correlation studies in stroke patients, and functional imaging studies in healthy people all provide ample evidence for participation of the lateral temporal, inferior parietal, and inferior frontal cortex in picture naming. These regions contribute to naming in very different ways, i.e., by search and selection of concepts and word forms (inferior frontal cortex), representation of multimodal concepts (lateral temporal and inferior parietal cortex), and representation of phonological word forms (posterior temporal and inferior parietal cortex). The high-level visual recognition deficit associated with left ventral ATL resection is one type of impairment that can affect naming, but other types are possible from lesions in other locations.

The role of the hippocampus in picture naming has been controversial. Observing that left TLE patients with hippocampal sclerosis (HS) show less severe naming decline after ATL surgery than patients without HS, some authors hypothesized that patients with HS are more likely to have shift of language functions to the right hemisphere, accounting for the ‘protective’ effect of HS [9, 19]. While plausible, this hypothetical language reorganization provides no direct evidence that the hippocampus itself participates in language processing. HS could be simply a marker of more severe temporal lobe dysfunction, in which case language reorganization away from the left temporal lobe might occur even if the hippocampus itself has no role in language. In fact, there is evidence that patients with HS have more severe structural and functional abnormalities, on average, than patients without HS, both within the temporal lobe and in other ipsilateral structures [38–40]. A lower risk of decline in HS patients could also occur even if there was no language reorganization, since removal of a less functional temporal lobe would be expected to have a less detrimental effect. Evidence against a critical role for the hippocampus in naming comes from numerous studies showing that patients with hippocampal amnesia perform normally on vocabulary knowledge and picture naming tasks [41–43].

Naming decline in the current study was not statistically related to hippocampal damage at the individual voxel level (i.e., VLSM). We also found no evidence of decline in a subgroup of patients who underwent selective hippocampal laser ablation, and no evidence that the

extent of hippocampal damage accounted for variance in naming outcome after accounting for extent of damage in the basal temporal region. This result converges with previous evidence from a between-group comparison study of left TLE patients who underwent standard ATL resection and left TLE patients who underwent stereotactic laser amygdalohippocampectomy (i.e., selective hippocampal or amygdalohippocampal ablation) [20]. The standard ATL group showed typical levels of decline on the BNT, whereas the laser amygdalohippocampectomy group showed no decline. Together, these studies provide strong evidence that surgical lesioning of the left hippocampus, at least in patients with left temporal lobe epilepsy, is unlikely to produce significant impairment in picture naming.

Resection of the temporal pole, including tissue from the temporal tip to ~4 cm posterior to the tip, was not significantly correlated with picture naming decline. This outcome was somewhat unexpected given the early appearance of anomia in patients with ATL neurodegeneration [13, 14] and associated claims that the temporal pole functions as a semantic "hub" [44]. On the other hand, functional neuroimaging data suggest that the semantic system is extensively distributed throughout much of the higher-level temporal and parietal cortex [45]. In the case of semantic PPA, neurodegenerative changes characteristically occur bilaterally and involve most of the temporal lobe even at relatively early stages [46, 47]. Thus, the special role attributed to the temporal pole in semantic memory may have been overestimated in some accounts. Another possibility is that chronic left TLE in our patients produced reorganization of the semantic system such that the left temporal pole no longer played a critical role. This account would only be tenable if the hypothesized reorganization affected the pole more than other temporal lobe regions, since many of our patients did show naming decline and therefore must have depended on the left temporal lobe for this task. In any case, resection of the temporal pole in patients with left TLE does not appear to affect postoperative picture naming ability. We note the important caveat that naming in this study was tested using common object categories rather than naming of specific individuals. Previous studies suggest a greater dependence on the temporal pole for naming specific individuals, especially famous faces, compared to common object categories [48–50]. Therefore, the present results do not necessarily identify critical regions for naming unique entities, such as individual people.

The current study was limited to patients undergoing surgery in the left temporal lobe, so it provides no information regarding the likelihood of naming deficits from surgery in other brain regions. As shown in Fig. 2A, coverage of the superior and posterolateral portions of the temporal lobe was also limited. As with any group-level analysis, the results identify commonalities across participants and are mute regarding individual variations. Despite these limitations, we hope the current results will help define a left TLE surgical approach that will more reliably spare object naming abilities in patients undergoing this treatment.

Acknowledgments

The study was supported by grant R01 NS35929 (J. Binder, PI) from the National Institute of Neurological Disorders and Stroke. The authors thank the participating patients for their generous commitment of time and effort. We also thank the following individuals who assisted with the study as members of the FATES consortium: Bassel Abou-Khalil, MD; Ellen Air, MD, PhD; Jeanette Albertson; Erik Beall, PhD; Michael Berg, MD; William Bingaman, MD; Truman R. Brown, PhD; Nancy J. Cohen; Noreen Connolly; Alex Dagley; Sheri Davis; Jonathan C. Edwards, MD; Lisa Ferguson; Steven S. Glazier, MD; Jorge Gonzalez-Martinez, MD; Xiaoping Hu, PhD;

Mirjana Ivanisevic; Colleen Kenney; Peter Konrad, MD, PhD; Megan LeDoux; Lucy Mendoza; Katherine Murphy; Imad Najm, MD; Andrew Nencka, PhD; Gloria Novak; Jeffrey Ojemann, MD; Vaishali Phatak, PhD; Webster Pilcher, MD; Michael Privitera, MD; Brian Renner; Kristen O. Riley, MD; Fred W. Sabb, PhD; Lisa Schwartz; Diane E. Smith; William A. Vandergrift III, MD; Mark Wagner, PhD; and Hwa Shain Yeh, MD.

REFERENCES

1. Wiebe S, Blume W, Girvin JP, Eliasziw M. A randomized, controlled trial of surgery for temporal-lobe epilepsy N Engl J Med. 2001;345:311–318. [PubMed: 11484687]
2. Tellez-Zenteno JF, Dhar R, Wiebe S. Long-term seizure outcomes following epilepsy surgery: a systematic review and meta-analysis Brain. 2005;128:1188–1198. [PubMed: 15758038]
3. Sherman E, Wiebe S, Fay-McClymont TB, Tellez-Zenteno J, Metcalfe A, Hernandez-Ronquillo L, et al. Neuropsychological outcomes after epilepsy surgery: systematic review and pooled estimates Epilepsia. 2011;52:857–869. [PubMed: 21426331]
4. Busch RM, Floden DP, Prayson B, Chapin JS, Kim KH, Ferguson L, et al. Estimating risk of word-finding problems in adults undergoing epilepsy surgery Neurology. 2016;87:2363–2369. [PubMed: 27815406]
5. Sabsevitz DS, Swanson SJ, Hammeke TA, Spanaki MV, Possing ET, Morris GL, et al. Use of preoperative functional neuroimaging to predict language deficits from epilepsy surgery Neurology. 2003;60:1788–1792. [PubMed: 12796532]
6. Bonelli SB, Thompson PJ, Yogarajah M, Vollmar C, Powell RHW, Symms MR, et al. Imaging language networks before and after anterior temporal lobe resection: Results of a longitudinal fMRI study Epilepsia. 2012;53:639–650. [PubMed: 22429073]
7. Davies KG, Risse GL, Gates JR. Naming ability after tailored left temporal resection with extraoperative language mapping: increased risk of decline with later epilepsy onset age Epilepsy and Behavior. 2005;7:273–278. [PubMed: 16040279]
8. Ruff IM, Swanson SJ, Hammeke TA, Sabsevitz DS, Mueller WM, Morris GL. Predictors of naming decline after dominant temporal lobectomy: Age at onset of epilepsy and age of word acquisition Epilepsy and Behavior. 2007;10:272–277. [PubMed: 17270499]
9. Davies KG, Bell BD, Bush AJ, Hermann BP, Dohan FC, Jaap AS. Naming decline after left anterior temporal lobectomy correlates with pathological status of resected hippocampus Epilepsia. 1998;39:407–419. [PubMed: 9578031]
10. Penfield W, Roberts L. Speech and brain-mechanisms New York: Atheneum; 1959.
11. Ojemann G, Ojemann J, Lettich E, Berger M. Cortical language localization in left, dominant hemisphere: An electrical stimulation mapping investigation in 117 patients J Neurosurg. 1989;71:316–326. [PubMed: 2769383]
12. Lüders H, Lesser RP, Hahn J, Dinner DS, Morris HH, Wyllie E, et al. Basal temporal language area Brain. 1991;114:743–754. [PubMed: 2043946]
13. Hodges JR, Patterson K, Oxbury S, Funnell E. Semantic dementia: Progressive fluent aphasia with temporal lobe atrophy Brain. 1992;115:1783–1806. [PubMed: 1486461]
14. Gorno-Tempini ML, Dronkers NF, Rankin KP, Ogar JM, Phengrasamy L, Rosen HJ, et al. Cognition and anatomy in three variants of primary progressive aphasia Ann Neurol. 2004;55:335–346. [PubMed: 14991811]
15. Price CJ, Devlin JT, Moore CJ, Morton C, Laird AR. Meta-analyses of object naming: effect of baseline Hum Brain Mapp. 2005;25:70–82. [PubMed: 15846820]
16. Tanaka K, Saito H, Fukada Y, Moriya M. Coding visual images of objects in the inferotemporal cortex of the macaque monkey J Neurophysiol. 1991;66:170–189. [PubMed: 1919665]
17. Lerner Y, Hendler T, Ben-Bashat D, Harel M, Malach R. A hierarchical axis of object processing stages in the human visual cortex Cereb Cortex. 2001;11:287–297. [PubMed: 11278192]
18. Grill-Spector K, Malach R. The human visual cortex Annu Rev Neurosci. 2004;27:649–677. [PubMed: 15217346]
19. Seidenberg M, Hermann B, Wyler AR, Davies K, Dohan FC, Leveroni C. Neuropsychological outcome following anterior temporal lobectomy in patients with and without the syndrome of mesial temporal lobe epilepsy Neuropsychology. 1998;12:303–316. [PubMed: 9556776]

20. Drane DL, Loring DW, Voets NL, Price M, Ojemann JG, Willie JT, et al. Better object recognition and naming outcome with MRI-guided stereotactic laser amygdalohippocampotomy for temporal lobe epilepsy Epilepsia. 2015;56:101–113. [PubMed: 25489630]
21. Bates E, Wilson S, Saygin AP, Dick F, Sereno M, Knight RT, et al. Voxel-based lesion-symptom mapping Nat Neurosci. 2003;6:448–450. [PubMed: 12704393]
22. Kaplan E, Goodglass H, Weintraub S. Boston Naming Test. Philadelphia: Lea and Febiger; 1983.
23. Binder JR, Frost JA, Hammeke TA, Cox RW, Rao SM, Prieto T. Human brain language areas identified by functional MRI J Neurosci. 1997;17:353–362. [PubMed: 8987760]
24. Binder JR, Sabsevitz DS, Swanson SJ, Hammeke TA, Raghavan M, Mueller WM. Use of preoperative functional MRI to predict verbal memory decline after temporal lobe epilepsy surgery Epilepsia. 2008;49:1377–1394. [PubMed: 18435753]
25. Janecek JK, Swanson SJ, Sabsevitz DS, Hammeke TA, Raghavan M, Rozman ME, et al. Language lateralization by fMRI and Wada testing in 229 patients with epilepsy: Rates and predictors of discordance Epilepsia. 2013;54:314–322. [PubMed: 23294162]
26. Ojemann G Individual variability in cortical localization of language J Neurosurg. 1979;50:164–169. [PubMed: 430127]
27. Steinmetz H, Seitz RJ. Functional anatomy of language processing: Neuroimaging and the problem of individual variability Neuropsychologia. 1991;29:1149–1161. [PubMed: 1791929]
28. Lüders H, Lesser RP, Hahn J, Dinner DS, Morris H, Resor S, et al. Basal temporal language areas demonstrated by electrical stimulation Neurology. 1986;36:505–510. [PubMed: 3960324]
29. Schaffler L, Lüders HO, Beck GJ. Quantitative comparison of language deficits produced by extraoperative electrical stimulation of Broca's, Wernicke's, and basal temporal language areas Epilepsia. 1996 5;37:463–475. [PubMed: 8617176]
30. Krauss GL, Fisher RS, Plate C, Hart J, Uematsu S, Gordon B, et al. Cognitive effects of resecting the basal temporal language areas Epilepsia. 1996;37:476–483. [PubMed: 8617177]
31. Ranck J Which elements are excited in electrical stimulation of mammalian central nervous system: A review Brain Res. 1975;98:417–444. [PubMed: 1102064]
32. Forseth KJ, Kadipasaoglu CM, Conner CR, Hickok G, Knight RT, Tandon N. A lexical semantic hub for heteromodal naming in middle fusiform gyrus Brain. 2018;141:2112–2126. [PubMed: 29860298]
33. Marr D. Vision. San Francisco: Freeman; 1982.
34. Vuilleumier P, Henson RN, Driver J, Dolan RJ. Multiple levels of visual object constancy revealed by event-related fMRI of repetition priming Nat Neurosci. 2002;5:491–499. [PubMed: 11967545]
35. Fernandino L, Binder JR, Desai RH, Pendl SL, Humphries CJ, Gross W, et al. Concept representation reflects multimodal abstraction: A framework for embodied semantics Cereb Cortex. 2016;26:2018–2034. [PubMed: 25750259]
36. Hamberger MJ, Seidel WT, McKhann GM, Goodman RR. Hippocampal removal affects visual but not auditory naming Neurology. 2010;74:1488–1493. [PubMed: 20335560]
37. Levelt WJM. Speaking: From intention to articulation. Cambridge, MA: MIT Press; 1989.
38. Coan AC, Campos BM, Yasuda CL, Kubota BY, Bergo FPG, Guerreito CAM, et al. Frequent seizures are associated with a network of gray matter atrophy in temporal lobe epilepsy with or without hippocampal sclerosis PLoS One. 2014;9:e85843. [PubMed: 24475055]
39. Mueller SG, Laxer KD, Schuff N, Weiner MW. Voxel-based T2 relaxation rate measurements in temporal lobe epilepsy (TLE) with and without mesial temporal sclerosis Epilepsia. 2007;48:220–228. [PubMed: 17295614]
40. Mueller SG, Laxer KD, Barakos J, Ian C, Garcia P, Weiner MW. Widespread neocortical abnormalities in temporal lobe epilepsy with and without mesial sclerosis Neuroimage. 2009;46:353–359. [PubMed: 19249372]
41. Verfaellie M, Koseff P, Alexander M. Acquisition of novel semantic information in amnesia: effects of lesion location Neuropsychologia. 2000;38:484–492. [PubMed: 10683398]
42. Kensinger EA, Ullman MT, Corkin S. Bilateral medial temporal lobe damage does not affect lexical or grammatical processing: evidence from amnesic patient HM Hippocampus. 2001;11:347–360.

43. Manns JR, Hopkins RO, Squire LR. Semantic memory and the human hippocampus Neuron. 2003;38:127–133. [PubMed: 12691670]
44. Patterson K, Nestor PJ, Rogers TT. Where do you know what you know? The representation of semantic knowledge in the human brain Nat Rev Neurosci. 2007;8:976–987. [PubMed: 18026167]
45. Binder JR, Desai R, Conant LL, Graves WW. Where is the semantic system? A critical review and meta-analysis of 120 functional neuroimaging studies Cereb Cortex. 2009;19:2767–2796. [PubMed: 19329570]
46. Rohrer JD, Warren JD, Modat M, Ridgway GR, Douiri A, Rossor MN, et al. Patterns of cortical thinning in the language variants of frontotemporal lobar degeneration Neurology. 2009;72:1562–1569. [PubMed: 19414722]
47. Rogalski E, Cobia D, Harrison TM, Wieneke C, Weintraub S, Mesulam MM. Progression of language decline and cortical atrophy in subtypes of primary progressive aphasia Neurology. 2011;76:1804–1810. [PubMed: 21606451]
48. Damasio H, Tranel D, Grabowski T, Adolphs R, Damasio A. Neural systems behind word and concept retrieval Cognition. 2004;92:179–229. [PubMed: 15037130]
49. Drane DL, Ojemann JG, Phatak V, Loring DW, Gross RE, Hebb AO, et al. Famous face identification in temporal lobe epilepsy: support for a multimodal integration model of semantic memory Cortex. 2013;49:1648–1667. [PubMed: 23040175]
50. Mehta S, Inoue K, Rudrauf D, Damasio H, Tranel D, Grabowski T. Segregation of anterior temporal regions critical for retrieving names of unique and nonunique entities reflects underlying long-range connectivity Cortex. 2016;75:1–19. [PubMed: 26707082]

Key Points

- Decline in picture naming ability after left temporal lobe epilepsy surgery is strongly related to resection of basal temporal cortex 4–6 cm posterior to the temporal pole.
- Picture naming decline was not related to resection of the hippocampus or temporal pole.
- Picture naming decline can likely be avoided in many left temporal surgery patients by limiting the posterior ventral extent of the resection.

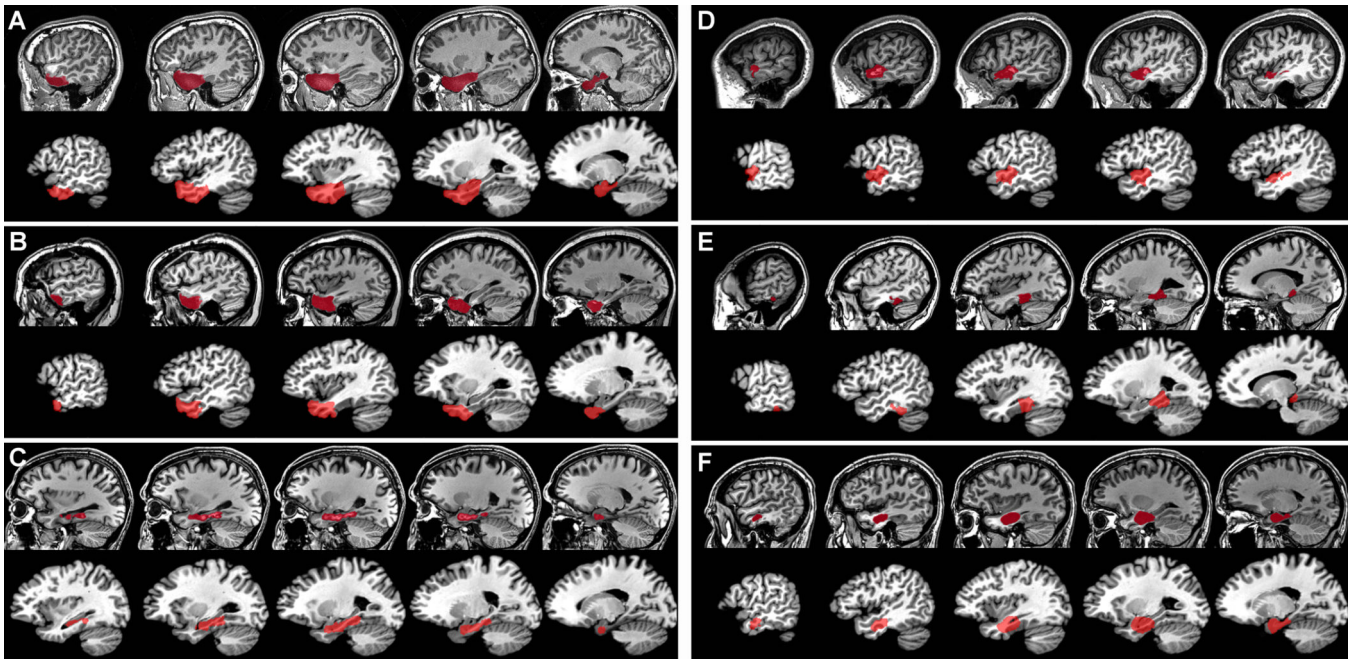

Figure 1. Examples of surgical resections.

Lesions are shown in each case on five serial sagittal sections through the left hemisphere of the patient's own MRI scan (top row of each panel) and the template space (bottom row in each panel). Cases included (A) standard left ATL resections, (B) temporal pole resections sparing the hippocampus, (C) hippocampal laser ablations, and (D, E, F) more focal resections throughout the temporal lobe.

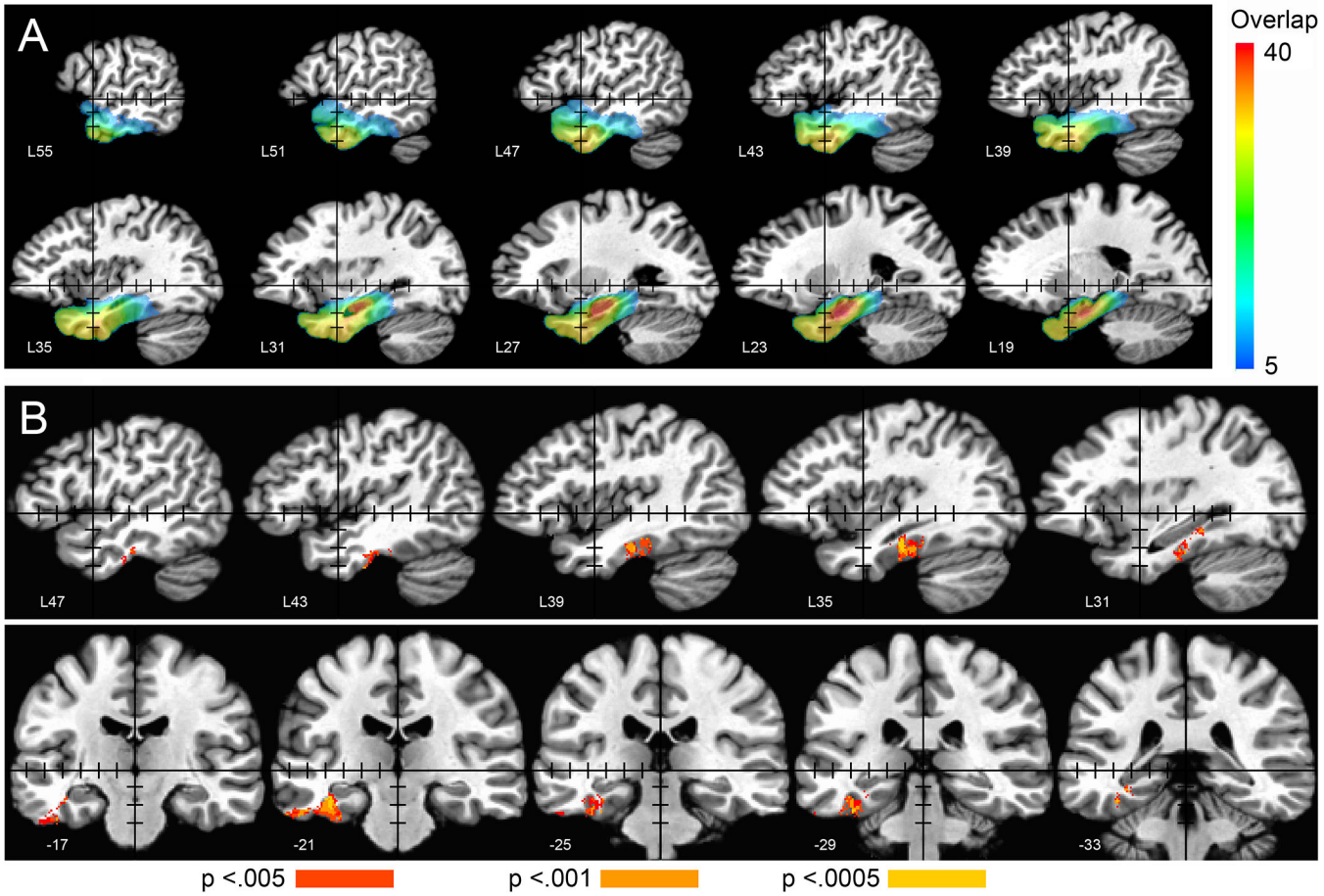

Figure 2. MRI results.

(A) Lesion overlap map, thresholded at ≥ 5 patients. (B) VLSM map of voxels where surgical resection was significantly related to postoperative decline in picture naming. Stereotaxic coordinates are given at the lower left of each image. Black tick marks indicate 10- mm intervals on axes centered at the stereotaxic origin.

Table 1:

Participant Characteristics

	Mean	SD
Age (yrs)	36.5	12.5
Education (yrs)	13.3	2.8
Age at Onset (yrs)	23.2	12.5
Weeks to Follow-Up	31.1	12.4

Table 2:

BNT preoperative, postoperative, and change scores

	Pre	Post	Change	%Change
Mean	47.6	40.4	−7.2	−15.3
SD	8.1	11.0	8.5	19.0
Min	26	17	−24	−57.5
Max	59	57	7	27.6

Table 3:

Correlations with BNT %change score

	R	p
Age	−.345	.007
Education	.228	.083
Age at Onset	−.364	.005
Preop Score	−.133	.317
Lesion Volume	−.763	<.0001

Table 4:

BNT change score as a function of resection type. See text for definitions.

Type	N	Pre	Post	Change	%Change
Standard ATLR	22	47.5	34.8	−12.7	−26.7
MTL Laser Ablation	11	46.3	46.8	0.6	2.0
Focal Neocortical	8	51.5	49.6	−1.9	−3.7
Anterior SAH	6	44.0	41.5	−2.5	−4.6
Temporal Pole	4	50.8	47.0	−3.8	−7.2
Ventral ATLR	3	47.0	34.0	−13.0	−28.4
Ventral Mid-Temporal	2	54.0	42.0	−12.0	−22.1
Extended ATLR	1	44	28	−16	−36.4
Ventral Temporal	1	34	18	−16	−47.1
Trans-Sylvian SAH	1	52	42	−10	−19.2

Abbreviations: ATLR = anterior temporal lobe resection, MTL = medial temporal lobe, SAH = selective amygdalohippocampectomy