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fMRI Prediction of Naming Change after Adult Temporal Lobe Epilepsy Surgery: Activation Matters

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Summary

Objective: We aimed to predict language deficits after epilepsy surgery. In addition to evaluating surgical factors previously examined, we determined the impact of the extent of fMRI activation resected on naming ability.

Method: Thirty-five adults (mean age 37.5+/-10.9 yr, 13 males) with temporal lobe epilepsy completed a pre-operative fMRI auditory description decision task, which reliably activates frontal and temporal language networks. Patients underwent temporal lobe resections (20 left). The Boston Naming Test (BNT) was used to determine language functioning before and after surgery.

Language dominance was determined for Broca's and Wernicke's area (WA) by calculating a laterality index following SPM processing. We used an innovative method to generate anatomical resection masks automatically from pre- and post-operative MRI tissue map comparison. This mask provided 1) resection volume; 2) overlap between resection and pre-operative activation; 3) overlap between resection and WA. We examined post-operative language change predictors using stepwise linear regression. Predictors included parameters described above as well as age of seizure onset (AOS), pre-operative BNT score, resection side and its relationship to language dominance.

Results: Seven out of thirty-five adults had significant naming decline (six dominant-side resections). The final regression model predicted 38% of the naming score change variance

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Disclosure of Conflicts of Interest

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

Ethical Publication Statement

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

(adjusted $r^2=0.28$, $p=0.012$). The percentage of top 10% fMRI activation resected ($p=0.017$) was the most significant contributor. Other factors in the model included WA LI, AOS, volume of WA resected, WA LI absolute value (extent of laterality).

Significance: Resection of fMRI activation during a word definition decision task is an important factor for post-operative change in naming ability, along with other previously reported predictors. Currently, many centers establish language dominance using fMRI. Our results suggest the amount of the top 10% of language fMRI activation in the intended resection area provides additional predictive power and should be considered when planning surgical resection.

Keywords

Epilepsy; Surgery; fMRI; Language; Naming

Introduction

Temporal lobectomy, an effective method of seizure control for drug-resistant patients, may lead to post-operative impairments in language functions such as naming ability¹. Functional magnetic resonance imaging (fMRI) is an increasingly common tool for pre-operative language evaluation. A high degree of hemispheric language lateralization on pre-operative fMRI may be associated with poor naming outcome²⁻⁴. However, a recent American Academy of Neurology Practice Guideline found only limited evidence for fMRI prediction of post-operative language deficits, emphasizing the need for additional studies⁵.

The degree of overlap between areas of fMRI language activation and surgical resection, a factor influenced by statistical thresholds and task selection effects on regional activation, has not been addressed. In order to investigate this parameter, we used a language task known to activate frontal and temporal brain regions⁶, and an unbiased approach to create individualized thresholds, defined by the top 10% of activated voxels for each individual¹². We also developed an automated pipeline to co-register post-operative with pre-operative structural MRI and create a neuroanatomical resection mask. This resection mask was applied to pre-operative fMRI to assess the volume of 'functional' cortex (based on activation) resected, as well as 'structural' cortex (Wernicke's area-WA) resected. We then performed an exploratory analysis to identify potential predictors of change in language performance after surgery, including previously reported factors (e.g. age of seizure onset, pre-operative language performance and language lateralization) in addition to a factor not previously examined, the amount of fMRI language activation area resected. We hypothesized that all factors would be significant predictors, with temporal activation resected being the strongest predictor for naming change.

Materials and Methods

Participants

Seventy-nine patients had surgery between 2004 and 2016 after referral to the Clinical Epilepsy Section, National Institute of Neurological Disorders and Stroke (NINDS) for evaluation of intractable epilepsy. We confined subject selection to English-speaking adult temporal lobectomy (TLE) patients who completed pre- and post operative Boston Naming

Test (BNT) for language function and pre-operative fMRI for language laterality. Thirty-five patients (mean surgery age 37.5+/-10.9, age of seizure onset ((AOS) 16.0+/-10.8 yrs) met study criteria; 20 had left and 15 had right temporal resections. Twenty-eight patients had anterior temporal lobectomy (ATL), four selective amygdalohippocampectomy (SAH), and three temporal lesionectomy/topectomy (Tables 1 and 2). Nineteen patients had mesial temporal sclerosis (MTS). Twenty-seven had Engel class 1 outcome.

All fMRIs were performed at NIH. The study was approved by the NIH Combined Neurosciences Institutional Review Board. Written informed consent was obtained from all subjects. Eleven were included in a previous study⁷.

Neuropsychological Language Testing

Patients completed the Boston Naming Test (BNT)⁸, a widely-used neuropsychological measure assessing confrontation naming ability as part of a larger comprehensive neuropsychological evaluation both pre- and post-operatively. Post-operative evaluation was conducted an average of 1.3 (SD = 0.8) years after surgery (range: 0.5–5.4 years). The BNT procedure includes showing up to 60 black and white line drawings depicting objects and asking individuals to name the picture. The BNT is sensitive to post-operative changes in language function, especially among adult TLE surgery patients^{9–11}. Post-operative BNT administration varied over a considerable range, and language deficits might improve with time after surgery. We evaluated the relation of the timing of post-operative assessment to change in BNT score (see Supplementary material).

Reliable Change Index (RCI) is a rigorous method to determine whether a change in score is clinically significant by accounting for change over time due to measurement error or

practice effects. RCI is defined by $RC = \frac{x_2 - x_1}{S_{diff}}$, where x_1 is the baseline score, x_2 is follow-up score, and S_{diff} is the standard error of the difference between scores¹². Significant RCI for raw BNT scores is calculated as greater than +/-4.55 (95% confidence interval) based on normal adult data¹³.

fMRI Language Paradigm

Patients completed the Auditory Description Decision Task (ADDT), a semantic word definition decision task based on BNT items that elicits strong, reliable activation in frontal and temporal language processing networks⁶. Word definitions (e.g. “a long yellow fruit is a banana”) were presented aurally; subjects were instructed to press a button for true (70% of items) but not false statements (30%). The control condition was reverse speech with tone identification; subjects were asked to press a button when hearing tones (70% with tones, 30% with foils). Thus, the number of push-button responses for task and control conditions was matched. The paradigm was presented as a block design of five one-minute cycles (30 seconds of control followed by 30 seconds of active stimuli) using E-Prime software versions 1.1 and 2.0 (Psychology Software Tools, Inc., Pittsburgh, PA). Performance during both task and control conditions was monitored.

Imaging Data Acquisition and Analyses

All subjects received pre-operative fMRI and anatomy scans on a 3T GE scanner. Post-operative anatomy scans were acquired on 3T Siemens, Phillips, or GE scanners. Anatomical scans were T1-weighted SPGR or MPRAGE images. Detailed scanning parameters are described in previous publications¹⁴.

Automatic Resection Mask Generation—We developed a method to calculate resection masks automatically, avoiding intra- and inter-user variability from manual drawing methods (see supplementary material for details). Briefly, we generated a 3D resection volume for each patient through T1 segmentation of pre- and post-operative anatomical scans to obtain gray matter (GM), white matter (WM), and CSF probability maps and binarized them to minimize edge overlap. Resection masks were defined by gray/white matter intersection in pre-operative and CSF in post-operative scans. To account for post-operative atrophy and brain tissue retraction after surgery (shrinkage), calculated resection masks were restricted to the resection lobe. Spatial differences between this resection lobe restricted mask and the original resection mask quantified shrinkage outside the resection lobe. We used automatically generated resection masks to compute resection volume, overlap with WA and fMRI activation volume as potential predictors of naming change. Brain shrinkage was also included in the stepwise regression model selection process as a possible factor.

fMRI—Language fMRI was obtained using echo planar imaging (EPI) blood oxygen level dependent (BOLD) techniques. Auditory stimuli were presented via earphones. Language fMRI data processing was performed using SPM12 (Wellcome Department of Imaging Neuroscience, University College, London, UK), including motion correction, indirect normalization to MNI space using a deformation field generated through T1 segmentation, and spatial smoothing using a Full Width Half Maximum 8mm Gaussian kernel. Single subject first-level analyses were done using the General Linear Model¹⁵, contrasting task and control conditions.

To assess the amount of ‘functional’ cortex resected, we used an unbiased approach to create individualized thresholds utilizing the top 10% activated voxels for each patient. Compared to a fixed p-value cutoff, this individualized threshold-weighted approach reduces inter-subject variability and increases reliability of spatial distribution within subjects across runs and time points^{16–18}, which is especially necessary for planned post-operative studies. For example, individuals may have substantially different activation patterns on the same language tasks during two different runs with classical p-value cutoff $p < .001$, while the top 10% activation maps will show similar activation patterns in Broca and WA (See supplementary Figure S1, data from a healthy volunteer who had repeated ADDT scans 6 months apart). To generate the top 10% activation maps, all positive activated voxels (contrasting task > control) were extracted from each individual SPM T map and ordered in descending T value order. The threshold that retains the top 10% of these voxels was determined, and then an activation map thresholded to this individualized threshold was created. Furthermore, we calculated the amount of the top 10% activation resected relative to

the total top 10% activation. This proportion is used to control for individual brain size differences and baseline differences of the pre-operative amount of activation.

Lateralization Index and Language Dominance

Two regions of interest (ROIs) were used for Laterality Index (LI) calculation: Broca's (inferior frontal gyrus [IFG]) and WA (Brodmann areas 21, 22, 39 and 40). ROI masks were obtained from the Wake Forest University PickAtlas toolbox^{19,20}. We chose a more extensive WA based on implications of Brodmann areas for language processing²¹. Laterality index was defined as $[(L-R)/(L+R)]$ for activated voxels in left and right ROIs where $LI > 0.4$ = left dominant, $-0.4 < LI < 0.4$ = bilateral, and $LI < -0.4$ = right dominant^{2,22}. ROI LI values were calculated using the LI toolbox²³ for SPM12 with bootstrapping. Recent evidence suggests that setting a higher LI threshold (0.4 vs 0.2) reduces language dominance ambiguity²². We also tested the effect of continuous LI in IFG and WA on naming change, as well as absolute WA ROI laterality (regardless if more left or right lateralized) as a continuous variable to indicate general extent of laterality.

Since patients had temporal lobe resections, WA LIs were used to determine overall language dominance and categorize resections as dominant or non-dominant. Patients (n=7) with bilateral WA LI were considered to have had dominant resections (Table 2). We reviewed available Wada results in cases with unexpected outcomes, such as significant decline with non-dominant or improvement with dominant side resection.

Statistical Analysis to Identify Potential Predictors of Naming Change

We first summarized the cohort's demographic, clinical, fMRI, and surgical variables by mean and standard deviation for continuous variables and by n (%) for categorical variables for the full sample as well as for subgroups of patients with significant BNT change (increase or decline), or no significant change. Plots of surgical variables against naming raw score change were created to show the complete distribution, and the possible presence or absence of outliers.

Due to the small number of patients with significant BNT decline (n=7) or improvement (n=2) based on RCI cutoff, we could not compare patients with decline, improvement, and no change statistically, but provided descriptive analyses. Statistical analyses focused on finding predictors for any BNT raw score change through stepwise regression. Predictors included: demographic data (age at surgery, age of seizure onset; pre-operative BNT score); clinical outcome (Engel class); volume of brain tissue or WA resected, brain shrinkage; pre-operative language fMRI LI in WA or IFG, both raw (emphasizing right to left dominance spectrum) and absolute value (i.e. extent of laterality regardless of direction); dominant versus non-dominant resection; resected volume and percentage of top 10% fMRI activation resected. The effect of changing the percentage threshold for activation was tested (see Supplementary materials for analysis and data). Stepwise regression analysis was performed in R (version 3.3.3) in RStudio with MASS package, through stepAIC function, with both forward and backward directions to identify the model explaining the greatest variance in BNT raw score change.

Results

Pre-operative MRI/fMRI related Findings

Language laterality and dominant resections: Overall, TLE patients showed left-lateralized language as reported for typical adults (IFG LI: 0.45 $\pm$ 0.31, WA LI: 0.45 $\pm$ 0.35). Absolute WA LI was 0.528 $\pm$ 0.22. Twenty-six had WA LI categorized as left, eight bilateral, and one right. Based on these LI categories, 23 had a dominant resection; 12 had a nondominant resection. No patient had discordance between Broca's and WA LI. Left resection patients had more frequent dominant resection (19/20, 4 bilateral LI) than right (4/15, 4 bilateral LI).

Surgical resection of brain volumes: An average of 18.1 $\pm$ 10.30 cm³ of brain was resected with 1.01 $\pm$ 2.4 cm³ shrinkage after surgery due to post-operative atrophy and brain tissue retraction.

Resection of fMRI activation: The range of volume of language activation resected was 0–4.2 cm³ for top 10% activated voxels. The percentage of language activation resected ranged from 0–26.0 (median 1.8). The corresponding p-values for the top 10% activated voxels ranges from $p < 0.0001$ to $p = 0.065$ uncorrected.

Descriptive Analyses of Surgery and Naming Change

Twenty-five patients had direct electro-cortical mapping (ECM) with object naming^{7,24} that guided surgical resection. In all cases fMRI lateralization, but not localization, was used to guide surgical planning. Mean pre-operative BNT raw score was 47.6 $\pm$ 8.7. After surgery, patients had an average raw BNT naming score change of -1.2 (range -18 to 8) (post-operative - pre-operative) (Figure 1). One patient with -18 point drop might be a potential outlier (see further sensitivity analysis below).

Nine patients had BNT score change exceeding the 95% confidence interval for RCI (± 4.55) (Supplementary Table S1). Seven had significant pre- to post-operative decline and two significant improvement. Six of the seven patients with significant decline had dominant side resections (five left dominant/left resection, one bilateral dominant/right resection). The other patient with a significant decline demonstrated right dominance pre-operatively and had a left resection. For this patient, to exclude the possibility of false fMRI lateralization, we reviewed the Wada test, which showed bilateral language. Two patients had significant BNT improvement; one had right resection with bilateral LI (Wada not performed); the other had a non-dominant resection (right side resection with left dominant LI). Age of seizure onset for the seven with significant decline was 16.4 $\pm$ 11.6 years, similar to the *no-change* group (14.6 $\pm$ 9.9), and younger than the *significantly-improved* group (33.5 $\pm$ 3.5). Mean resection volume was 22.7 $\pm$ 11.9 cubic centimeter, larger than both the *significantly-improved* (13.4 $\pm$ 9.0) and *no-change* patients (17.2 $\pm$ 10.1). Percentage of top 10% activation resected was larger for significant decline (10.4 $\pm$ 8.5 %) than both the *significantly-improved* (3.4 $\pm$ 4.8 %) and *no-change* patients (3.8 $\pm$ 5.1 %).

Stepwise Regression Final Model for the Full Cohort

The final stepwise regression model included percentage of top 10% functional MRI activation resected, age of seizure onset, continuous WA LI, WA LI absolute value, and volume of WA resected. The model predicted 38% of naming score change (adjusted $r^2=0.28$, $p=0.012$ see Table 3). The most significant predictor in the final multiple regression model was the percentage of top 10% functional MRI activation resected ($p=0.017$), with a higher percentage of top 10% functional MRI activation resected associated with greater post-operative BNT decline. In 11/12 patients in whom no top 10% activation was resected, BNT score was unchanged or improved post-operatively (Figure 2A). In contrast, 6/8 patients with more than 10% of the top 10% activation resected had decreased BNT scores post-operatively.

Younger seizure onset age ($p=.054$), greater overlap between resection and WA ($p=.061$), greater degree of laterality (absolute value of WA LI) regardless of left or right ($p=.064$) were all associated with greater post-operative BNT decline at a trend level (Figure 2C). Notably, lower WA LI values (Figure 2B, i.e., values indicative of bilateral or right dominance), predicted greater post-operative BNT decline ($p=.029$).

Stepwise regression results without the outlier

One patient with BNT decline of 18 points was a potential outlier (Figure 1). Stepwise regression omitting this patient for sensitivity analysis, produced a similar final model but with one additional variable: pre-operative BNT score. Patients with higher pre-operative BNT scores had greater decline in BNT score at a trend level ($p=0.11$). Removing the outlier strengthened the full prediction model (adjusted $r^2=0.35$, $p=0.005$, Table 3). We found similar results after conducting the analysis using the top 5% instead of the top 10% activation in the final stepwise regression model (see Supplementary material for more details).

DISCUSSION

We found that extent of resection of top 10% fMRI language activation predicts naming task decline after temporal lobectomy. This was the most significant predictor in a model that also found other significant predictors previously known to predict naming decline, including age of seizure onset, WA laterality, and volume of WA resected. This novel metric creates individualized language maps that are more reliable than conventional fixed statistical thresholds. Our results suggest that this metric of language activation should be considered when assessing the risk to a patient's language functioning following a proposed surgical resection.

Temporal lobectomy poses a risk for naming decline. Naming deficits may be related to interruption of ventral pathway fibers, the uncinate and extreme capsule, conveying information from temporal to inferior frontal language processing areas^{25,26}. Post-operative impairment was found in 41% of patients with left temporal, 5% of right temporal, and less than 20% of extratemporal resections²⁷. We found a lower proportion (20%) with significant

naming decline, which might be due to our rigorous RCI approach for defining “meaningful clinical change”.

Past studies have identified some risk factors for post-operative naming changes. Limited data suggest anterior temporal lobectomy (ATL) has better overall outcome for seizure control than selective amygdalo-hippocampectomy, but selective resection (smaller volume) is associated with better cognitive outcome^{28–30}. Left temporal resection leads to an increased risk of language function decline compared to right-sided surgery, which may in fact lead to improvement in some language measures²⁸. Resection of a structurally intact hippocampus has been shown to result in loss of visual naming ability, despite pre-operative mapping of cortical naming sites³¹. Much of current clinical practice for preserving language function after temporal lobectomy stems from studies that found post-operative language deficits with resection within 1cm of naming sites identified on cortical stimulation mapping; resection >2 cm did not lead to deficits^{32–34}. However, a large retrospective study by Hermann (1999) comparing naming changes on the BNT after dominant ATL in 50 patients with, and 118 without, electro-cortical mapping (ECM) found significant decline in BNT regardless of ECM³⁵. Similarly, Hamberger et al (2005) found naming decline in 6/7 patients with auditory naming sites removed, and 3/12 without removal after one year follow up³³. ECM was performed for both auditory and visual naming, but surgery was guided by preserving only visual and not auditory naming sites (which were anterior to visual naming). This work highlights the importance of the specific language tasks used for pre-operative planning, as well as the criteria used to determine language positive sites. The ADDT fMRI task identifies areas anterior to ECM-localized visual naming sites, that, if resected, may lead to naming impairment^{24,36}. In addition to the traditionally described Broca’s and Wernicke’s areas, language decline following temporal lobe surgery may also occur due to resection of the basal temporal language area. Multiple language functions can be disturbed during stimulation of this region^{24,37}.

Previous studies have suggested that several other factors affect post-operative language decline. Higher pre-operative language performance in general predicted decline^{27,38}. We found a similar relationship after excluding one potential outlier. Older age at seizure onset and surgery also predicted decline in previous studies²⁷; object names learned late in childhood were most vulnerable³⁹. Inter-hemispheric language reorganization may be responsible for the relative resistance of early-onset epilepsy patients to post-operative naming deficits⁶. However, we found younger age at seizure onset was related to greater naming decline. This might be due to our younger age of onset patients having both a larger area of activation resected and higher pre-operative BNT scores. Other predictors of BNT decline included absence of MRI lesions or structural pathology^{40–42}. As our patients had predominantly abnormal MRIs we could not address this factor.

Several previous studies evaluated fMRI for predicting post-operative language deficits, primarily based on identifying the dominant language hemisphere; none addressed effects of extent of resection of activated regions. Atypical language dominance predicted BNT decline^{40–42}. Decreased left lateralization in left TLE patients was associated with better post-operative naming²⁷. We used lobar rather than total hemispheric language ROIs to determine LI and dominance⁴³. The degree of language laterality as well as the extent of WA

resected predicted outcome, agreeing with previous reports. Several studies support the concept that language dominance is not hemispheric but varies on regional and individual bases^{22,44,45}.

Operating on the “dominant” hemisphere, however identified, creates a risk of post-operative language impairment, and thus, in this sense fMRI determination of language dominance is associated with the risk of language decline⁴⁶. Using fMRI, language dominance usually is determined by LI in both IFG and Wernicke’s Area. In our current study, LI as a continuous variable in Wernicke’s Area (temporal lobe) was included in the final regression model for temporal lobe resection patients. However, there is no specific cut-off level that predicts decline. LI in IFG did not play an important role in predicting naming change in our data, perhaps as IFG LI was significantly correlated with Wernicke LI ($r=0.73$).

We did not find an effect of dominant versus non-dominant resection for naming change, even though the majority of our significant decline patients had dominant resection. Other studies have found decline in language measures, particularly visual naming, following dominant resection^{41,47}. It is possible that our inclusion of the continuous WA LI variable accounts for the variance that would have been explained by dominant or non-dominant resection.

Twenty-five of our patients had ECM with object naming^{7,24}. Eleven were included in a recent study comparing language fMRI and direct cortical stimulation using the same fMRI task, ADDT, that showed fMRI dependably excluded eloquent language cortex in patients without language positive sites during stimulation mapping⁷. ADDT had the best sensitivity and specificity of four fMRI tasks evaluated. ECM has significant practice variability across centers and 41% of centers report at least one adverse language outcome despite mapping eloquent cortex before surgery⁴³. ADDT activation is often anterior to impairment of object naming found on ECM⁴³ and may in part explain diminished post-operative language measures, as cortex thought to be silent for language processing was consequently resected. Several studies suggest resection of fMRI-negative areas is safe but there are no data on consequences of resecting fMRI language task activation as it is difficult to assess activation critical for, versus associated with, language processing^{7,48,49}. Our data suggest resection of language positive areas in the temporal lobe carries risk of language function decline.

Our study has several limitations. Only a few patients had post-operative BNT decline based on the rigorous RCI approach. Therefore our descriptive findings about patients with significant naming decline need cautious interpretation. The stepwise regression model is data-driven but reflects assumptions about potentially significant predictors. The final model is chosen through the stepwise process to have the best predictive power. Each variable on its own might not be significant but they function together to predict BNT. The model was partially sensitive to outliers, showing the need for confirmation in a subsequent study. It is important to note that after the elimination of the single outlier in the BNT test results, the p-value for the “PCT top 10% activation resected” fell, while the significance of other factors such as “WA LI” increased. This might have been due to the “outlier” having a relatively high amount of top 10% activation resected. Opposite relationships for continuous signed WA LI (negative) and absolute WA LI (positive) to BNT decline need cautious

interpretation, as the difference might be driven by the one right dominant patient with LI of -0.6 who had a 10 point drop after surgery. However, due to the low incidence of right dominance in our sample, we need larger datasets to conclude whether this case is indeed an outlier that drives the finding.

fMRI task selection may play a more important role in guiding resection than previously appreciated. ADDT, a task based on BNT items that activates both frontal and temporal language areas⁶, produces greater temporal activation than naming tasks currently described in the literature²². It tests auditory comprehension, a better analogue for naming than verbal fluency performance or single word semantic decision tasks. Furthermore, our data raise the possibility that language “activation” in the “non-dominant” hemisphere in some epilepsy patients may contribute to language capability.

Our results suggest in addition to identifying hemispheric laterality, localizing fMRI activation and determining how much activation is in the intended resection area may be useful in predicting post-operative naming change. The best fMRI analysis method for predicting language decline has not been established. A recent appraisal of the role of fMRI in pre-operative evaluation of patients with epilepsy emphasized the need to compare fMRI analysis methods with one another⁵. Our data suggest that language localization using the top 10% of activated areas may be an approach worthy of additional study and that resecting such fMRI activation areas in eloquent regions may be deleterious to neurological outcomes following epilepsy surgery.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Key Points:

- 20% of patient had significant naming decline after temporal lobectomy, and 6% had significant naming improvement after temporal lobectomy.
- Several factors predicted outcome: Age of seizure onset, laterality and the amount of tissue resected in Wernicke's area.
- The percentage of the top 10% of voxels activated during an auditory language task is one of the important factors in predicting more naming score decline
- Functional MRI can help predict neuropsychological outcome after temporal lobectomy

Figure 1. Boxplot of BNT score distribution. Dotted lines are the RCI cut-offs (4.5 and -4.5). One potential outlier of BNT score change of -18. Subjects were jittered horizontally to display in a nonoverlap fashion.

Figure 2.

Distribution between BNT score change and percentage of top 10% activation resected (top) and LI on Wernicke area (continuous and absolute value). A: symbol size corresponds to resected tissue volume (cm³), symbol shape corresponds to dominant side resection or not, dotted lines are the RCI cut-offs (4.5 and -4.5). B and C: WA LI regular and absolute value vs BNT Score change. Vertical dotted lines denotes left language dominance (0.4) and right language dominance (-0.4). Blue color denotes cases that were with negative LI value, red denotes positive LI value.

Table 1.

Patients' demographic information summary

	Adult (N = 35)
Median (SD) age, years	37.5 (10.9)
Age range, years min-max	18–61
Sex, M/F	13-M 22-F
Handedness	29 Right, 3 Left, 3 Ambidextrous
Mean age at onset (SD), years	16.0(10.8)
No. of patients in class I, II, III or IV after surgery *	21,7,2,4 (1 Missing)
Resection Side:	
Left	20
Right	15
Type of Resection:	
ATL	28
SAH	4
Temporal Lesionectomy/Topectomy	3

* According to the Engel's classification. Follow-up period at least 6 months (median 31, range 6–96 months).

Detailed patients' demographic and surgery information

Table 2.

ID	BNT Score Change	Age at Surgery	Age Onset	Sex	Handedness	Etiology	Resection Side	Resect Procedure	LI IFG	LIWER	LI Dominance Overall	Dominant Hem Resect	Engel Class
1*	-18	34	6	F	R	MTS	L	ATL	0.61	0.55	L	Yes	1
2*	-9	43	38	F	L	MTS	L	ATL	-0.46	-0.6	R	No	1
3*	-7	49	4	F	R	MTS	L	SAH	0.83	0.82	L	Yes	3
4*	-7	28	19.5	F	R	MTSPlus	L	ATL	0.08	0.71	L	Yes	1
5*	-7	30	10	M	R	Tumor	L	ATL	0.91	0.73	L	Yes	NA
6*	-5	54	22	F	R	FCD	R	ATL	-0.27	0.11	B	Yes	1
7*	-5	28	15	F	R	Unknown	L	ATL	0.49	0.67	L	Yes	1
8	-4	49	10	F	R	MTS	R	ATL	0.61	0.52	L	No	1
9	-3	36	12	M	R	MTS	R	ATL	0.73	0.71	L	No	2
10	-3	38	4	M	R	MTS	L	SAH	0.74	0.68	L	Yes	1
11	-2	33	20	M	R	Microdysgenesis	L	ATL	0.33	0.65	L	Yes	3
12	-2	33	18	F	R	Microdysgenesis	L	TOP	0.15	-0.21	B	Yes	4
13	-2	20	7	M	R	Microdysgenesis	L	TOP	0.77	0.55	L	Yes	4
14	-2	61	0.25	F	L	MTS	L	ATL	0.3	-0.27	B	Yes	1
15	-2	30	14	F	L	MTS	L	SAH	0.33	0.46	L	Yes	2
16	0	36	21	M	R	Cavernoma	R	Temp LES	0.52	0.65	L	No	4
17	0	18	11	F	R	FCD	R	ATL	0.47	0.72	L	No	1
18	0	33	23	M	R	Microdysgenesis	L	ATL	0.22	0.12	B	Yes	1
19	0	59	9	F	L	MTS	L	ATL	0.78	0.55	L	Yes	1
20	0	38	27	M	R	MTS	R	ATL	0.95	0.74	L	No	2
21	0	44	9	F	R	MTS	L	ATL	0.64	0.68	L	Yes	1
22	0	29	9	F	R	MTS	R	ATL	0.53	0.73	L	No	2
23	0	49	8	M	R	Unknown	R	ATL	0.29	0.44	L	No	2
24	0	26	21	M	R	Unknown	L	ATL	0.67	0.61	L	Yes	1
25	1	41	4	F	L	MTS	R	ATL	0.56	0.28	L	Yes	1
26	1	44	35	F	R	MTS	R	SAH	0.35	0.49	L	No	1
27	2	23	6	F	R	MTS	R	ATL	0.58	0.54	L	No	1
28	2	23	0.75	F	R	MTS	L	ATL	0.49	0.86	L	Yes	4
29	2	45	29	F	R	Unknown	L	ATL	0.4	0.17	B	Yes	2
30	3	52	35	F	R	Meningioma	R	ATL	0.36	-0.11	B	Yes	1
31	3	35	24	M	R	Unknown	L	ATL	0.67	0.56	L	Yes	1
32	4	46	9	F	R	MTS	L	ATL	0.44	0.43	L	Yes	1

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ID	BNT Score Change	Age at Surgery	Age Onset	Sex	Handedness	Etiology	Resection Side	Resect Procedure	LI IFG	LI WER	LI Dominance Overall	Dominant Hem Resect	Engel Class
33	4	25	12.5	M	L	Unknown	R	ATL	0.64	0.69	L	No	1
34	5	43	36	F	R	Unknown	R	ATL	-0.21	-0.13	B	Yes	1
35	8	37	31	M	R	MTS	R	ATL	0.4	0.68	L	No	2

MTS= Mesial temporal sclerosis, FCD= Focal Cortical Dysplasia, ATL = anterior temporal lobectomy, FL = frontal lobectomy, PL=parietal lobectomy, SAH = selective amygdalohippocampectomy, HEM=hemispherectomy, LES= Lesionectomy, TOP= Topectomy. If a significant decline occurred, the change is noted in the ID column (*). If patient had no invasive electro-cortical mapping, it is noted in the Resection Side column (†).

Table 3

Stepwise regression final models summary (with and without the BNT outlier)

Coefficients	BNT Score Change							
	Full Sample				Without Outlier			
	Estimate	Conf. Int.	std. Error	p	Estimate	Conf. Int.	std. Error	p
(Intercept)	1.41	-3.86 – 6.69	2.58	.588	8.90	-0.39 – 18.20	4.53	.060
Age of Seizure Onset	0.15	-0.00 – 0.30	0.07	.054	0.09	-0.03 – 0.21	0.06	.117
WA Absolute LI	-9.45	-19.49 – 0.60	4.91	.064	-13.36	-21.84 – -4.88	4.13	.003
WA LI	7.40	0.81 – 13.99	3.22	.029	8.86	3.62 – 14.11	2.56	.002
WA Resection Vol	-0.83	-1.71 – 0.04	0.43	.061	-0.68	-1.35 – -0.01	0.32	.046
PCT Top10% Activation Resected	-0.28	-0.51 – -0.05	0.11	.017	-0.16	-0.34 – 0.02	0.09	.075
Pre-operative BNT					-0.12	-0.27 – 0.03	0.07	.111
Observations		35				34		
R ² / adj. R ²		.381 / .275				.471 / .354		
F-statistics		3.574*				4.012**		
AIC		204.076				179.867		

WA=Wernicke's Area, PCT=Percentage, Preop=Pre-operative