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Comprehensive presurgical functional MRI language evaluation in adult patients with epilepsy

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Abstract

Functional magnetic resonance imaging (fMRI) has the potential to replace the intracarotid amobarbital procedure (IAP) in presurgical evaluation of patients with epilepsy patients. In this study, we compared fMRI verb generation (VG) and semantic decision/tone decision (SDTD) tasks and the IAP in their ability to localize language functions in patients with epilepsy undergoing presurgical evaluation. We enrolled 50 healthy controls to establish normal language activation patterns for VG and SDTD tasks at 3 or 4 T, and to design language regions of interest (ROIs) that were later applied to 38 patients with epilepsy (28 of 38 also underwent the IAP). We calculated laterality indices (LIs) for each task for each subject based on the ROIs, and we used general linear modeling to analyze the fMRI data. All healthy and epileptic subjects activated language areas with both fMRI tasks. We found significant correlations in language lateralization between the fMRI tasks ($r = 0.495$, $P \leq 0.001$) and between VG and IAP ($r = 0.652$, $P < 0.001$) and SDTD and IAP ($r = 0.735$, $P < 0.001$). The differences in LIs between SDTD and VG tasks were small and not affected by age, gender, epilepsy status, handedness, or performance. SDTD and VG tasks combined explained approximately 58.4% in the variability of the IAP/language. In the general linear modeling, only the SDTD task significantly contributed to the determination of language lateralization in patients with epilepsy undergoing presurgical evaluation. Results indicate a moderate convergent validity between both fMRI language tasks and between IAP and fMRI tasks. The results of this study indicate that either of these fMRI tasks can be used for language lateralization in patients with epilepsy undergoing presurgical evaluation, but that the SDTD task is likely to provide more information regarding language lateralization than the VG task.

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Keywords

Epilepsy; Temporal lobe epilepsy; Surgery; Functional magnetic resonance imaging; Intracarotid amobarbital procedure; Language

1. Introduction

Approximately 30−40% of patients with epilepsy fail medical treatment and are considered for epilepsy surgery [1–3]. Such decisions are made on the basis of ictal EEG recordings, with the results of other studies (imaging, neuropsychological testing, and intracarotid amobarbital procedure) providing outcome and neurological risk data to the patient before she or he decides whether to undergo the resective procedure. Reliable language evaluation is therefore a crucial part of the presurgical evaluation. It is currently performed by means of the intracarotid amobarbital procedure (IAP), which provides information about language lateralization. Although the IAP has remained the "gold standard" for language lateralization, it has several risks and disadvantages [4–8]. It may be falsely lateralizing [9,10]; the precise pattern of sodium amobarbital perfusion rate is unknown even with angiography showing the intracranial vessels [11]. Performing the procedure may not be possible in patients with complicated vascular anatomy or a known allergy to iodine-based contrast agents or barbiturates. Finally, the IAP does not provide information about the localization of the language functions. Because of the risks associated with the IAP and the availability of functional MRI (fMRI) as an alternative, it is necessary to fully explore the effectiveness of fMRI for presurgical language assessment.

In recent years, several studies have compared fMRI and the IAP with respect to language lateralization, or evaluated the ability of fMRI to localize language functions in children and adults with epilepsy [12–24]. These and other authors used various language fMRI tasks including semantic decision [14,16,21,25–27], verb generation/verbal fluency [13,19,20,23, 28–30], word generation [15,18,22,24], and sentence reading [17,31]. Some studies have also reported the use of more than one fMRI paradigm for language localization and lateralization [10,12,13,29,32,33], but the results of these studies have been mixed, with some tasks showing good and some poor correlation with the results of IAP. It is still not clear whether performing more than one fMRI task will contribute to the presurgical evaluation of patients with epilepsy and whether different tasks (e.g., semantic decision and word production) are of similar importance in predicting language lateralization.

The main goal of this study was to establish an effective fMRI language evaluation protocol for presurgical evaluation of patients with epilepsy and to evaluate the concordance between the two most widely used fMRI language tasks—a semantic decision/tone decision task (SDTD) and a verb generation task (VG)—and the IAP in patients with medication-resistant epilepsy undergoing presurgical staging. Our hypothesis was that the fMRI language tasks used in this study should be similar in their lateralization patterns in healthy controls and those with epilepsy, and that the results of language lateralization with fMRI would be concordant with the results of the IAP.

2. Material and methods

2.1. Subjects

Fifty healthy controls were recruited by word of mouth; 38 epilepsy subjects were recruited from the Epilepsy Monitoring Unit at the University Hospital in Cincinnati, OH, USA. In all subjects with epilepsy, the diagnosis of epilepsy was confirmed by prolonged video/EEG monitoring (PVEM) in conjunction with the neuropsychological testing, PET, and MRI data. All subjects signed an informed consent approved by the institutional review board of the

University of Cincinnati and completed the Edinburgh Handedness Inventory (EHI) [34] prior to the scanning procedure; one subject less than 18 years of age signed assent and her parent signed informed consent approved by the Cincinnati Children's Hospital Medical Center.

2.2. Language tasks

2.2.1. Verb generation task (VG)—The design of this blocked language fMRI paradigm was based on the description by Petersen et al., later used by many others including our group to study language development and localization in healthy subjects and those who had a stroke or epilepsy [30,35–38]. Briefly, in the active condition, a noun is presented binaurally every 5 seconds, and the subject is required to silently generate verbs that are associated with each noun. For example, if the noun *stove* is presented, the subject might generate the verbs *cook, bake*, and *clean*. The subject is instructed to generate verbs without saying them, to minimize the motion artifact associated with speech. Five periods of active condition lasting 30 seconds each are separated by control periods, each also lasting 30 seconds. During the control periods, the subject is instructed to perform sequential, bilateral finger taps starting with the thumb/fifth digit opposition in response to each frequency-modulated tone centered on 400 Hz presented every 5 seconds. The rate of the sequential tapping was self-paced, and the subjects were instructed to stop after touching each finger once. The finger tapping part of this paradigm was designed to control for the auditory prompt used in VG and to distract the subjects from performing verb generation, as this type of activity is relatively incompatible with continued engagement in verbal processing; finger tapping is known to decrease the ability to generate fluent speech in adults [39,40]. Monitoring finger tapping via closed-circuit TV also provided a gross assessment of task performance by the subjects. This word fluency fMRI task is known to activate areas involved in lexical processing including the inferior frontal gyrus, dorsolateral prefrontal cortex, superior and middle temporal gyri, and anterior cingulated gyrus [41]. The total duration of this task is 5 minutes 30 seconds. As previously [42], to evaluate subjects' engagement in the verb generation part of the task, a noun recall was administered to all subjects scanned at 4 T (N = 49: 25 healthy controls and 24 patients with epilepsy) immediately on leaving the scanner.

2.2.2. Semantic decision/tone decision task (SDTD)—This language fMRI paradigm consists of two intervening (block design) conditions: the control condition (tone recognition, performed eight times) and the active condition (semantic recognition, performed seven times) [14,43]. Presentation of each condition lasted 30 seconds (15 seconds for the first tone recognition), with stimuli presented every 3.75 seconds. In the tone condition, subjects heard eight brief sequences of four to seven 500- and 750-Hz tones. They responded with a nondominant hand button press for any sequence containing either two 750-Hz tones ("1") or other than two 750-Hz tones ("2"). In the active condition, subjects heard eight spoken English nouns designating animals and responded "1" with a nondominant hand button press to stimuli that met two criteria: "native to the United States" and "commonly used by humans." In all other cases, they responded with button press "2." This task is known to activate numerous brain areas involved in language processing, including the prefrontal cortex of the inferior, middle, and superior frontal gyri, posterior cingulated gyrus and retrosplenial cortex, anterior/superior temporal sulcus and middle temporal gyrus, posterior/inferior temporal gyrus, fusiform and anterior parahippocampal gyri, anterior hippocampus, angular gyrus, and posterior cerebellum [44]. The total duration of this task is 7 minutes 15 seconds.

Prior to entering the scanner, all subjects learned the fMRI tasks. Their understanding of the language tasks was tested by performing a mock run that included, for the SDTD task, a sequence of five sets of tones followed by a sequence of five nouns designating animals. For the VG task, the subjects listened to a sequence of six nouns presented every 5 seconds. Subjects were allowed to proceed to the scanner only if they responded correctly to all 10 SDTD items

and if they were able to generate at least one verb associated with each of the presented nouns within the allotted time.

2.3. Functional MRI

On completion of the standard MRI screening procedures, all subjects underwent fMRI using VG and SDTD tasks with either a 3-T Bruker Bio-spec 30/60 (Bruker Medizintechnik, Karlsruhe, Germany, in the Imaging Research Center at the Cincinnati Children's Hospital Medical Center (IRC)) or a 4-T Varian (Oxford Magnet Technology, Oxford, UK, in the Center for Imaging Research at the University of Cincinnati (CIR)) MRI scanner. A detailed description of the differences between the procedures at 3 and 4 T is provided elsewhere [37]. Here, we provide only a brief description of the MRI procedure for the Bruker 3-T MRI scanner, followed by a description of the differences between the Bruker and Varian procedures.

The 3-T Bruker MRI scanner is equipped with an audiovisual system for presentation of task stimuli (SV 4120; Avotech Systems Inc., Jensen Beach, FL, USA). Foam padding and a head restraint were used to control head movement. The subjects were given a button box for generating measurable responses, as well as to alert the MRI technologist to a problem if necessary. Echo planar imaging (EPI) was performed in thirty-two 5-mm-thick planes suffcient to cover areas extending superiorly from below the inferior aspect of the cerebellum to the apex of the cerebrum in an adult brain. The specific protocol was a T2*-weighted gradient-echo EPI pulse sequence (TR/TE = 3000/38 ms, FOV = 25.6 × 25.6 cm, matrix 64 × 64 pixels, slice thickness = 5 mm, flip angle = 90°). Finally, a high-resolution T1-weighted three-dimensional anatomical scan was obtained using a modified driven equilibrium Fourier transform (MDEFT) protocol (TR = 15 ms, TI = 550 ms, TE = 4.3 ms, FOV = 25.6 × 19.2 × 16.2, flip angle = 20°, spatial resolution of 1 × 1 × 1.5 mm) to provide images for anatomical localization of the activation maps. For the scans obtained at 4 T, 30 axial planes to be imaged in the fMRI procedures were identified from initial scout images. The specific protocol for the EPI scans was TR/TE = 3000/25 ms, FOV 25.6 × 25.6 cm, matrix 64 × 64 pixels, slice thickness = 4 mm, flip angle array: 85/180/180/90; and that for the anatomical scans was TR = 13 ms, TE = 6 ms, FOV = 25.6 × 19.2 × 15.0, flip angle array of 3: 22/90/180 with the voxel size of 1 × 1 × 1 mm.

For all data, the fMRI image postprocessing was performed using software developed in the IRC in the IDL software environment (IDL 6.3; Research Systems Inc., Boulder, CO, USA). Geometric distortion due to *B*0 field inhomogeneity was corrected for during reconstruction using a multi-echo reference scan [45]. Next, data were first co-registered and motion corrected using a pyramid iterative algorithm [46]. Finally, affne spatial transformation was used with the brain rotated into AC–PC coordinate frame and then linearly scaled into the Talairach reference frame prior to statistical analysis [47].

Individual participant data for each task were analyzed using a general linear model to identify voxels with a time course similar to the time course of stimulus presentation. Signal drift and respiratory and cardiac signals were accounted for by using a set of cosine basis functions as covariates. *Z*-score maps were computed from the results of this analysis. Individual participant maps for each task were concatenated, and a random-effects analysis was performed to determine regions of significant group activation. All composite activation maps were generated using a threshold *Z* score of 2.58. This nominal *Z*-score value, combined with a cluster size of at least 10, resulted in a corrected *P* value of 0.001 for all images as determined via Monte-Carlo simulation.

To calculate the laterality indices (LIs), we designated specific functional regions of interest (ROI) based on the activation maps from healthy subjects' fMRI data defined from the global

composite map separately for each task (Fig. 1). These primary ROIs include the lateral frontal region (corresponds to Broca's area) and the lateral/posterior temporal region (corresponds to Wernicke's area) in the left hemisphere and corresponding homologs in the right hemisphere. Further, we combined the frontal and temporal ROIs into one “global language ROI.” ROIs defined by active regions on the left and right were mirrored onto the contralateral side, and the Talairach coordinates of all active pixels encompassed within these regions were stored. ROIs designed this way correspond to the classically recognized areas responsible for language. Only voxels with Z scores ≥ 2.58 within an ROI were used in the calculation of LIs. Pixels were counted, and a LI was defined as the difference in the number of activated voxels, summed independently for the left and right regions of interest, divided by the total of active voxels in the left and right regions of interest. This approach yielded LIs ranging from −1 (complete right lateralization) to 1 (complete left lateralization). Laterality indices for the patients with epilepsy were calculated using the ROIs generated based on the healthy subjects' fMRI data. On the basis of previous studies, we assumed VG to be symmetric if the LI ranged between −0.1 and 0.1, to be left hemisphere dominant if the LI was >0.1, and to be right hemisphere dominant if the LI was less than −0.1; for the SDTD, the cutoff points were −0.2 and 0.2 [27,41].

2.4. Intracarotid amobarbital procedure (IAP)

On injection of 100−150 mg of amobarbital into the hemisphere opposite the seizure focus as documented by PVEM, and allowing 10−20 seconds for the patient's initial confusion to subside, a brief evaluation of receptive and expressive language functions was performed by asking the patient to follow two simple commands, answer four simple yes/no questions, and name four pictures of common objects. Subjects scored a point for performing each of the language tasks; an additional 3 points were added to the hemispheric score if paraphasic errors were not observed during the procedure. The language-dominant hemisphere was based on the modified formula provided by Binder et al. [14]:

$$\mathrm{LI} = (L)/(L \quad \text{maximal possible score}) - (R)/(R \quad \text{maximal possible score}),$$

where L is the left hemisphere score and R is the right hemisphere score. This approach yields LIs that range between strongly left dominant (1) and strongly right dominant (−1). Based on a previous study, we assumed IAP of language to be left hemispheric if the LI was >0.25 and atypical if the LI was <0.25 [14].

Language recovery from hemispheric anesthesia was tested by asking the patient to read two standard sentences. Language recovery was deemed complete after the patient read the sentences without hesitation or paraphasic errors. Approximately 30−40 minutes after the first injection, the catheter was moved to the contralateral side and the procedure was repeated with different sets of language items. The EEG was monitored during all IAPs. Initial language testing started only if slowing was observed ipsilateral to the injection site. Second hemisphere testing was always done after the slowing from the first injection observed on the EEG had resolved.

2.5. Statistical analysis

Data are described using means and SD for continuous variables and frequencies and percentages for categorical variables. Data are compared between groups with and without epilepsy using χ^2 tests for categorical variables and independent sample t tests for continuous variables. The primary hypotheses are that VG and SDTD similarly indicate language lateralization, and that lateralization determined by IAP is similar to that determined by VG

and SDTD. To test these hypotheses, it is common to consider correlation; a high correlation suggests that a high score on one task or test corresponds to a high score on the other task or test. A high correlation does not preclude systematic bias; two tasks can be highly correlated, but one may be biased high or low when compared with the other. Limits of agreement can be used to estimate the extent of any bias; these limits, defined as the mean difference ±2 SD of the differences, determine the range within which 95% of the differences will fall. In this study, Pearson's correlation coeffcients, paired samples *t* tests, and limits of agreement are used to compare LIs obtained using different methods. In addition, mean differences were considered a dependent variable in generalized linear models to determine whether factors impacting lateralization also impact systematic bias (i.e., as a test of effect modification). Generalized linear models were also used to determine whether LIs assessed by VG and SDTD tasks were predictive of LIs assessed by IAP. Analyses were conducted using SPSS 14.0 (SPSS Inc., Chicago, IL, USA).

3. Results

We recruited 50 healthy controls without any history of neurological disease aged 22−59 and 38 patients with epilepsy aged 16−59. Characteristics and primary measurements for study subjects are summarized in Table 1. One healthy control received only the VG task, and this subject's data were excluded from analysis. The only difference between groups was in task performance; subjects with epilepsy performed significantly worse than healthy controls. For the SDTD task, this difference was similar to the results obtained in a previous study using this task in healthy controls and patients with epilepsy [27]. There were no other differences between healthy controls and subjects with epilepsy, or between 3- and 4-T scanners, except for language lateralization (see below). Therefore, we combined the results obtained from both scanners for further, hypothesis-driven analysis.

We noted significant correlations between the fMRI tasks for all three LIs (frontal, temporal, and global; all $P \leq 0.037$) (Table 2). The correlation between language lateralization (global ROI) with the SDTD or VT task and IAP was strong (for both, Pearson's $r \geq 0.652$, $P < 0.001$). In Table 3 are listed the clinical characteristics of subjects with epilepsy who underwent both fMRI and the IAP. Of note is that four patients who had atypical language lateralization with the IAP also had atypical language lateralization with fMRI. Further testing of the effects of age, sex, epilepsy, handedness, performance, and scanner type on differences in the LI between the SDTD and VG tasks revealed that these variables had either no effect or a very small effect (Table 4).

Next, we tested the contribution of the fMRI language tasks to the determination of LIs using the IAP as the “gold standard” for language lateralization. Unadjusted model testing revealed that the SDTD and VG tasks combined explained approximately 58.4% in the variability of the IAP/language, and that only the SDTD task significantly contributed to this determination (in other words, the VG task did not add to the prediction from the SDTD task). Further analysis adjusted for other variables revealed that the effects of handedness and age were significant, whereas other variables tested did not contribute to the model; age, handedness, and SDTD combined explained approximately 75.5% of the IAP/language variability (Table 5). We also tested the effects of side of epilepsy onset on language lateralization (Table 6), and we found that there was a much higher chance of atypical language lateralization in patients with left but not right hemispheric epilepsy ($P = 0.013$ for the SDTD task, $P = 0.088$ for the VG task). This relationship was not seen when IAP results were analyzed, which may be the effect of the small number of subjects who received this test.

4. Discussion

In this study evaluating fMRI as a presurgical tool for language cortex localization, we first established normal language activation patterns using two frequently used fMRI tasks: verb generation and semantic decision/tone decision. We then applied the results of language localization in healthy controls to the presurgical evaluation of patients with epilepsy. Both fMRI tasks used in this study showed robust BOLD signal changes in the language cortices in healthy controls (Fig. 1) and patients with epilepsy. The validity of language localization with fMRI tasks in epilepsy was later verified by comparing the fMRI results with the results of the IAP in patients with epilepsy (Fig. 2). Our findings confirm the clinical utility of the fMRI tasks used in this study for localization of the eloquent cortex in presurgical evaluation, and are consistent with prior literature. Several studies have already documented the ability of fMRI to lateralize language in patients with epilepsy, and have shown a strong correlation between presurgical fMRI performed using various language tasks and IAP [14,16,18,23,24,29]. For example, Binder and colleagues found a very strong correlation (Pearson's $r = 0.96$, $P < 0.0001$), and Desmond and colleagues observed a perfect (“100%”) correlation between the IAP and fMRI in the ability to lateralize language in patients with epilepsy [14,16]. Correct localization and lateralization of language functions in patients undergoing surgical treatment of epilepsy is of utmost importance, as patients who undergo surgery in the language-dominant hemisphere are known to suffer from word finding deficits. The possibility of such deficits may be predicted by fMRI with the SDTD task [26,48]. These and our results confirm the utility of fMRI in presurgical evaluation of patients with pharmacoresistant epilepsy and add to the growing body of evidence that fMRI can be used for presurgical language localization.

Some of the more recent studies used a combination of fMRI tasks for evaluation of language functions in patients with epilepsy, and at least one study proposed using fMRI instead of the IAP [33,49]. Furthermore, one fMRI study using the SDTD task in patients with left temporal lobe epilepsy has already shown 100% sensitivity and 73% specificity in predicting significant naming decline after epilepsy surgery when language was lateralized to the left hemisphere, confirming the clinical utility of this fMRI task in presurgical evaluation of epilepsy surgery patients [26]. We extended the results of the preceding studies by adding a comparison of the two most frequently used fMRI tasks and by demonstrating the excellent ability of both tasks in language localization and a strong correlation between fMRI and the IAP. In one of the previous studies, Benson and colleagues reported a discrepancy in the ability of three language tasks to lateralize language in patients with brain lesions; only the verb generation task showed good language lateralizing capability and correlation with the IAP, whereas object naming and single-word reading tasks did not perform well at lateralizing language functions [29]. Bahn and colleagues reported that language lateralization with IAP and that with fMRI tasks agreed in all patients, but only the results of visual analysis were presented [13]. In contrast to the aforementioned studies, Galliard and colleagues used five different language fMRI tasks to determine language lateralization in 26 predominantly right-handed patients with epilepsy with left hemispheric seizure onset [33]. These authors reported significant agreement between the IAP and language lateralization with a panel of fMRI tasks, and they suggested that the panel may improve designation of language laterality in patients with epilepsy when compared with a single task.

In view of the findings by various research groups, it is not surprising to find a strong correlation between each of the fMRI tasks and the IAP and between the fMRI tasks themselves. But, when we examined the contribution of each of the tasks to the correlation with the IAP, we found that the additional contributions of the verb generation task to the estimation of language lateralization by the SDTD task proved to be not significant. In other words, it appears that performing one task, preferably the SDTD task, would be suffcient for correct language lateralization, provided the patient was able to cooperate with the requirements of the task.

These results have important clinical implications. The results of fMRI language localization can be analyzed independently and compared with each other later or, in the case when one study fails (e.g., because of equipment failure, excessive movement, or lack of activation), the results of the second study would still be available, preventing the patient from undergoing a second procedure (and, in the case of IAP, repeated exposure to radiation and contrast agents). Therefore, including two or more language tasks in the presurgical evaluation has the advantage of possibly streamlining presurgical evaluation and avoiding the need for test repetition.

In addition to the above findings, we noted that the SDTD task provided LIs that were more left-lateralized than the LIs generated with the VG task. This shift is likely related to the semantic nature of the SDTD task and to subtracting from the active paradigm the tone decision component, which allows for control of attention/working memory, auditory processing, and motor responses with this task [43]. This LI difference is also likely related, in part, to the differences in the activation patterns between the tasks that are due to various language components involved in the SDTD task versus the VG task. In contrast to the SDTD task, the VG task uses spontaneous verb generation in response to common nouns while finger tapping is used as a control [36,41]. Therefore, in this task, subtracting auditory and working memory components of language processing is not possible. This may have contributed to the differences in LIs. Further, the VG task does not include intrascanner performance monitoring. Although the subjects performed very well during the mock run and on the postscan recall of the nouns outside the scanner immediately on completion of the fMRI procedure, we have not been able to assess the performance inside the scanner due to the covert nature of this task. This possibly could have affected the LI values generated with this task, but we do not think that this is the case, as a recent study showed that language LIs generated with fMRI are performance independent [50]. Nevertheless, despite the significant differences between the tasks and between the lateralization of the BOLD signal changes, the LIs were highly correlated, and the results of both fMRI tasks strongly agreed with the results of language evaluation with the IAP and cortical stimulation mapping. This supports the notion that either both fMRI tasks combined or each task independently can be used for language localization in health and disease.

We noted differences between the LIs in patients with right and left hemispheric epilepsy onset with either task. The differences in the LIs obtained with the VG and SDTD tasks was between healthy controls and patients with left hemispheric seizure onset (more symmetric language distribution). These findings suggest the possibility that the recurrent ictal and interictal activity causes redistribution of language function in the developing brain to compensate for injury to the traditional left-dominant language areas or connections to them. These findings are in concordance with the study by Powell et al., who observed reorganization of functional tracts (i.e., changes in connectivity) in patients with left medial temporal but not right temporal seizure onset [51]. An alternative explanation is that the preexisting brain injury that leads to the development of epilepsy causes a shift in language localization/lateralization. The latter possibility is partially supported by a recent study indicating that early brain injury (defined as any insult, e.g., meningitis, febrile seizure, trauma) is associated with more symmetric language distribution [27]. Further, the findings of differences in language lateralization in patients with left hemispheric epilepsy are in agreement with an fMRI study that examined the effects of left and right hemispheric epilepsy on language distribution using a word generation task [28]. We also noted a trend toward more symmetric language distribution in patients with longer duration of epilepsy. This trend was not significant, in contrast to previous studies [27,52], but it was consistent with our previous study that focused on the effects of epilepsy on language in children [30] and other studies examining this issue in adult patients with epilepsy [53,54]. Such a lack of significance may be the result of the relatively small sample of patients with epilepsy included in our study or the enrollment in this study of subjects with various etiologies of epilepsy including stroke, tumor, and hippocampal sclerosis, as well as

subjects with normal anatomical MRIs (Table 1). However, a study that included a large number of patients with left medial temporal lobe epilepsy did not find such a relationship [53]. Hence, it is still somewhat unclear what factors affect language lateralization, and to what degree, in patients with epilepsy.

In summary, our data demonstrate that fMRI is a useful clinical tool for language lateralization. Here, we have identified several focus areas for future work. Of primary interest is the use of fMRI to elucidate the effects of epilepsy on language, which will support research on the physiological underpinning of language.

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References

1. Engel J Jr. Finally, a randomized, controlled trial of epilepsy surgery. N Engl J Med 2001;345:365–7. [PubMed: 11484695]
2. Kwan P, Brodie MJ. Early identification of refractory epilepsy. N Engl J Med 2000;342:314–9. [PubMed: 10660394]
3. Wiebe S, Blume WT, Girvin JP, Eliasziw M. A randomized, controlled trial of surgery for temporal-lobe epilepsy. N Engl J Med 2001;345:311–8. [PubMed: 11484687]
4. Jones-Gotman M, Sziklas V, Djordjevic J, et al. Etomidate speech and memory test (eSAM): a new drug and improved intracarotid procedure. Neurology 2005;65:1723–9. [PubMed: 16344513]
5. Loring DW, Meador KJ, Lee GP, et al. Cerebral language lateralization: evidence from intracarotid amobarbital testing. Neuropsychologia 1990;28:831–8. [PubMed: 2247209]
6. Rasmussen T, Milner B. The role of early left-brain injury in determining lateralization of cerebral speech functions. Ann NY Acad Sci 1977;299:355–69. [PubMed: 101116]
7. Wada J, Rasmussen T. Intracarotid injection of sodium amytal for the lateralization of cerebral speech dominance. J Neurosurg 1960;17:226–82. [PubMed: 13826545]
8. Wada JA, Clarke R, Hamm A. Cerebral hemispheric asymmetry in humans: cortical speech zones in 100 adults and 100 infant brains. Arch Neurol 1975;32:239–46. [PubMed: 1124988]
9. Jayakar P, Bernal B, Santiago Medina L, Altman N. False lateralization of language cortex on functional MRI after a cluster of focal seizures. Neurology 2002;58:490–2. [PubMed: 11839861]
10. Kho KH, Leijten FS, Rutten GJ, Vermeulen J, Van Rijen P, Ramsey NF. Discrepant findings for Wada test and functional magnetic resonance imaging with regard to language function: use of electro-cortical stimulation mapping to confirm results [case report]. J Neurosurg 2005;102:169–73. [PubMed: 15658111]
11. Hong SB, Kim KW, Seo DW, Kim SE, Na DG, Byun HS. Contralateral EEG slowing and amobarbital distribution in Wada test: an intracarotid SPECT study. Epilepsia 2000;41:207–12. [PubMed: 10691118]
12. Baciu MV, Watson JM, McDermott KB, et al. Functional MRI reveals an interhemispheric dissociation of frontal and temporal language regions in a patient with focal epilepsy. Epilepsy Behav 2003;4:776–80. [PubMed: 14698719]
13. Bahn MM, Lin W, Silbergeld DL, et al. Localization of language cortices by functional MR imaging compared with intracarotid amobarbital hemispheric sedation. AJR Am J Roentgenol 1997;169:575–9. [PubMed: 9242780]

14. Binder JR, Swanson SJ, Hammeke TA, et al. Determination of language dominance using functional MRI: a comparison with the Wada test. Neurology 1996;46:978–84. [PubMed: 8780076]
15. Cuenod CA, Bookheimer SY, Hertz-Pannier L, Zeffiro TA, Theodore WH, Le Bihan D. Functional MRI during word generation, using conventional equipment: a potential tool for language localization in the clinical environment. Neurology 1995;45:1821–7. [PubMed: 7477975]
16. Desmond JE, Sum JM, Wagner AD, et al. Functional MRI measurement of language lateralization in Wada-tested patients. Brain 1995;118(Pt 6):1411–9. [PubMed: 8595473]
17. Gaillard WD, Balsamo L, Xu B, et al. Language dominance in partial epilepsy patients identified with an fMRI reading task. Neurology 2002;59:256–65. [PubMed: 12136067]
18. Hertz-Pannier L, Gaillard WD, Mott SH, et al. Noninvasive assessment of language dominance in children and adolescents with functional MRI: a preliminary study. Neurology 1997;48:1003–12. [PubMed: 9109891]
19. Lehericy S, Cohen L, Bazin B, et al. Functional MR evaluation of temporal and frontal language dominance compared with the Wada test. Neurology 2000;54:1625–33. [PubMed: 10762504]
20. Liegeois F, Connelly A, Salmond CH, Gadian DG, Vargha-Khadem F, Baldeweg T. A direct test for lateralization of language activation using fMRI: comparison with invasive assessments in children with epilepsy. Neuroimage 2002;17:1861–7. [PubMed: 12498760]
21. Spreer J, Arnold S, Quiske A, et al. Determination of hemisphere dominance for language: comparison of frontal and temporal fMRI activation with intracarotid amytal testing. Neuroradiology 2002;44:467–74. [PubMed: 12070719]
22. Woermann FG, Jokeit H, Luerding R, et al. Language lateralization by Wada test and fMRI in 100 patients with epilepsy. Neurology 2003;61:699–701. [PubMed: 12963768]
23. Worthington C, Vincent DJ, Bryant AE, et al. Comparison of functional magnetic resonance imaging for language localization and intracarotid speech amytal testing in presurgical evaluation for intractable epilepsy: preliminary results. Stereotact Funct Neurosurg 1997;69:197–201. [PubMed: 9711754]
24. Yetkin FZ, Swanson S, Fischer M, et al. Functional MR of frontal lobe activation: comparison with Wada language results. AJNR Am J Neuroradiol 1998;19:1095–8. [PubMed: 9672017]
25. Fernandez G, Specht K, Weis S, et al. Intrasubject reproducibility of presurgical language lateralization and mapping using fMRI. Neurology 2003;60:969–75. [PubMed: 12654961]
26. Sabsevitz DS, Swanson SJ, Hammeke TA, et al. Use of preoperative functional neuroimaging to predict language deficits from epilepsy surgery. Neurology 2003;60:1788–92. [PubMed: 12796532]
27. Springer JA, Binder JR, Hammeke TA, et al. Language dominance in neurologically normal and epilepsy subjects: a functional MRI study. Brain 1999;122(Pt 11):2033–46. [PubMed: 10545389]
28. Adcock, J.; Smith, S.; Matthews, P. Human Brain Mapping. Brighton, UK: 2001. Comparison of fMRI with the Wada test for lateralization of language in pre-surgical epilepsy patients.. 2001
29. Benson RR, FitzGerald DB, LeSueur LL, et al. Language dominance determined by whole brain functional MRI in patients with brain lesions. Neurology 1999;52:798–809. [PubMed: 10078731]
30. Yuan W, Szaflarski JP, Schmithorst VJ, et al. FMRI shows atypical language lateralization in pediatric epilepsy patients. Epilepsia 2006;47:593–600. [PubMed: 16529628]
31. Ries ML, Boop FA, Griebel ML, et al. Functional MRI and Wada determination of language lateralization: a case of crossed dominance. Epilepsia 2004;45:85–9. [PubMed: 14692913]
32. Bookheimer SY, Zeffiro TA, Blaxton TA, Gaillard PW, Theodore WH. Activation of language cortex with automatic speech tasks. Neurology 2000;55:1151–7. [PubMed: 11071493]
33. Gaillard WD, Balsamo L, Xu B, et al. fMRI language task panel improves determination of language dominance. Neurology 2004;63:1403–8. [PubMed: 15505156]
34. Oldfield RC. The assessment and analysis of handedness: the Edinburgh Inventory. Neuropsychologia 1971;9:97–113. [PubMed: 5146491]
35. Jacola LM, Schapiro MB, Schmithorst VJ, et al. Functional magnetic resonance imaging reveals atypical language organization in children following perinatal left middle cerebral artery stroke. Neuropediatrics 2006;37:46–52. [PubMed: 16541368]
36. Petersen SE, Fox PT, Posner MI, Mintun M, Raichle ME. Positron emission tomographic studies of the cortical anatomy of single-word processing. Nature 1988;331:585–9. [PubMed: 3277066]

37. Szaflarski JP, Holland SK, Schmithorst VJ, Byars AW. fMRI study of language lateralization in children and adults. Hum Brain Mapp 2006;27:202–12. [PubMed: 16035047]
38. Szaflarski JP, Schmithorst VJ, Altaye M, et al. A longitudinal functional magnetic resonance imaging study of language development in children 5 to 11 years old. Ann Neurol 2006;59:796–807. [PubMed: 16498622]
39. Friedman A, Polson MC, Dafoe CG, Gaskill SJ. Dividing attention within and between hemispheres: testing a multiple resources approach to limited-capacity information processing. J Exp Psychol Hum Percept Perform 1982;8:625–50. [PubMed: 6218226]
40. Kemper S, Herman RE, Lian CH. The costs of doing two things at once for young and older adults: talking while walking, finger tapping, and ignoring speech or noise. Psychol Aging 2003;18:181–92. [PubMed: 12825768]
41. Holland SK, Plante E, Weber Byars A, Strawsburg RH, Schmithorst VJ, Ball WS Jr. Normal fMRI brain activation patterns in children performing a verb generation task. NeuroImage 2001;14:837–43. [PubMed: 11554802]
42. Chiu CY, Schmithorst VJ, Brown RD, Holland SK, Dunn S. Making memories: a cross-sectional investigation of episodic memory encoding in childhood using FMRI. Dev Neuropsychol 2006;29:321–40. [PubMed: 16515409]
43. Binder JR, Frost JA, Hammeke TA, Cox RW, Rao SM, Prieto T. Human brain language areas identified by functional magnetic resonance imaging. J Neurosci 1997;17:353–62. [PubMed: 8987760]
44. Szaflarski JP, Binder JR, Possing ET, McKiernan KA, Ward BD, Hammeke TA. Language lateralization in left-handed and ambidextrous people: fMRI data. Neurology 2002;59:238–44. [PubMed: 12136064]
45. Schmithorst VJ, Dardzinski BJ, Holland SK. Simultaneous correction of ghost and geometric distortion artifacts in EPI using a multiecho reference scan. IEEE Trans Med Imaging 2001;20:535–9. [PubMed: 11437113]
46. Thevenaz P, Unser M. A pyramid approach to sub-pixel registration based on intensity. IEEE Trans Image Process 1998:7–41.
47. Talairach, J.; Tournoux, P. Co-planar stereotaxic atlas of the human brain. Thieme; New York: 1988.
48. Langfitt JT, Rausch R. Word-finding deficits persist after left anterotemporal lobectomy. Arch Neurol 1996;53:72–6. [PubMed: 8599562]
49. Medina LS, Bernal B, Dunoyer C, et al. Seizure disorders: functional mr imaging for diagnostic evaluation and surgical treatment—prospective study. Radiology 2005;236:247–53. [PubMed: 15987978]
50. Weber B, Wellmer J, Schur S, et al. Presurgical language fMRI in patients with drug-resistant epilepsy: effects of task performance. Epilepsia 2006;47:880–6. [PubMed: 16686653]
51. Powell HW, Parker GJ, Alexander DC, et al. Abnormalities of language networks in temporal lobe epilepsy. NeuroImage 2007;36:209–21. [PubMed: 17400477]
52. Saltzman J, Smith ML, Scott K. The impact of age at seizure onset on the likelihood of atypical language representation in children with intractable epilepsy. Brain Cogn 2002;48:517–20. [PubMed: 12030499]
53. Janszky J, Jokeit H, Heinemann D, Schulz R, Woermann FG, Ebner A. Epileptic activity influences the speech organization in medial temporal lobe epilepsy. Brain 2003;126(Pt 9):2043–51. [PubMed: 12821521]
54. Brazdil M, Chlebus P, Mikl M, Pazourkova M, Krupa P, Rektor I. Reorganization of language-related neuronal networks in patients with left temporal lobe epilepsy: an fMRI study. Eur J Neurol 2005;12:268–75. [PubMed: 15804243]

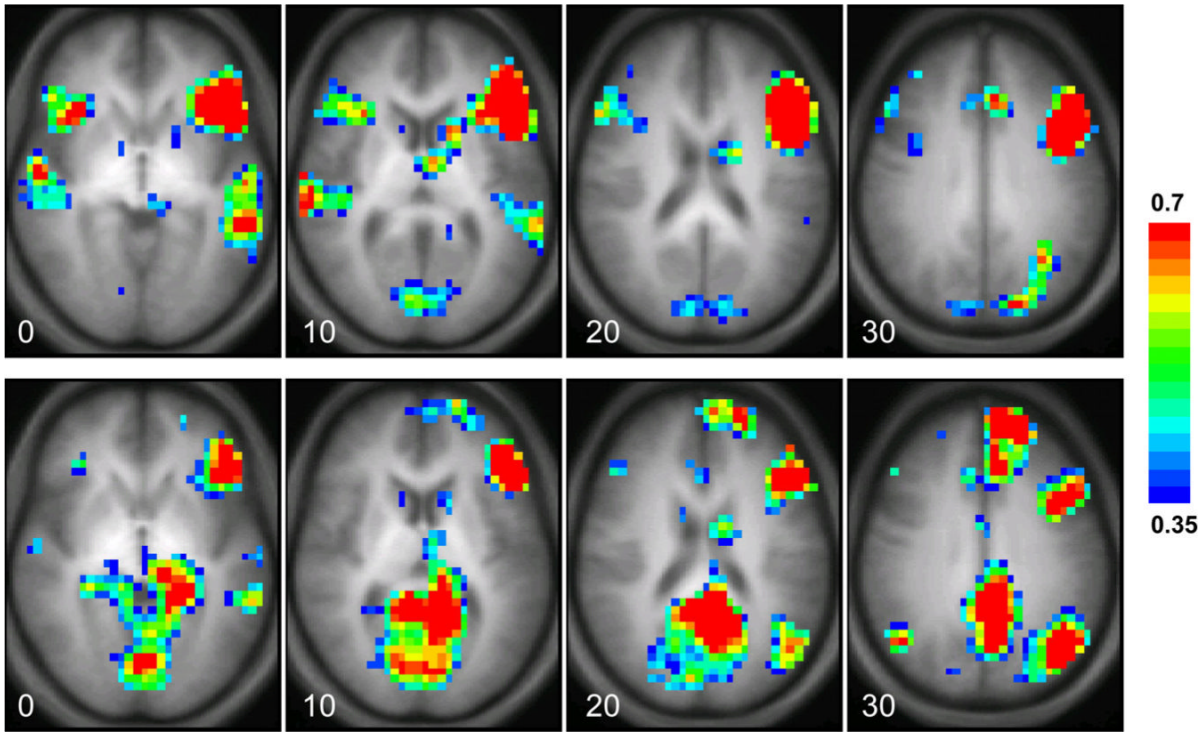

Fig. 1.

Functional MRI language maps in healthy subjects. Cross-correlation activation maps showing areas of increased BOLD signal during the verb generation task (upper row) and semantic/tone decision task (lower row). Activations for VG task are located over the inferior/medial frontal gyri (centroid: −50, 15, 15) and medial/superior temporal gyri (centroid: −58, −25, 5). Activations for SDTD (lower row) are located over the inferior/medial frontal gyri (centroid: −42, 27, 15) and middle/inferior temporal and supramarginal gyri (centroid: −46, −41, −10).

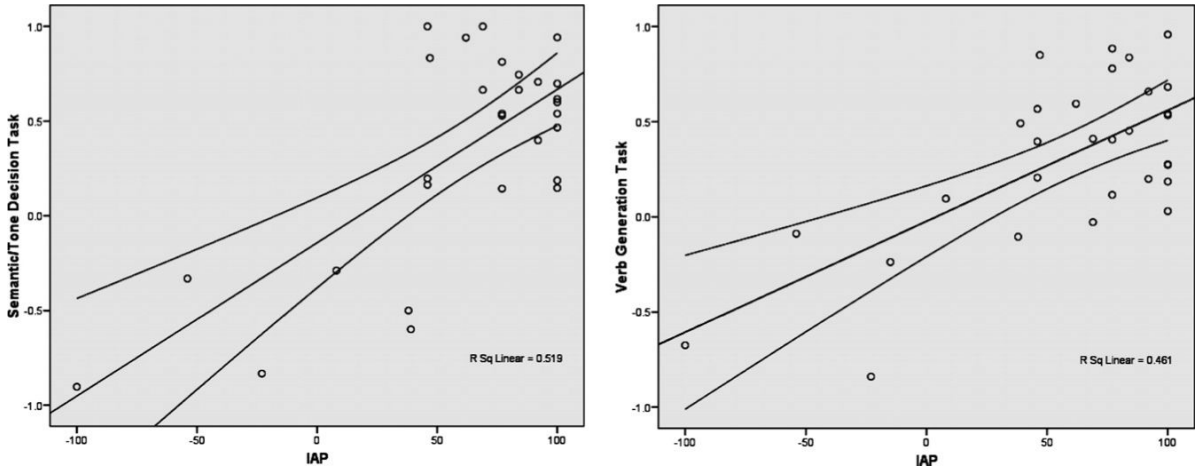

Fig. 2.
Correlation between language lateralization with the IAP and the verb generation (left) and semantic/tone decision tasks (right).

Table 1

Characteristics and primary measurements for study subjects

	Healthy subjects (*N* = 49)	Subjects with epilepsy (*N* = 36)	All subjects (*N* = 85)	*P* value
Age	39.5 (12.2)	37.9 (11.7)	38.8 (11.9)	0.544
Male	37 (75.5)	22 (61.1)	59 (69.4)	0.155
Female	12 (24.5)	14 (38.9)	26 (30.6)	
Personal handedness[a]	84.4 (38.2)	77.9 (50.3)	81.6 (43.5)	0.505
Family handedness[b]	84.0 (18.3)	86.0 (23.6)	84.9 (20.6)	0.665
Age at epilepsy onset		16.6 (15.2)		
Duration of epilepsy		21.1 (13.2)		
Left hemisphere epilepsy	0 (0.0)	18 (50.0)	18 (50.0)	
Right hemisphere epilepsy	0 (0.0)	18 (50.0)	18 (50.0)	
3-T scanner	24 (49.0)	13 (36.1)	37 (43.5)	0.237
4-T scanner	25 (51.0)	23 (63.9)	48 (56.5)	
Performance, verbs[c]	98.8 (2.1)	83.1 (15.8)	91.3 (13.5)	<0.001
Performance, TD[d]	93.7 (6.1)	77.3 (17.0)	87.0 (14.3)	<0.001
Performance, SD[e]	81.0 (11.4)	71.7 (12.8)	77.3 (12.8)	0.001
Frontal VG	0.42 (0.31)	0.45 (0.47)	0.43 (0.38)	0.396
Temporal VG	0.11 (0.44)	0.18 (0.46)	0.14 (0.45)	0.135
Global VG	0.35 (0.29)	0.38 (0.41)	0.36 (0.34)	0.180
Left	41 (83.7)	29 (80.6)	70 (82.4)	
Right	3 (6.1)	3 (8.3)	6 (7.1)	0.912
Symmetric	5 (10.2)	4 (11.1)	9 (10.6)	
Frontal SDTD	0.54 (0.36)	0.45 (0.55)	0.50 (0.45)	0.690
Temporal SDTD	0.36 (0.46)	0.19 (0.58)	0.29 (0.52)	0.486
Global SDTD	0.49 (0.30)	0.36 (0.54)	0.44 (0.42)	0.769
Left	47 (95.9)	24 (66.7)	71 (83.5)	
Right	1 (2.0)	7 (19.4)	8 (9.4)	0.002
Symmetric	1 (2.0)	5 (13.9)	6 (7.1)	
IAP		0.57 (0.49)		
Left		23 (85.2)		
Right		2 (7.4)		
Symmetric		2 (7.4)		

Note. Data are reported as means and SD or frequency and proportions, as appropriate. The significance of the difference between subjects with and without epilepsy is given. Lateralization for VG and SDTD was determined from the global laterality index.

[a] Five subjects had values ≤-50, values for all other subjects were >50.

[b] All subjects had a positive score; data were not available for one subject.

[c] Assessed only for subjects scanned at 4 T.

[d] Not assessed for six subjects.

[e] Not assessed for five subjects.

Table 2

Correlation, difference, and limits of agreement for LIs measured using the VG task, SDTD task, and IAP

	Pearson's *r*	*P* value		Mean difference	Lower limit of agreement	Upper limit of agreement
		Correlation	Difference			
Frontal (SDTD–VG)	0.530	<0.001	0.124	0.07	−0.74	0.88
Temporal (SDTD–VG)	0.227	0.037	0.022	0.15	−1.06	1.36
Global (SDTD–VG)	0.495	<0.001	0.088	0.07	−0.71	0.85
IAP–VG	0.652	<0.001	0.002	0.25	−0.52	1.03
IAP–SDTD	0.735	<0.001	0.007	0.22	−0.56	1.01

Note. For comparison of IAP and fMRI data, the global fMRI measure has been used. (One patient with epilepsy did not have valid VG and SDTD lateralization measures, and one healthy control and one patient with epilepsy did not have a valid VG measure. Nine subjects with epilepsy did not have IAP data; these subjects are excluded for analyses relating VG and SDTD to IAP language lateralization.)

Table 3

Clinical information for the patients with epilepsy who underwent IAP and fMRI

	Age	Age of onset	Sex	EHI	Seizure onset	Structural MRI	Etiology/risk factor	LI		
								VG	SDTD	IAP
1	24	14	F	88	R MT	R MTS	Febrile seizures	0.67	0.41	0.69
2	38	4	F	100	R MT	Bilateral hippocampal volume loss R > L; no signal change	Febrile seizures	0.54	0.78	0.77
3	30	11	M	100	R temporal	R posterior temporal DNET	DNET	0.71	0.66	0.92
4	52	36	M	85	Bitemporal	L MTS	Meningitis	0.67	0.45	0.84
5	51	<1	M	100	L MT	s/p L lateral temporal resection/L MTS	Perinatal insult	0.16	0.40	0.46
6	51	5	M	33	L MT	L MTS	Febrile seizures	−0.83	−0.84	−0.23
7	17	16	F	58	R MT	R temporal tip ring-enhancing lesion	Lesion	0.40	0.20	0.92
8	39	5	F	100	R temporal	R hemispheric atrophy	Meningitis	1.00	0.57	0.33
9	30	9	F	100	R MT	R MTS	Febrile seizures	0.20	0.21	0.46
10	33	19	F	67	L MT	Normal	None	0.54	0.03	0.27
11	39	20	F	−50	L MT	Normal	None	−0.33	−0.09	−0.54
12	53	13	M	100	R MT	R MTS	Meningitis	0.14	0.41	0.77
13	47	27	M	100	R MT	R MTS	None	1.00	−0.03	0.69
14	21	2	M	91	R temporal	R posterior medial lesion	Lesion	0.60	0.96	1.00
15	21	14	F	52	L temporal	Normal	None	0.75	0.84	0.84
16	43	2	M	−89	L temporal	L lateral ventricle enlargement/L MTS	None	−0.90	−0.68	−1.00
17	35	1	M	100	L MT	L MTS	Premature 11 weeks	−0.60	0.49	0.39
18	20	15	M	100	L parietotemporal	L posterior hippocampal DNET	Lesion	0.94	0.19	1.00
19	35	9	F	83	R MT	R anterior temporal resection/ residual hippocampus remaining	Febrile seizures	0.81	0.88	0.77
20	33	19	F	83	L frontal	L frontal arachnoid cyst	Cyst; s/p shunting	−0.50	−0.10	0.38
21	41	7	F	100	R MT	R MTS	Febrile seizures	0.15	0.28	1.00
22	27	17	M	100	L MT	Posttraumatic white matter changes	TBI	0.70	0.27	0.77
23	22	<1	F	100	R frontotemporal	R cerebral hemispheric atrophy	Meningitis and stroke at 3 weeks of age	0.53	0.12	0.77
24	46	40	M	75	L MT	L MTS	TBI	−0.29	0.1	0.08
25	22	4	F	73	R temporal	R MTS	TBI	0.47	0.54	1.00
26	49	27	F	100	L MT	L medial temporal glioma	Lesion	0.83	0.85	0.47
27	28	27	F	−100	R MT	R MTS	Thyroiditis-related encephalopathy	−0.24		−0.15
28	41	36	F	100	L temporal	L anterior temporal cortical dysplasia	Lesion	0.94	0.59	0.62

Note. $N = 28$; one patient underwent the fMRI/VG task only due to difficulties with understanding the SDTD task; the patient is a non-native English speaker. Patients 1−11 underwent fMRI at 3 T, and the remaining patients, at 4 T. Not included in the table are patients who did not undergo IAP ($N = 10$). Of these 10 subjects, 8 decided not to undergo further evaluation for epilepsy surgery,1 subject was allergic to barbiturates (the decision regarding surgery was based on fMRI results), and 1 subject underwent IAP and fMRI but could not hear the prompts for language tasks and, hence, his fMRI data were excluded from analysis. MT, mesial temporal lobe; MTS, mesial temporal sclerosis; DNET, dysembryoplastic neuroepithelial tumor; s/p, status post.

Table 4

Models testing the effect of age, sex, epilepsy, handedness, performance, and scanner type on differences in the LI between the SDTD and VG tasks

	B	95% CI (*B*)	*P* value
Frontal			
Intercept	−0.94	(−1.67 to −0.21)	0.012
Age	−0.01	(−0.01 to 0.00)	0.096
Male vs female	−0.01	(−0.20 to 0.18)	0.904
Personal handedness	0.00	(0.00 to 0.00)	0.180
Healthy subjects vs subjects with epilepsy	0.03	(−0.18 to 0.23)	0.780
Performance (TD)	0.00	(0.00 to 0.01)	0.231
Performance (SD)	0.01	(0.00 to 0.02)	0.029
4 T vs 3 T	0.03	(−0.15 to 0.21)	0.760
Temporal			
Intercept	0.40	(−0.82 to 1.63)	0.516
Age	0.01	(−0.01 to 0.02)	0.264
Female vs male	0.00	(−0.32 to 0.33)	0.995
Personal handedness	0.00	(0.00 to 0.00)	0.909
Healthy subjects vs subjects with epilepsy	0.35	(0.01 to 0.70)	0.044
Performance (TD)	−0.01	(−0.02 to 0.01)	0.442
Performance (SD)	0.00	(−0.02 to 0.01)	0.623
4 T vs 3 T	0.00	(−0.31 to 0.30)	0.989
Global			
Intercept	−0.54	(−1.26 to 0.19)	0.144
Age	−0.01	(−0.01 to 0.00)	0.105
Female vs male	−0.05	(−0.24 to 0.14)	0.623
Personal handedness	0.00	(0.00 to 0.00)	0.157
Healthy subjects vs subjects with epilepsy	0.13	(−0.07 to 0.33)	0.204
Performance (TD)	0.00	(−0.01 to 0.01)	0.852
Performance (SD)	0.01	(0.00 to 0.02)	0.056
4 T vs 3 T	0.03	(−0.15 to 0.21)	0.750

Note. Performance on the verb task is not included; this was only measured for subjects scanned using the 4-T scanner. The intercept is shown for completeness.

Table 5

Models relating LI determined by SDTD and VG tasks to LI determined by IAP

	B	95%CI (*B*)	P value	R^2
Intercept	0.30	(0.14 to 0.47)	0.001	0.584
SDTD	0.47	(0.15 to 0.78)	0.006	
VG	0.32	(−0.09 to 0.74)	0.121	
Intercept	0.35	(0.19 to 0.51)	<0.001	0.539
SDTD	0.63	(0.39 to 0.87)	<0.001	
Intercept	0.61	(0.07 to 1.14)	0.030	0.767
4 T vs 3 T	0.04	(−0.20 to 0.28)	0.642	
Female vs male	−0.09	(−0.34 to 0.17)	0.481	
Personal handedness	0.00	(0.00 to 0.01)	0.004	
Age	−0.01	(−0.02 to 0.00)	0.041	
Hemisphere	−0.07	(−0.33 to 0.18)	0.562	
SDTD	0.26	(−0.04 to 0.56)	0.071	
VG	0.01	(−0.40 to 0.42)	0.932	
Intercept	0.50	(0.10 to 0.91)	0.026	0.755
Personal handedness	0.01	(0.00 to 0.01)	0.001	
Age	−0.01	(−0.02 to −0.00)	0.036	
SDTD	0.27	(0.01 to 0.52)	0.046	

Note. Both unadjusted models and models adjusted for age, sex, handedness, scanner type, and hemisphere are shown.

Table 6

Comparison of language lateralization between healthy controls, patients with left hemisphere epilepsy, and patients with right hemisphere epilepsy

	Controls	Left hemisphere epilepsy	Right hemisphere epilepsy	*P* value comparing lateralization between left and right hemisphere epilepsy
SDTD				
Left	47 (95.9)	9 (50.0)	15 (83.3)	0.013
Right	1 (2.0)	7 (38.9)	0 (0.0)	
Symmetric	1 (2.0)	2 (11.1)	3 (16.7)	
VG				
Left	41 (83.7)	12 (66.7)	17 (94.40	0.088
Right	3 (6.1)	3 (16.7)	0 (0.00	
Symmetric	5 (10.2)	3 (16.7)	1 (5.6)	
IAP				
Left		10 (71.4)	13 (100.0)	0.113
Right		2 (14.3)	0 (0.0)	
Symmetric		2 (14.3)	0 (0.0)	