Language Lateralization in Patients with Temporal Lobe Epilepsy: A Comparison between Volumetric Analysis and the Wada Test

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Objective: Determining language lateralization is important for the presurgical evaluation of patients with medically intractable epilepsy. The Wada test has been the gold standard for lateralization of language dominance before epilepsy surgery. However, it is an invasive test with risk, and have some limitations.

Methods: We compared the volumetric analysis with Wada test, and studied the clinical potential of volumetric analysis to assess language laterality in large surgical candidates with temporal lobe epilepsy (TLE). To examine the efficacy of volumetric analysis to determine language lateralization during presurgical evaluation, we compared the volumetric analysis of the bilateral planum temporale with the results of Wada test in 59 patients with chronic intractable TLE (rTLE, n=32; ITLE, n=27) who underwent epilepsy surgery. We measured the gray matter volumes of planum temporale (PT) of each patients using the VoxelPlus2 program (Mevisys, Daejeon, Korea).

Results: Overall congruence of the volumetric analysis with the Wada test was 97.75% in rTLE patients and 81.5% in ITLE patients. There were more significant leftward asymmetry of the PT in rTLE patients than ITLE patients. In ITLE patients, relatively high proportion (37%) of the patients showed bilateral or right hemispheric language dominance.

Conclusion: These results provide evidence that the volumetric analysis of the PT could be used as an alternative in language lateralization. Also, the results of the Wada test suggested that there was considerable plasticity of language representation in the brains of patients with intractable TLE and it was associated with an earlier age of brain injury.

KEY WORDS: Cerebral dominance • Temporal lobe epilepsy • Wada • Volume.

INTRODUCTION

The determination of language lateralization is important in the presurgical evaluation of patients with medically intractable epilepsy. Surgical treatment offers the possibility of successful seizure control in a selected group of patients, particularly in those with temporal lobe epilepsy (TLE). However, it also puts them at risk for the development of new cognitive deficits. Post-operative aphasia, simple naming, or other word-finding difficulties has been reported in 6 to 30% of patients after left temporal lobectomy. The risk of postoperative language and memory deficits is related directly to the preoperative lateralization of language functions in the brain. The intracarotid amobarbital procedure (IAP), or the Wada test, is the most commonly used method at present and represents the gold standard in the assessment of language lateralization. However, this test has major shortcomings due to its invasiveness, lack of standardization, absence of spatial resolution, and difficulties related to application and interpretation. Therefore, non-invasive alternatives to the Wada test are continually evaluated. Repetitive magnetic stimulation is a non-invasive alternative that works by deactivating the language cortex. The majority of other promising alternatives including functional magnetic resonance imaging (fMRI), positron emission tomography (PET), single photon emission computerized tomography (SPECT), transcranial Doppler, and near infrared spectroscopy are based on brain activation and detect hemodynamic responses to language cortex activation. Magnetoencephalography directly measures event-related physi-
ological brain activation. Some techniques provide localization of language functions, while the Wada test is strictly a lateralization method. The fMRI will likely serve as the most widespread alternative due to broad availability. But, there are very few studied comparisons between volumetric analysis and the IAP.

The planum temporale (PT), which constitutes part of Wernicke’s area, was postulated to be an important area for language processing with speculation that this region facilitates the conversion of auditory phonemes to visual graphemes. The PT is located in the posterior superior temporal gyrus (Brodman’s area 22) and is associated with auditory phonological processing. The 3D gradient echo magnetic resonance imaging (MRI) allows acquisition of high resolution consecutive millimeter sections. This allows in vivo quantitative analysis of the PT. Steinmetz et al. used this technique to study the relationship of PT asymmetry to hand preference. The left-handers had a less significant leftward asymmetry of the PT as compared to the right-handers. In 1994, Foundas et al. measured the PT on MRI scans of patients with selective hemispheric anesthesia or Wada testing for language lateralization. All individuals with language area lateralized to the left hemisphere (right-handed individuals) had leftward asymmetry in the PT, and one subject with language area lateralized to the right hemisphere (left-handed individual) exhibited a strong rightward asymmetry of the PT. This suggested that MRI-determined PT asymmetries are associated with language dominance and may predict language laterality. Therefore, we compared language-related lateralization by the IAP test and with volumetric analysis to test potential of PT volumetry to detect language lateralization in patients with intractable temporal lobe epilepsy.

MATERIALS AND METHODS

Patients

This study included 59 patients with TLE who underwent temporal lobectomy at our institution from March 2004 to December 2007. Preoperative evaluations included detailed clinical and neurologic examinations, video-EEG monitoring, high-resolution MRI, SPECT, PET, neuropsychological examination, the IAP, and volumetric analysis of the PT. Patients were grouped according to seizure onset in subjects with right (rTLE, n=32) or left (lTLE, n=27) TLE. Clinical and demographic data of patients are summarized in Table 1.

| Variable       | Right TLE (n=32) | Left TLE (n=27) | p value |
|----------------|-----------------|----------------|---------|
| Age (yr)       | 28.0±10.4 (7-51) | 37.9±9.7 (21-65) | <0.001  |
| Education (yr) | 10.2±3.9 (1-16)  | 9.5±3.5 (1-16)    | 0.470   |
| Gender         |                 |                 | 0.082   |
| Male           | 16 (50.0%)      | 20 (74.1%)       |         |
| Female         | 16 (50.0%)      | 7 (25.9%)        |         |
| Onset age (yr) | 11.2±6.9 (1-27)  | 12.5±4.1 (1-31)   | 0.467   |
| Epilepsy duration (yr) | 16.8±9.2 (2-35) | 25.3±11.0 (6-51) | 0.002   |
| Pathology      |                 |                 |         |
| Sclerosis      | 18 (56.3%)      | 18 (66.7%)       |         |
| Tumor          | 2 (6.2%)        | 3 (11.1%)        |         |
| Gliosis        | 4 (12.5%)       | 4 (14.8%)        |         |
| NMD            | 8 (25.0%)       | 2 (7.4%)         |         |

TLE: temporal lobe epilepsy; NMD: neuronal migration disorder

**Table 1. Clinical details of patients groups**

**Intracarotid amobarbital procedure (IAP)**

The patients were prepared for an intracarotid injection of anesthetic, typically thiopental sodium, after the cerebral angiogram. The cerebral hemispheres suspected to harbor the epileptogenic focus were always studied first. Paralysis of the contralateral arm and the arrest of finger wiggling usually indicated that the hemisphere has been anesthetized and that language and memory testing could begin. In general, language testing was performed first. The patient was asked to name objects, follow simple commands, repeat sentences, and count or name the days of the week. We recorded whether the patients showed correct naming, dysarthria or global aphasia. So, if the patients showed dysarthria when right side injection, and global aphasia when left side injection, we determined that the patients showed left language dominance. Memory items were presented in order to test memory reserves in the non-anesthetized hemisphere. Memory for the presented items was tested after complete recovery of neurological functions. To account for the different number of items used in some presentation, a percentage of retention (number of objects recalled or recognized divided by the number displayed to the patient) was calculated for the right and left hemisphere memory scores. It recommended that both injections were spaced by at least 30 minutes to avoid residual amobarbital effects in the hemisphere where functions were to be tested.

**MRI scan acquisition and measurements**

Volumetric MR images were acquired in all patients on a Siemens 1.5 Tesla system. T1 weighted images were obtained as a series of 104 to 124 coronal image sections of 2.0 mm thickness. The gray matter volumes in the PT were measured with the VoxelPlus2 program (Mevisys, Daejeon, Korea).
VoxelPlus2 allows the simultaneous measurement of images in all three orthogonal planes and this enhances the ability to discern whether specific tissues are part of a particular structure (Fig. 1). Galaburda13) noted that "coronal, axial, and sagittal views were all necessary for the appropriate measurement of the PT" (p. 457). The gray matter of each of the regions of interest (ROI) was traced with a mouse-driven, computer guided cursor and the sagittal, coronal, and axial planes were simultaneously viewed. Boundaries were marked and saved in all three planes, allowing for accurate identification of the boundaries of each region. Therefore, the full gray matter volume could be measured through this three-dimensional approach, as described by Honeycutt19). The examiner of volumetry did not know results of wada test.

The planum temporale (PT) measurements

The PT is the flat plane that forms the surface of the superior temporal gyrus caudal to Heschl's gyrus (HG). The anatomic delineation of the PT on the 3D MR scan was defined by methodologies established by Steinmetz et al.34) and refined by Kulynych et al.22). The anterior border is defined by the transverse sulcus caudal to HG, and the posterior border is defined by the caudal extent of the posterior horizontal ramus as it bifurcates into the posterior ascending and descending rami. The medial tip of the roughly triangular PT is the retroinsular point where the anterior and posterior borders of the PT coincide. We defined the lateral border of the PT as the superlateral margin of the bulging rim of the superior temporal convolution. We drew the PT in the sagittal plane from medial to lateral with visualization of the axial plane according to these definitions (Fig. 2).

The normal brain anatomy was characterized by one transverse gyrus on the left and two transverse gyri on the right supratemporal plane according to Pfeifer28). However, this is typically seen in only 50% of brains. Additionally, HG sometimes appears to be divided into anterior and posterior portions by an additional "transverse sulcus" running along the HG edge. These portions are characterized as two parts of HG and not as part of the PT since they appear to originate from a common medial stem. This is consistent with Pfeifer's anatomic descriptions. However, if two transverse gyri originate separately from the retroinsular region and are separated by HG, the posterior gyrus is regarded as part of the PT regardless of side.

Analyses

Asymmetry quotients (AQs) were calculated as (Left-Right)/[(Left+Right)/2] in accordance with calculations established by previous investigators. An AQ greater than or
equal to 0.025 was defined as leftward asymmetry and an AQ of less than or equal to -0.025 was defined as rightward asymmetry. Symmetry is defined as greater than 5% interhemispheric differences, with a value range between -0.025 and +0.025. This is consistent with previous studies. AQs were calculated for the PT in all patients.

**Interobserver correlation**

The volume of the PT was measured according to previous designations with the VoxelPlus2. The Planimetric volumes of the PT are listed in Table 2. The volumetric differences in the PT area measurements between two observers were not significant (p>0.05).

**RESULTS**

**Intracarotid amobarbital procedure (IAP)**

The side of speech dominance was clearly elucidated in all individuals. Language lateralization was distributed as follows in the rTLE group: 96.8% (31 of 32 individuals) had left hemisphere language dominance and 3.2% (1 of 32) had bilateral language dominance. Corresponding values in the ITLE group were 63% (17 of 27) with left hemisphere language dominance, 7.4% (2 of 27) with bilateral language dominance, and 29.6% (8 of 27) with right hemisphere language dominance (Table 3). The ITLE group showed the high incidence of atypical (right hemisphere or bilateral) language dominance pattern (about 37%).

These incidences of atypical language dominance pattern in ITLE group was correlated with the age at the time of operation and the seizure duration (Table 4). In the atypical language dominance group, the mean age at the time of operation was older and the seizure duration was longer than the left language dominance group. But, there was no significant difference between two groups with respect to the age of seizure onset and education.

The volume of the PT in rTLE and ITLE patients is shown in Table 2. The volume of the PT in rTLE patients was bigger than that of the right PT in ITLE patients (p<0.001). But, there was no significant difference between the right and left PT volumes in the ITLE patients (p=0.061).

**Language lateralization in TLE patients according to the asymmetry quotients (AQs) of the Planum Temporale (PT)**

We calculated AQs after the PT measurements in all patients. The results of the volumetric analysis and the congruence between volumetric language dominance and the Wada test can be seen in Table 3. The figures in bold are representing that the results of the language lateralization for both Wada test and volumetry are the same. Overall congruence with the Wada test was 93.75% (30 of 32 individuals) in rTLE patients and 85.1% (23 of 27) in ITLE patients. Left hemisphere language dominance was present in 96.8% (31 of 32) of patients in the rTLE group, and right dominance was seen in 3.2% (1 of 32) of patients in the rTLE group. In the ITLE group, left hemisphere language dominance was present in 63% (17 of 27) of patients, bilateral dominance was present in 7.4% (2 of 27) of patients, and right dominance was present in 29.6% (8 of 27) of the patients. There was a significant leftward asymmetry of the planum temporale noted in rTLE patients (Fig. 3).
The determination of language dominance is important in epilepsy surgery to prevent postoperative language deficits. The intracarotid amobarbital procedure or the Wada test has been the gold standard for pre-surgical lateralization of language dominance\textsuperscript{36}. However, the Wada test is an invasive test that involves an arteriogram. Previous studies have reported the risk of carotid artery dissection at 0.7%\textsuperscript{25}. Further, the Wada test is not standardized across clinical centers\textsuperscript{31}, has difficulties in application and interpretation\textsuperscript{3}, and exhibits the waning drug effect\textsuperscript{27}. Therefore, noninvasive procedures are preferred. Several studies have compared the IAP with fMRI in patients with epilepsy. In 2003, Adcock et al.\textsuperscript{2} studied 12 healthy right-handed controls and 19 right-handed preoperative patients with TLE, and found concordance between the Wada test and the fMRI results. This suggested that the fMRI method may be implemented in a similar way to the Wada test. Benke et al.\textsuperscript{10} compared the fMRI with the Wada test in 68 patients with chronic intractable right and left temporal lobe epilepsy and reported that the overall congruence between fMRI and the Wada test was 89.3% in rTLE patients and 72.5% in iTLE patients. In 1998, Choi et al.\textsuperscript{7} reported MRI-based sulcal, gyral patterns and volumetric asymmetry of inferior frontal gyrus correlate with speech lateralization of Wada test. Our volumetric analysis of the planum temporale revealed an overall congruence with the Wada test of 97.75% in rTLE patients and 81.5% in iTLE patients (Table 3). Left speech was correctly allocated in 96.8% of rTLE and in 88.2% of iTLE patients. Our results suggest that volumetry of the planum temporale as well as fMRI could serve as alternatives for the Wada test in determination of language dominance.

The PT lies between the HG and the posterior border of sylvian fissure. Flechsig\textsuperscript{9} first recognized the gross left-right asymmetry of this postero-lateral part of the supratemporal plane. Correlation between PT asymmetry and functional cerebral lateralization is a subject of extensive discussion\textsuperscript{15,16}. Quantitative anatomic data have reported an asymmetry excess of the left PT in 63%\textsuperscript{14} to 82%\textsuperscript{37} of brains studied post mortem. The PT is covered by the auditory cortex, and therefore planum temporale asymmetry was thought to represent a structural substrate for speech lateralization. Geschwind and Levitsky\textsuperscript{16} found highly significant differences between the left and right hemispheres in the planum temporale. Steinmetz et al.\textsuperscript{14} first reported MR-derived PT planimetric measurements in 10 human cadaver brains and found that the left PT was larger in 8 brains. Foundas et al.\textsuperscript{10} measured the PT on MRI scans of right- and left-handed patients with selective hemispheric anesthesia or Wada testing performed for language lateralization. All subjects with language lateralized to the left hemisphere (right-handed patients) had a leftward asymmetry of the PT and one subject with language lateralized to the right hemisphere (left-handed patient) had a strong rightward asymmetry of the PT. This suggested that PT asymmetries determined by MR were associated with language dominance and could predict language laterality. To our knowledge, our study is the first to compare PT asymmetries determined by MR volumetry with the Wada test in temporal lobe epilepsy patients. A potential drawback of MR volumetry is the time involved in measurement. It takes approximately 3 to 4 hours for an experienced rater to measure both the right and left PT. However, calculation of the planum temporale volume using software for volumetry is easy and noninvasive.

Previous studies have suggested that fMRI measures may be useful in the presurgical evaluation of patients with TLE\textsuperscript{35}, demonstrated that bilateral language-related fMRI activations were detected more frequently in iTLE patients than in healthy controls or in patients with rTLE\textsuperscript{20,21,33}. Our results were concordant with those seen in previous studies. Left language dominance was seen in 96.8% of rTLE patients and 63% of iTLE patients (Table 3). Approximately 37% of iTLE patients showed bilateral or right hemispheric language dominance. This finding concurs with previous studies demonstrating a close relationship between atypical language dominance and iTLE patients\textsuperscript{36,30,38} and suggests that pathological processes in epilepsy exert a common set of influences on the development of language lateralization. There may be considerable plasticity of language representation in the brains of patients with intractable TLE. Sakai\textsuperscript{32} suggested that cortical plasticity for second language acquisition was guided toward first language specialization of the left inferior frontal gyrus, at least at the age of 13. Springer et al.\textsuperscript{33} suggested that atypical language dominance in the
epilepsy group was associated with an earlier age of brain injury and with weaker right hand dominance. In our study, the seizure duration of the atypical language dominance group was significantly longer than the left hemispheric language dominance group in ITLE patients (Table 4). Thus, we suggested that atypical language dominance in the epilepsy group was associated with the seizure duration.

CONCLUSION

The present study confirms the usefulness of language lateralization using volumetric analysis in presurgical evaluation in temporal lobe epilepsy patients. We suggest that volumetric analysis of the PT can be an effective alternative to the Wada test in the determination of language dominance. Our data identified a close relationship between atypical language dominance and ITLE patients, and suggested the presence of considerable cerebral plasticity of language representation in the brains of patients with intractable TLE.

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