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Functional MRI and Direct Cortical Stimulation: Prediction of Postoperative Language Decline

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SUMMARY

Objective: To assess functional MRI's (fMRI) ability to predict postoperative language decline compared to direct cortical stimulation in epilepsy surgery patients.

Methods: In this prospective case series, 17 patients with drug-resistant epilepsy had intracranial monitoring and resection from 2012 to 2016 with one-year follow up. All patients completed preoperative language fMRI, mapping with direct cortical stimulation of subdural electrodes, pre and postoperative neuropsychological testing for language function, and resection. Changes in language function before and after surgery were assessed. fMRI activation and direct cortical stimulation electrodes in the resection were evaluated as potential predictors of language decline.

Results: Four of 17 patients (12 female; median[range] age, 43[23–59] years) experienced postoperative language decline one year after surgery. Two of four patients had overlap of fMRI activation, language positive electrodes in basal temporal regions (within 1cm), and resection. Two had overlap between resection volume and fMRI activation, but not direct cortical stimulation. fMRI demonstrated 100% sensitivity and 46% specificity for outcome compared to direct cortical stimulation (50% and 85%, respectively). When fMRI and direct cortical stimulation language findings were concordant, the combined tests showed 100% sensitivity and 75% specificity for language outcome. Patients with language decline tended to have more fMRI activated voxels overlapping resection (Mann-Whitney test, $p=0.068$). Seizure onset age, resection side, type, volume, or one year seizure outcome did not predict language decline.

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Significance: Language localization overlap of fMRI and direct cortical stimulation in the resection influences postoperative language performance. Our preliminary study suggests fMRI may be more sensitive and less specific than direct cortical stimulation. Together they may predict outcome better than either test alone.

Keywords

Epilepsy/Seizures; Intracranial electrodes; Neuropsychological assessment; Epilepsy Surgery; Neuroimaging

Introduction

Cognitive deficits, particularly visual naming and word-finding declines, occur in up to 35% following dominant hemisphere epilepsy surgery.^{1,2} Later age at epilepsy onset, absence of hippocampal sclerosis, strong left-hemisphere language lateralization, and resection within 1–2 centimeters (cm) of direct cortical stimulation (DCS) identified naming sites are associated with postoperative deficits.³

DCS is used widely for preoperative evaluation of patients with drug-resistant epilepsy^{3,4} when surgery is considered in functionally important regions. Disadvantages include additional surgical risk, discomfort, extended hospital stay and limited cortical coverage. Persistent language deficits may occur even when all positive sites are excluded from resection.³

Functional magnetic resonance imaging (fMRI), an increasingly established alternative to intracarotid amytal procedure (IAP) for language lateralization, can provide hemispheric and regional language mapping.^{5,6,7,8} Several studies showed fMRI predicts postoperative language decline at least as accurately as IAP.⁹ However, the value of fMRI compared to DCS language localization is uncertain.

In a previous study, we compared DCS language localization with fMRI echo-planar imaging (EPI) blood oxygen level-dependent (BOLD) activation.¹⁰ fMRI sensitivity and specificity, compared to DCS, varying with stimuli and task, were 80.6% and 72.7% for the best combination. fMRI reliably excluded the presence of eloquent cortex. We now report the accuracy of DCS and fMRI for predicting postoperative language decline after epilepsy surgery.

Methods

Patient Selection

Thirty-five patients underwent intracranial electrode implantation and subsequent epilepsy surgery at the National Institutes of Health Epilepsy Center between 2012 and 2016. We included 17 native English-speaking patients 18 years or older who received pre-surgical evaluation including fMRI, DCS mapping, and neuropsychological testing pre- and postoperatively between August 16, 2006 and April 20, 2017. Thirteen were included in a previous study.¹⁰ This study was approved by the NIH Combined Neurosciences Institutional Review Board. Written informed consent was obtained from all patients.

fMRI task paradigm, acquisition, and analysis

Patients underwent fMRI using EPI BOLD techniques during an Auditory Description Decision Task (ADDT). This paradigm, described in previous studies, followed a block design alternating between 30 second active and 30 second control conditions for five cycles.^{5,10} Briefly, during the active condition, participants were instructed to listen to auditory clues with 6–8 word sentences defining items from the Boston Naming Test (BNT) and press a button when they thought the definition true (67% true, 33% false definitions). The control condition was tones intermixed throughout reverse speech. Participants were instructed to listen and press when they heard a tone (70% tones, 30% no tones).

Patients were scanned on a 3.0 Tesla General Electric scanner. Gradient echo-planar images were collected with the following parameters: TR=2000ms, TE=30ms, flip angle=65°, FOV=22×22cm, and 64×64 acquisition matrix. Images were acquired in the axial plane parallel to the AC-PC line. Between 2012 and 2016 when images were obtained, brain volumes were either: 30 slices with 4.0mm thickness and 3.4×3.4×4.0mm voxel sizes, or 40 slices with 3.0mm thickness and 3.0×3.0×3.0mm voxel sizes.

Functional data were analyzed in the patient's native space using Analysis of Functional NeuroImages (AFNI) software.¹¹ Echo-planar images collected during ADDT were preprocessed as a single 4-dimensional dataset containing 150 time points. Pre-steady state volumes collected before equilibrium magnetization was reached were discarded and remaining slices shifted to correct timing. T1 weighted MPRAGE was registered to the EPI base volume using a Local Pearson correlation absolute value cost function. A concatenated transform was applied to align remaining EPI volumes. During registration, EPI data were resampled to 4.0mm isotropic voxels to ensure consistency and avoid additional interpolation. Volumes were spatially blurred with a 4.0mm FWHM Gaussian kernel. Motion regression was computed using de-meaned motion parameters. Motion exceeding 0.30mm for any time point was censored from the final EPI dataset.

The voxelwise response magnitude to the active condition was modeled using a generalized least squares timeseries fit with restricted maximum likelihood equation of temporal autocorrelation for regression with a voxel-wise ARMA (1,1) model. Monte Carlo simulation with 3dClustSim corrected for multiple comparisons by using cluster size frequency counts to estimate false positive probabilities, determining cluster size thresholds for uncorrected p values to achieve family-wise error (FWE) corrected $p < 0.05$.¹²

Stimulation Mapping

DCS mapping was performed in all 17 patients. Stimulation parameters included: pulse width 0.50ms, pulse rate 50Hz, duration of stimulus approximately 3–5 seconds. Current amplitude increased from 2mA to a maximum of 16mA in 1mA increments. To screen for language function, adjacent electrodes (1cm apart) were stimulated bipolarly. In some cases, when electrode pairs elicited positive responses they were tested individually with monopolar stimulation. Testing threshold was determined during a continuous recitation task while current amplitude gradually increased. Threshold was determined as the amplitude where reproducible functional change was observed, or 1–2mA lower than after-discharge

threshold. If neither condition was present, further testing was done at 16mA. At threshold, patients named pictures of objects aloud (Visual Naming), read sentences aloud (Reading), or pointed to objects after an experimenter's verbal description (Token Test).

Electrodes were considered language positive and overlaying a critical language area if stimulation at any amplitude reproducibly disrupted language function during any task. Electrodes were considered clear if language function was not disrupted for any task during stimulation at threshold. If stimulation was limited by pain at <10mA, electrodes were excluded from our analysis. We also excluded electrodes that caused sensory or motor effects, electrographic seizures during stimulation, or electrodes where stimulation caused language disruption in the setting of after-discharges. Electrodes cleared in the presence of after-discharges were included in analysis.

No resection was performed within 1cm of clearly language positive electrodes from DCS in Wernicke's or Broca's areas. After discussion with patients, inclusion of positive stimulation sites in basal temporal language areas were considered for resection.

Electrode localization

Electrode centers were identified on the post-implantation CT scan and transformed to preoperative T1 MPRAGE space. Correction for brain shift was accomplished using a modified elastic algorithm¹³ to reconstruct subdural electrode locations on the outer-smoothed pial surface using Freesurfer (<http://surfer.nmr.mgh.harvard.edu>) and publicly available custom software (<https://neuroscience.nih.gov/ninds/zaghloul/downloads.html>). Intraoperative digital photography was used to identify several landmark electrodes. Locations were marked on the pial surface with 3D-Slicer (<http://www.slicer.org>), informing the automated localization algorithm for remaining electrodes.¹³

Creation of Resection Masks

Pre and postoperative T1 MPRAGE scans were collected for all patients. Scans were deobliqued (3dWarp), skull-stripped (3dSkullStrip), and aligned (3dAllineate) via 12-parameter affine transformation. An exclusion mask was manually drawn on postoperative scans, covering resection cavities, to prevent them from influencing alignment. In three patients, alignment failed and nonlinear transformation was successfully applied (3dQwarp).

To create a resection cavity mask, the now-aligned postoperative volume was subtracted from the preoperative volume (3dCalc). The raw resection mask was dilated (3dMaskTool), adding five layers of voxels to each open edge. Next, six levels of voxels were eroded from contiguous voxel cluster edges, eliminating thin parts of the mask not part of the resection cavity. Clusters smaller than 2,000 voxels were eliminated (3dClust). A second dilation was performed on the clustered resection mask, extending mask boundaries by two levels, to create the final mask in the automatic pipeline (Figure 1).

An experimenter visually inspected resection masks overlaid on postoperative scans. Manual intervention, if needed, included eliminating voxels outside the cavity and expanding resection mask boundaries. This was only necessary in one patient. We determined the number of voxels contained in each patient's resection mask.

Overlap Detection

We determined if any stimulated electrode sites (both language positive and cleared) and functional activation maps (FWE corrected threshold, $p < 0.05$) overlapped with the resection cavity. If positive DCS or fMRI intersected with postoperative margins, the mask was saved and the number of overlapping voxels determined.

To determine whether DCS electrode sites overlapped with the resection cavity, each electrode coordinate was transformed into a spherical region of interest (ROI) with 10mm radius. Electrodes stimulated bipolarly were modeled as a single ROI of two intersecting spheres. A mask containing only overlapping voxels between the resection cavity mask and ROI for each electrode stimulation site was created, and the number of overlapping voxels within the intersection mask counted.

To assess fMRI activation map intersection with the resection cavity, an fMRI activation map containing only significant clusters surviving FWE corrected threshold $p < 0.05$ was created. The map was resampled to the preoperative T1 MPRAGE grid spacing; the overlap mask was based in 1mm isotropic grid space. A mask containing only overlapping voxels between functional activation and the resection cavity mask was created, and the number of overlapping voxels determined.

Neuropsychological Testing

To assess changes in language function, we collected pre and postoperative scores on the 60-item Boston Naming test (BNT), Controlled Oral Word Association F-A-S total corrected score, and Verbal IQ (VIQ) from the Wechsler Adult Intelligence Scale III (WAIS-III). Three patients completed the Wechsler Adult Intelligence Scale IV (WAIS-IV), and the Verbal Comprehension Index (VCI) was used instead of VIQ.

Preoperative tests were collected a mean of 356 days before surgery (range, 25 to 2197 days) and postoperative scores a mean of 448 days after surgery (range, 321 to 1019 days). To be included in this study, patients were required to complete at least one of three language measures on both pre and postoperative neuropsychological tests.

We calculated raw change scores (postoperative minus preoperative) for each available neuropsychological test. Scores were classified as either improved, no change, or declined, using established reliable change indices (RCI) for epilepsy. RCI uses cutoff scores corrected for practice effect to describe statistically reliable change in which any change score exceeding the cutoff would occur in an unoperated epilepsy population less than 5% of the time (90% confidence interval).¹⁴ The RCI cutoff values for each test are as follows:

$$VIQ-6 \geq RCI \geq +8$$

$$BNT-5 \geq RCI \geq +5$$

$$\text{FAS}-12 \geq \text{RCI} \geq +14$$

We simplified outcomes into “decline” and “no decline” (no change + improved scores).

Results

Demographics, characteristics of surgery and seizure outcome are included in Table 1 (12 females; median[range] age, 43[23–59] years). fMRI was used to lateralize language before surgery in accordance with the American Academy of Neurology practice guidelines for presurgical evaluation.⁸ IAP was also conducted in five patients, but was found to be inconclusive in three out of five. Fourteen out of 17 patients had language dominance lateralized to the left, two patients lateralized to the right, and one patient who had bilateral language function (Table 1).

Four patients showed language decline on one or more neuropsychological tests (Table 2). All four with decline had activated fMRI within the resection margin, including two patients (#1 and #16) who were ‘cleared’ on DCS (Figure 2A and Table 2). Of the two patients who had postoperative language decline and language positive electrodes within 1cm of the resection margin, language positive electrode sites were in basal temporal cortex (Figure 3A). Two patients with positive electrodes within 1cm and fMRI voxels included in the resection did not experience language decline (Figure 3B). Seven with only fMRI activation in the resection did not experience decline (Figure 2B).

Patient 1 had a right frontal topectomy that presented a postoperative pathology of focal cortical dysplasia and had postoperative language decline on FAS (Table 2). While WADA was inconclusive, fMRI showed right language dominance. There were no language positive electrodes from DCS in the resection, but fMRI activation overlapped the resection cavity (Figure 2A).

Patient 16, who had a right temporal resection and was ‘cleared’ on DCS but not fMRI, had postoperative language decline on VCI (Table 2). fMRI showed left language dominance. DCS was limited by pain, and excluded from our analysis, in four basal temporal electrode sites, compared to six cleared basal temporal sites. This patient had a history of viral encephalitis; MRI showed bilateral increased hippocampal FLAIR signal, suggesting potential damage contralateral to the seizure focus (Table 1).

fMRI activation was present in the resection in all four patients who experienced language decline; no patient experienced language decline when fMRI activation did not overlap the resection cavity. Two patients who declined had DCS overlap as well, but two did not. However, in seven patients fMRI activation overlapped the resection without postoperative language decline; two patients had DCS overlap without decline (Table 2). Based on our small preliminary series, fMRI showed sensitivity of 100%, specificity of 46%, positive predictive value of 36%, and negative predictive value of 100% for postoperative language decline, compared to 50%, 85%, 50%, and 85% respectively for DCS. When fMRI and DCS findings were concordant, which occurred in 10 out of 17 patients, sensitivity of the

combined tests was 100%, specificity 75%, positive predictive value 50%, and negative predictive value 100%. Overall, DCS language positive stimulation site or fMRI activated voxel overlap with resection cavity did not predict language decline after surgery (Fisher's exact test, $p=0.22$ and $p=0.24$, respectively).

Eight of 17 patients had resections in their language dominant hemisphere. While mapping with DCS was done in all patients, language positive electrodes were only found in the resection margins of patients with dominant resections. In addition, there was a larger proportion of patients with fMRI overlapping the resection in those with dominant resections compared to those with nondominant resections (88% vs. 44%, respectively) (Table 2). In all patients with fMRI activation overlap, the number of fMRI activated voxels in the resection tended to be higher in patients who experienced language decline (Mann-Whitney Test, $p=0.068$). The number of DCS ROI voxels from language positive electrodes overlapping the resection did not differ between patients who experienced language decline and those who did not (Figure 4).

In this small series, seizure onset age, resection side, type (standard anterior temporal lobectomy, amygdalo-hippocampectomy or topectomy), volume, and seizure outcome at one year were not associated with neuropsychological outcome. Mean age at surgery was 45 (SD=7.1) for patients with postoperative decline and 37.6 (SD=11.6) for those without decline (N.S.).

Discussion

We found complementary results between DCS and fMRI activation in predicting postoperative language decline. While overall predictive success was low, patients were less likely to have language decline after surgery if fMRI activation and direct cortical stimulation language positive sites did not overlap resection cavities. Two patients with fMRI positive voxels but not DCS electrode sites overlapping the resection also declined. In addition, when language findings between fMRI and DCS were concordant, there was an improvement in the trade-off between sensitivity and specificity. This suggests that fMRI and DCS together may provide more information than either alone. Patients experiencing language decline after surgery tended to have more fMRI activation within the resection margin, which may provide predictive value when DCS is not available.

We used the fMRI ADDT task, showing the best correlation with DCS language sites in our previous study.¹⁰ Other studies used various approaches comparing fMRI and intraoperative DCS localization, with reported sensitivity compared to DCS ranging from 22% to 100%, and specificity from 68% to 97%.^{15–22} Comparisons with extra-operative DCS using subdural electrodes showed similar results.^{22–26}

There are limited data on the relative value of fMRI and DCS for prediction of postoperative language decline. In a study comparing high gamma electrocorticography and fMRI to DCS, two patients who had both positive stimulation electrodes and fMRI voxels in the resection suffered postoperative deficits; fMRI voxels identified within 1cm of electrodes on co-registered post-implantation CT were considered co-localized.²⁴ Another study examined

fMRI laterality index for predicting postoperative naming outcome, showing 100% sensitivity and 57% specificity, similar to our 100% fMRI sensitivity and 46% specificity.⁹

Differences between fMRI and DCS tasks and testing methods need to be considered when comparing imaging and stimulation results. ADDT, involving both auditory processing and semantic retrieval, may be more complex than DCS tasks.^{27,28} While spontaneous speech, Visual Naming, Reading, and Token Test each test various aspects of language-related cortex, they are adjusted to fit DCS time constraints.²⁹ fMRI identifies language regions via behavior-associated activation, but DCS via focal disruption. Regions activated on fMRI were more extensive than those identified on DCS, which could lead to more conservative surgical decisions. Since we used DCS and not fMRI to plan the boundaries for resection, the results of this study were not affected. fMRI may be able to localize language function in sulcal regions inaccessible to DCS.^{29,30}

fMRI is subject to a variety of technical problems.⁸ BOLD signal may be disrupted by tumors with edema and mass effect, vascular malformations and other cerebral circulatory disorders, or postictal states. Some patients cannot comply with procedures due to difficulty hearing or reading, or poor language skills. fMRI advantages include its availability as a safe, noninvasive, cost-effective test as well as ability to test young children.^{5,31}

DCS can make surgery a viable option for patients with suspected epileptogenic onset zones close to functional cortex. However, its application is not standardized.²⁹ A survey of data from 56 epilepsy centers (69% in the US) found marked variability in technical approaches, including stimulation parameters, language functions tested, definitions of errors, and size of resection margins.³ Forty-one percent of centers reported at least one persistent adverse language outcome despite preserving all eloquent sites defined by their mapping procedure.

Patients with epilepsy often demonstrate mixed or atypical patterns of language dominance;²⁷ therefore, we included patients with both dominant and nondominant resections. While patients with dominant resections are considered most at risk for poor language outcome, some have shown cognitive decline after nondominant surgery.^{32,33} Only a few of our patients had IAP tests. However, data support using fMRI for language lateralization in patients with epilepsy being considered for surgery.⁸

Two of our patients had resection of language positive electrodes in the 'basal temporal language area (BTLA).' These electrode sites were included in resections based on evidence that immediate postoperative language deficits after BTLA resection typically resolve within one year; the risk associated with resecting BTLA is acceptable in cases of severe focal epilepsy.^{30,34,35} Functions identified in BTLA include visual naming, auditory naming, and verbal comprehension.²⁹ In an international survey, persistent postoperative deficits were reported by 13% of centers reported after resecting BTLA regions; interestingly, only 56% reported mapping this region.³ Eighty percent of patients developed transient language deficits with stimulation, particularly on confrontation naming and comprehension, primarily in the fusiform gyrus 1–9cm from the temporal tip, but persistent naming deficits were reported in a minority of patients after resection.³⁰ In a series of 29 patients, BTLA stimulation interfered with function in 13. The basal temporal area most consistently

involved with language function was fusiform gyrus.³⁶ Basal temporal electrical stimulation can be limited by pain caused by branches of the trigeminal nerves, which may limit ability to sufficiently identify eloquent cortex in this region.³⁷ Complementary information from fMRI may be most useful to identify language function in basal temporal areas where DCS is limited.

Within the limits of technical issues such as co-registration error, fMRI appears to complement DCS with subdural electrodes for predicting postoperative language decline. Both have strong negative predictive value to identify patients who are less likely to experience postoperative deficits. fMRI appears to be less specific than DCS. However, future studies may confirm our observation that the number of fMRI activated voxels within the resection cavity may be an important predictor of language decline in patients after surgery. Combined, language localization overlap of fMRI and DCS with resection influences postoperative patient performance on language measures.

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Key points:

- The value of fMRI compared to DCS for predicting postoperative language decline after epilepsy surgery is unclear
- Two patients with postop language decline had fMRI activation and DCS sites overlapping resection; two only had fMRI activation overlap
- fMRI and DCS present a trade-off between sensitivity and specificity that improves when test findings are concordant
- Combined, fMRI and DCS may predict language outcome after epilepsy surgery better than either test alone

Figure 1. Progression through semi-automated resection mask pipeline

(A) Pre and postoperative T1 MPRAGE anatomical scan (top) and AFNI generated pre and postoperative Automask of anatomical scan (bottom). (B) The number of voxels included in raw, intermediate, and final resection masks throughout the semi-automated editing pipeline. (C) Progression (left to right) through resection mask pipeline for a single patient. Raw = first resection mask created from subtraction of aligned Automasks (pre – post), DE1 = second step and first simultaneous dilation and erosion step. The mask was dilated by adding 5 layers of voxels to each open edge voxel, then 6 levels of voxels were eroded from the edges of contiguous clusters of voxels to eliminate thin parts of the mask that were not part of the resection cavity. CD = Cluster detection to eliminate clusters less than 2,000 contiguous voxels, DE2 = A second dilation was performed on the clustered resection mask, extending the boundaries of the mask by 2 levels to create the final mask in the automatic pipeline. Final = Final resection mask after manual editing (when necessary).

Figure 2. Two patients with fMRI activation overlap in resection cavity and different neuropsychological outcomes

(A) Patient 1 had a right frontal topectomy and postoperative language decline on Controlled Oral Word Association (FAS). fMRI activation overlapped with the resection cavity, but no language positive DCS electrodes were found in the resection cavity. (a) Resection cavity (b) fMRI activation at $p < 0.05$ FWE, where colors indicate distinct clusters (c) Intersection of fMRI activation and resection cavity (B) Patient 12 had a left anterior temporal lobectomy and no change in neuropsychological testing. fMRI activation overlapped with the resection cavity, but no language positive DCS electrodes were found in the resection cavity. (a) Resection cavity (b) fMRI activation at $p < 0.05$ FWE, where colors indicate distinct clusters (c) Intersection of fMRI activation and resection cavity. Left = Left.

Figure 3. Two patients with DCS language positive electrode overlap in resection cavity and different neuropsychological outcomes

(A) Patient 3 had a left anterior temporal lobectomy including basal temporal areas and experienced postoperative language decline on Controlled Oral Word Association (FAS) and Verbal IQ. Both language positive electrodes and fMRI activation overlapped with the resection cavity. (a) Language positive dipolar electrode stimulation site modeled as two intersecting spheres of 10mm radius (b) Resection cavity (c) fMRI activation at $p < 0.05$ FWE, where colors indicate distinct clusters (d) Intersection of language positive electrode pair and resection cavity (e) Intersection of fMRI activation and resection cavity (B) Patient 9 had a left temporal topectomy and no change in neuropsychological testing. Both language positive electrodes and fMRI activation overlapped with the resection cavity. (a) Language positive monopolar electrode stimulation site modeled as a 10mm radius sphere (b) Resection cavity (c) fMRI activation at $p < 0.05$ FWE, where colors indicate distinct clusters

(d) Intersection of language positive electrode and resection cavity (e) Intersection of fMRI activation and resection cavity. Left = Left.

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Figure 4. Number of overlapping voxels in resection and language outcome

(A) Number of voxels where fMRI activation overlapped resection cavity. Patients who experienced language deficit after surgery tended to have a greater number of voxels from fMRI activation overlapping the resection than patients with no postoperative language decline (Mann-Whitney test, $p=0.068$). (B) Number of DCS ROI voxels from language positive electrodes that overlapped the resection cavity. There is no significant difference between number of overlapping voxels in patients who experienced language decline and those who did not.

Table 1.

Patient Demographics

Patient	Sex	Onset Age	Surgery Age	Procedure	MRI findings	fMRI Language Laterality	IAP Language Laterality	Pathology	Seizure Outcome Engel Class
1	F	8	43	R frontal topectomy	R mesial frontal and orbitofrontal blurring of gray – white matter	R	Inconclusive	FCD	3a
2	F	35	52	R ATL	R frontal meningioma	L		Mild MCD and R frontal meningioma	1a
3	F	9	44	L ATL	L MTS	L	Inconclusive	MTS	1a
4	M	13	25	R ATL	Normal	L		Gliosis	1a
5	M	15	31	R parietal topectomy	Normal	L		FCD 2B	1a
6	F	35	43	R ATL	R MTS	L		Mild neuronal loss	1a
7	F	31	54	R ATL+	FCD	R		FCD + DNET	1a
8	M	42	49	R ATL	Normal	L		Mild gliosis neuronal loss	1a
9	F	18	37	L temporal topectomy	Normal	L	L	Microdysgenesis	2b
10	F	6	23	R ATL	Bilateral MTS R>L	L	Inconclusive	MTS, microdysgenesis	1b
11	F	14	34	L SAH	L hippocampal abnormal folding	L	BL	MTS, microdysgenesis	2b
12	F	3	63	L ATL	L MTS	L		MTS	1a
13	F	4	49	L SAH	L MTS	L		MTS	3a
14	M	32	45	R frontal topectomy	Normal	L		Microdysgenesis	1a
15	F	9	32	R ATL+	R MTS	L		MTS	2b
16	F	19	37	R ATL	Subtle increased FLAIR bilateral hippocampus	L		MTS +	1a
17	M	24	33	L ATL+	Migration abnormalities	BL		Microdysgenesis	1a

ATL(+)=anterior temporal lobectomy (removal of lesion). SAH=selective amygdalo-hippocampectomy. MTS=mesial temporal sclerosis, FCD=focal cortical dysplasia, MCD=malformations of cortical development, DNET=dysembryoplastic neuroepithelial tumor. Blank Wada indicates the test was not done. Engel Classes: 1a=Completely seizure free since surgery, 1b=Non-disabling simple partial seizures only since surgery, 2b=Rare disabling seizures since surgery, 3a=Worthwhile seizure reduction.

Table 2.

Characteristics of resection, overlap, and neuropsychological deficit for 17 patients

Patient	Resection Side	Total Resection Volume (cuMM)	Language Positive DCS in Resection	fMRI Activation in Resection	Neuropsychological Tests with Postop Language Decline (raw change score: post-pre)	Surgical Notes
1	R	34263		Y	FAS (-19)	
2	R	44368		Y		
3	L	56782	Y	Y	FAS (-23), VIQ (-12)	1
4	R	47870		Y		
5	R	43833				
6	R	31150				
7	R	78900	Y	Y		2
8	R	90494				
9	L	14769	Y	Y		
10	R	76337				
11	L	71237				
12	L	58250		Y		
13	L	30587	Y	Y	BNT (-7), VIQ (-14)	1,2
14	R	66392		Y		
15	R	83252				
16	R	133923		Y	VCI (-20)	
17	L	142732		Y		

Surgical Notes. 1=Language positive electrodes in basal temporal resection 2=Perioperative Infarct. Postoperative decline was measured during neuropsychological testing one year after surgery. Abbreviations: BNT= Boston Naming Test, FAS=Controlled Oral Word Association total corrected score, VIQ=Verbal IQ, VCI=Verbal Comprehension Index; all patients completed the WAIS-III, except three patients, who completed the WAIS-IV and VCI was used in place of VIQ.