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Determination of language dominance with synthetic aperture magnetometry: comparison with the Wada test☆

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Cerebral dominance for language function was investigated with synthetic aperture magnetometry (SAM). The results were compared with those of the Wada test. SAM is a spatial filtering technique that enables demonstration of the spatiotemporal distribution of oscillatory changes (synchronization and desynchronization) in magnetoencephalography (MEG) signals elicited by specific brain activation. MEG was conducted during a silent reading task in 20 consecutive preoperative neurosurgical patients who also underwent a Wada test. The spatial distribution of oscillatory changes related to silent reading was shown tomographically with SAM as statistical images. Language dominance was estimated by the laterality index, which scales the lateralization of the beta (13–25 Hz) and low gamma (25–50 Hz) band desynchronizations in the inferior frontal gyrus (IFG) or middle frontal gyrus (MFG). Oscillatory changes were distributed multifocally and bilaterally in the occipital cortex, IFG or MFG, and temporo-parieto-occipital border regions. In 19 patients (95%), language lateralization estimated by the laterality index was congruent with the result of the Wada test. In left-handed patients, SAM analysis clearly differentiated language dominance (left, right, or bilateral), and the findings were confirmed by the Wada test. Lateralization of beta or low gamma band desynchronizations in the IFG or MFG is a good indicator of the side of language dominance. Reliability of MEG imaging with SAM is sufficient to evaluate language dominance preoperatively in neurosurgical patients.

Keywords: Language dominance; Synthetic aperture magnetometry; Wada test

Introduction

Synchronous oscillations in specific frequencies such as the alpha and beta bands are well known as basic brain rhythms. The signal power of these basic brain rhythms changes upon brain activation. Event-related desynchronization (ERD) is an attenuation of, and event-related synchronization (ERS) is an increase of, the oscillation amplitude of a specific frequency related to specific neural activity (Pfurtscheller, 1992; Pfurtscheller and Aranibar, 1977). Recently, several magnetoencephalography (MEG) studies suggested that cerebral oscillatory changes in the gamma band reflect higher cognitive processes such as attention, perception, and language processing (Braeutigam et al., 2001; Eulitz et al., 1996; Pulvermüller et al., 1997). Pulvermüller and colleagues assumed that elements of cognitive processing are distributed over both hemispheres as transcortical cell assemblies that generate specific spatiotemporal activity patterns (Pulvermüller and Mohr, 1996; Pulvermüller et al., 1997). However, in these MEG studies, data were analyzed with relatively low spatial resolution (hemispheric or lobar level). To elucidate neurophysiological mechanisms of these higher cognitive processes, it is important to investigate the spatial localization and temporal distribution of cerebral oscillatory changes with high resolution.

Pioneering studies with functional imaging modalities, i.e., positron emission tomography (PET) (Howard et al., 1992; Petersen et al., 1988), functional magnetic resonance imaging (fMRI) (Binder et al., 1996; McCarthy et al., 1993), and MEG (Martin et al., 1993; Salmelin et al., 1994) provided information about language localization. Several fMRI and PET studies successfully estimated language dominance in agreement with the Wada test (Benson et al., 1999; Binder et al., 1996; Lehéricy et al., 2000), which is the gold standard for determining language dominance. MEG is noninvasive and provides direct information about activity over the whole brain by measuring the magnetic fields generated by minute neuronal intracellular electrical currents. MEG has excellent spatiotemporal resolution compared with that of other imaging modalities such as fMRI and PET. Thus, it is a good tool for elucidating neurophysiological processes within the brain. Several previous MEG studies estimated language dominance by the equivalent current dipole (ECD) method (Papanicolaou et al., 1999; Szymanski et al., 2001). Compared with short-latency magnetic fields such as somatosen-

☆ Synthetic aperture magnetometry and language dominance.

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sory, auditory, and visual evoked fields, linguistic components of magnetic fields evoked by a language task have long latency and include activities from multiple areas. Many of the successful language studies (Helenius et al., 1998; Levelt et al., 1998; Salmelin et al., 1994) used a multidipole model that requires a hypothesis about the number and location of active sources. An epoch-making tool was required to break through the limitations of the ECD method.

Synthetic aperture magnetometry (SAM) is a spatial filtering technique based on the nonlinear constrained minimum-variance beamformer and is capable of detecting current density in an arbitrarily chosen voxel within the whole brain with high resolution (Baillet et al., 2001; Robinson and Rose, 1992; Robinson and Vrba, 1999). Thus, the spatiotemporal distributions of ERD and ERS can be visualized precisely. We introduced this technique to investigate language processing and previously reported the spatial localization and temporal distribution of oscillatory changes during silent reading in healthy subjects (Hirata et al., 2002a; Ihara et al., 2003a). In these studies, ERD in the beta and gamma bands was seen consistently in language-related areas, especially in the left inferior frontal gyrus (IFG) and middle frontal gyrus (MFG), and both serial and parallel processing were suggested to be involved in language processing (Hirata et al., 2002a). Xiang et al. (2001) found, also with SAM, that a language task evoked the gamma band ERD in Broca's and Wernicke's areas in healthy subjects. Another MEG study with a spatial filtering technique (Kober et al., 2001) showed the spatiotemporal distribution of current sources during silent reading and silent naming tasks. It was also suggested that both serial and parallel processing were involved in language processing. But in that study, the results for only a few patients were compared with those of the Wada test. It is important to confirm the results of these spatially filtered MEG studies with a larger population by comparing them with the Wada test or cortical stimulation results. However, such justification studies have not been done. It is also of great significance to estimate language dominance directly based on the cerebral neurophysiological mechanisms of language processing. Thus, we investigated the spatial distribution of cerebral oscillatory changes related to silent reading, quantitatively evaluated language lateralization of oscillatory changes, and compared our results with those of the Wada test.

Materials and methods

Data acquisition

Twenty consecutive neurosurgical patients who underwent the Wada test for preoperative examination participated in this study (Table 1). MEG study for patients in this institute is approved as Advanced Medical Treatment and regulated by the Ministry of Health, Labor and Welfare of Japan. Informed consent was obtained from all participants. During the recording, each participant sat with eyes open in a comfortable chair in a magnetically shielded room. A three-character Japanese hiragana semantic word was presented every 6 s on a liquid crystal monitor 2 m away. Each word was presented for 3 s. One session consisted of 100 different word presentations. Words were selected from an elementary school dictionary so as to be understood quickly and easily by all participants. Participants were instructed to read each word only once and without phonation. The word stimuli subtended a horizontal visual angle of 3° and a vertical angle of 1°. Thus, no eye movements were necessary to scan the presented word.

Table 1
Summary of cases

Case	Age (years)	Sex	Location	Diagnosis	Wada	Handedness	HQ
1	60	M	rt parietal	glioblastoma	R	L	−18
2	18	M	lt parietal	epilepsy	R	L	−92
3	46	F	lt temporal	epilepsy	L > R	R[a]	83
4	31	M	rt parietal	infarction	L	L	−64
5	35	F	lt frontotemporal	cavernoma	L	R	83
6	45	F	lt temporal	astrocytoma	L	R	100
7	19	M	lt temporal	epilepsy	L	R	100
8	37	M	lt insular	astrocytoma	L	R	100
9	41	F	lt temporal	astrocytoma	L	R	100
10	24	M	lt temporal	epilepsy	L	R	100
11	22	F	lt temporal	epilepsy	L	R	100
12	58	M	lt temporal	cavernoma	L	R	100
13	25	F	lt frontal	astrocytoma	L	R	91
14	14	M	lt temporal	epilepsy	L	R	100
15	15	F	frontal	epilepsy	L	R	100
16	29	F	lt temporal	astrocytoma	L	R	100
17	24	F	lt frontal	epilepsy	R	L	−17
18	25	F	frontal	epilepsy	L	R	83
19	19	F	rt temporal	epilepsy	L	R	100
20	41	F	rt temporal	epilepsy	L	R	92

Sex: F = female, M = male; location: site of lesion, lt = left, rt = right.
Wada: right (R) or left (L) language dominance as determined by the Wada test.
Handedness: subjects judged to be (R) right or (L) determined by HQ.
HQ: handedness quotient based on the Edinburgh handedness inventory.
[a] This subject was natively left-handed but acquired right handedness.

Data were recorded with a 64-channel whole-head MEG system equipped with first-order SQUID gradiometers (NeuroSQUID Model 100, CTF Systems Inc., Port Coquitlam, Canada). MEG signals were digitized at a sampling rate of 625 Hz and filtered with a 200-Hz on-line, low pass filter. Notch filters were used at 60 and 120 Hz to eliminate AC line noise. Data of 5000-ms duration with a 2500-ms prestimulus interval were collected for each of the 100 trials. At the beginning and end of each measurement, the participant's head position was registered with localization coils that were placed at the nasion and the bilateral preauricular points. For each participant, magnetic resonance (MR) images were obtained with a 1.0 T (Magnetom Impact, Siemens, Erlangen, Germany) or 1.5 T (Signa GE Medical Systems, Milwaukee, WI) MR imaging systems in a T1-weighted sequence of 130 sagittal slices (1.5-mm thickness) with fiducial skin markers at the nasion and bilateral preauricular points. By registration of the head position at these three points, the MEG data could be superimposed on the individual MR images with an anatomical accuracy of a few millimeters.

SAM analysis

The spatial distributions of ERDs and ERSs were estimated by SAM statistical analysis (Hirata et al., 2002a,b; Ihara et al., 2003a,b; Robinson and Vrba, 1999; Taniguchi et al., 2000). The detailed algorithm for SAM is described elsewhere (Baillet et al., 2001; Robinson and Vrba, 1999; Taniguchi et al., 2000). SAM estimates the source power with high spatial resolution by forming a linear combination of sensors that can suppress the signals from environmental noise without attenuating power from the target voxel (Robinson and Vrba, 1999; Taniguchi et al., 2000). Because the SAM method does not require averaging, high-frequency components are not attenuated, even in the middle or long latency periods.

The MEG data were divided into five frequency bands as follows: theta (3–8 Hz), alpha (8–13 Hz), beta (13–25 Hz), low gamma (25–50 Hz), and high gamma (50–100 Hz) bands. The region of interest (ROI) was set to include the whole cerebral cortex with a 5-mm voxel resolution. A spherical area 1.5 cm in diameter, located at the center of the spherical head model, was excluded from the ROI because the noise-to-signal ratio increases in areas remote from the SQUID sensors. The current density of each voxel was estimated by SAM. Changes in the current density for each voxel between the active state (0 to 1000 ms after stimulus) and the control state (1000 to 0 ms before stimulus) were analyzed statistically with Student t values. The distribution of t values was displayed on the individual MR images for each frequency band (SAM statistical image). Negative and positive t values indicate ERD and ERS, respectively. Voxels with a P value of less than 0.001 were considered statistically significant.

Laterality index for estimating language dominance

Our preliminary study of healthy right-handed participants detected oscillatory changes mainly in the triangular or opercular part of the left IFG, the dorsal part of the left MFG, the posterior part of the superior or middle temporal gyrus, the temporo-parieto-occipital border areas, and the medial occipital area (Hirata et al., 2002a). To confirm where oscillatory change is most lateralized in these areas, the following six regions of interest (ROIs) with the highest t values were investigated statistically (Fig. 1): the triangular or opercular part of the IFG, the dorsal part of the MFG, the posterior part of the middle or superior temporal gyrus, the angular gyrus and the lateral occipital area, the temporo-occipital base, and the medial occipital area.

The laterality index (LI) was defined to estimate the degree of laterality of oscillatory changes quantitatively as follows:

$$\mathrm{LI} = 2(T_\mathrm{R} - T_\mathrm{L})/(|T_\mathrm{R}| + |T_\mathrm{L}|)$$

The t values of the most prominent ERD in the specified band within the related region and its contralateral homologous region were selected, and, of these two selected values, the t value on the right side was defined as T_R and the t value on the left side as T_L. When both left and right ROIs had no significant voxels, the LI was not calculated. If ROIs on either left or right sides had significant voxels and the other side had no significant voxels, the LI was calculated using the maximum t value of the significant side and that of the insignificant side. A positive LI means that oscillatory change is lateralized to the left, and a negative LI indicates right lateralization. When the LI is near 0, oscillatory change is present bilaterally. Based on the data from our preliminarily study, language lateralization was empirically defined to be left when the LI was more than 0.1, right when the LI was less than −0.1, and bilateral when the LI was between −0.1 and 0.1. Finally, the results were compared with those of the Wada test and handedness.

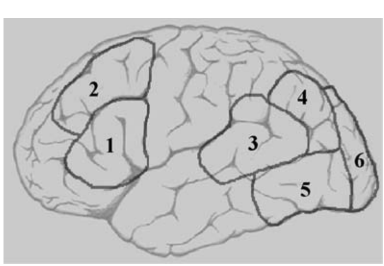

Fig. 1. The six areas analyzed in this study: (1) the triangular or opercular part of the inferior frontal gyrus, (2) the dorsal part of the middle frontal gyrus, (3) the posterior part of the middle or superior temporal gyrus, (4) the angular gyrus and the lateral occipital area, (5) the temporo-occipital base, and (6) the medial occipital area.

Our preliminary studies also showed that, during silent reading, the ERDs in the beta and low gamma bands were localized consistently in the left IFG or MFG (Hirata et al., 2002a). Based on this result, the criteria for estimating language dominance using the LI was defined empirically according to the following priorities. ERD in the IFG was of higher priority than ERD in the MFG. For both ERD in the IFG and ERD in the MFG, the beta band was of higher priority than the alpha band and of lower priority than the low gamma band. For example, if low gamma ERD in the IFG was not statistically significant but beta ERD in the IFG was significant, the LI was calculated with the t value of ERD in the IFG in the beta band. Also, if ERD in the IFG was not statistically significant, the t value of ERD in the MFG was used to calculate the LI. When there was no ERD fitting these criteria, dominance could not be judged.

Handedness and the Wada test

Handedness was determined by the handedness quotient based on the Edinburgh handedness inventory (Oldfield, 1971). The handedness quotient ranged from −100 (extremely left-handed) to 100 (extremely right-handed). Language dominance was determined by the Wada test (Wada and Rasmussen, 1960) in all patients. After a catheter was placed into one extracranial internal carotid artery, amobarbital was injected slowly until complete paralysis of the contralateral hand was observed obviously. Approximately 100 mg of amobarbital was needed for the hemispheric anesthesia. The patients were subjected to language tasks (object naming, picture naming, repetition, word reading). More than 30 min after the injection of amobarbital and after confirmation that paralysis was no longer present, the opposite side was tested. Test results were judged by neuropsychologists who were blinded to the MEG results. The investigators who analyzed the MEG data were also blinded to results of the Wada test.

Results

Handedness and the Wada test

Sixteen patients were judged to be right-handed. Fifteen of these patients had left language dominance as determined by the Wada test. In 1 case (case 4), handedness was judged to be right, but the patient turned out to be left-handed natively and had switched to using the right hand. This patient had bilateral language representation (left > right) according to the Wada test.

The remaining 4 patients were judged to be left-handed. Language dominance was determined to be right for 3 and left for 1 of these 4 patients (Table 1).

Localization of oscillatory changes

ERDs and ERSs (Fig. 2; Table 2) were distributed mainly in the medial occipital area (18 of 20 patients), the opercular and triangular region of the IFG (18/20), the dorsolateral region of the MFG (11/20), the temporo-occipital base (13/20), the angular gyrus or the lateral occipital area (10/20), and the posterior region of the middle or superior temporal gyrus (10/20). The areas and frequency bands of detected oscillatory changes were consistent with the results of our previous study in healthy subjects (Hirata et al., 2002a). ERD in the beta or low gamma bands in the left IFG (14/20) and ERS in the high gamma band in the bilateral occipital cortices (18/20) were detected most consistently.

In the control state (1000 to 0 ms before stimulus), the power spectrum of MEG signals had a clear monophasic peak in the low gamma band in the left frontal MEG sensors (Fig. 3). This low gamma peak attenuated markedly after the word presentation (0 to 1000 ms after stimulus), which corresponds to ERD in the IFG lateralized to the left.

Lateralization of oscillatory changes in significantly detected areas

For the 16 patients found to be left-dominant by the Wada test, left–right comparison of the largest t values of regional oscillatory changes was performed for each analyzed area. This left–right comparison revealed statistically significant left lateralization in the IFG (P = 0.0004) (Fig. 4). Left lateralization in the MFG was not significant (P = 0.115). No apparent laterality was present in the remaining four areas (the posterior part of the middle or superior temporal gyrus, the angular gyrus, the temporo-occipital base, and the medial occipital cortices).

Table 2
Location, incidences, and peak band of detected oscillatory changes

Location	ERD					ERS					Total incidence	%
Peak band	θ	α	β	Low γ	High γ	θ	α	β	Low γ	High γ		
Inferior frontal	0	4	3	11	0	0	0	0	0	0	18/20	90.0%
Middle frontal	0	0	3	4	2	0	0	1	1	0	11/20	55.0%
Temporo-occipital base	0	7	2	0	1	0	0	0	1	2	13/20	65.0%
Angular/lateral occipital	2	1	2	1	0	1	1	2	0	0	10/20	50.0%
Posterior superior/middle temporal	0	2	2	5	0	0	1	2	0	0	12/20	60.0%
Medial occipital	0	(1)[a]	(9)[a]	(2)[a]	0	0	0	0	0	18	18/20	90.0%

ERD: event-related desynchronization; ERS: event-related synchronization.
[a] In the medial occipital area, both high gamma ERS and alpha to low gamma ERD were found simultaneously; alpha to low gamma ERD were found less consistently, and their incidences are shown in parentheses.

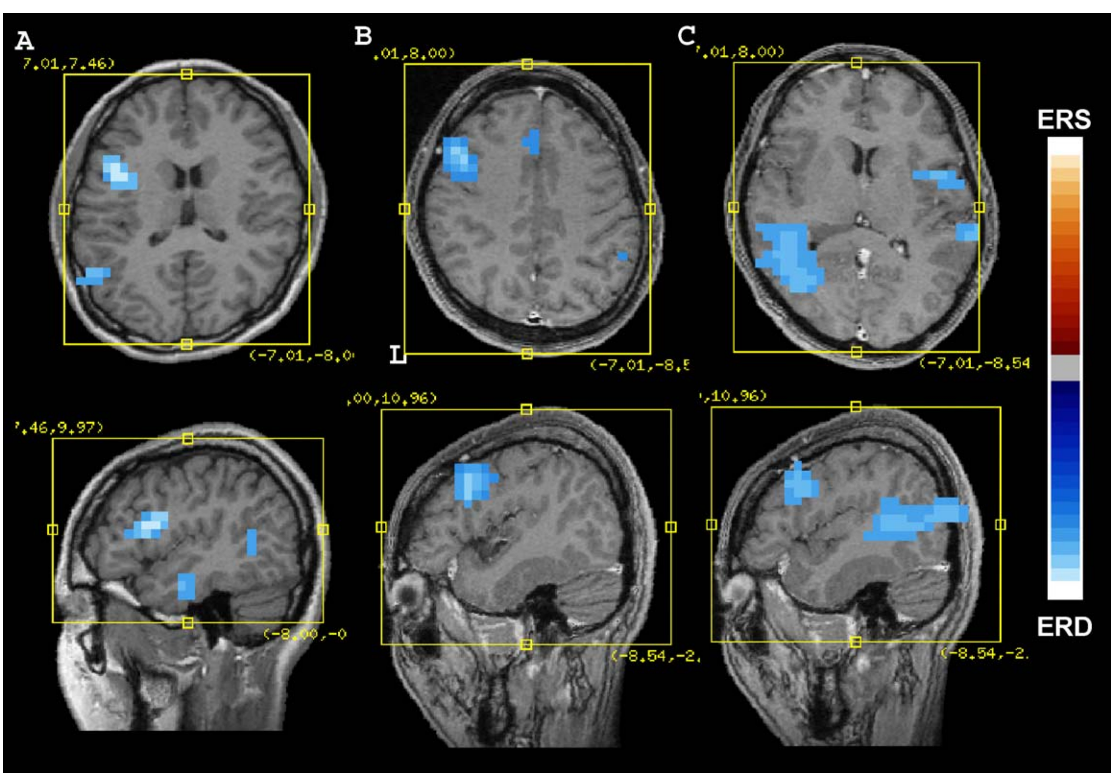

Fig. 2. Representative SAM statistical images displayed on the individual MR images showing the desynchronization related to silent reading in the low gamma band (25–50 Hz) in the left inferior frontal gyrus (A), the left middle frontal gyrus (B), and the bilateral middle and superior temporal gyrus (C). Blue areas surrounded by a black line indicate significant ERD. SAM: synthetic aperture magnetometry. ERD: event-related desynchronization.

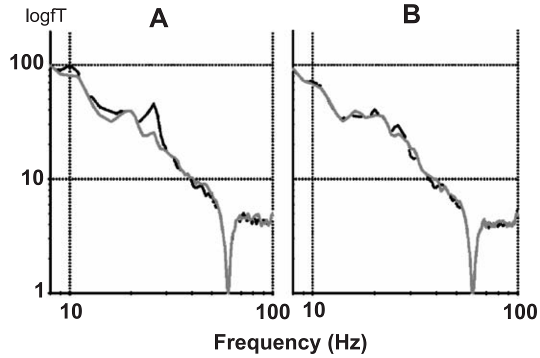

Fig. 3. Power spectra in the left (A) and right (B) frontal magnetoencephalography (MEG) sensors. The low gamma desynchronization in the inferior frontal gyrus (IFG) is strongly lateralized to the left side. In the control state (1000 to 0 ms before the presentation of a word), power spectra in the MEG sensors (black line) have a clear monophasic peak in the low gamma band in the left frontal MEG sensor (A). The low gamma peak is attenuated prominently in the active state (0 to 1000 ms after the presentation of a word, gray line), which corresponds to desynchronization in the left IFG related to silent reading.

ERD in the IFG and MFG

In all cases, ERD was found in the IFG or MFG. ERD in the beta and low gamma bands in the IFG or MFG was detected in 16 patients (80%; 12 left-dominant patients, 4 right-dominant patients). The remaining 4 patients, determined to be left-dominant by the Wada test, also had left-dominant ERD in the IFG; but the most prominent ERD was observed in the alpha band. In 19 of these 20 patients, lateralization of ERD was consistent with the language dominance determined by the Wada test.

Criteria for estimating language dominance

Language dominance estimated by our criteria based on the LI in the frontal area was consistent with the results of the Wada test in 19 of 20 patients (95%). Moderate correlation (coefficient = 0.54) was found between the LI and the handedness quotient (Fig. 5). In 1 patient (case 16), the LI was 0.08, and language dominance was judged to be bilateral by SAM and left dominant by the Wada test.

Language dominance in left-handed patients

In left-handed patients, including one converted patient, right dominance (case 1, LI = −0.33; case 2, LI = −0.11; case 17, LI = −2.00), left dominance (case 4, LI = 0.41), and bilateral dominance (case 3, LI = 0.08) were discriminated clearly by ERDs in the low gamma band in the IFG. These results were consistent with the results of the Wada test (Fig. 6).

Discussion

The present study is the first reported clinical investigation of the laterality of oscillatory changes related to silent reading. We showed language dominance estimated by SAM to be consistent with that determined by the Wada test. Kober et al. (2001) showed language dominance determined with spatially filtered MEG to be consistent with handedness, but their results were verified by the Wada test in only two cases, and they did not investigate the oscillatory changes.

Oscillatory changes induced by silent word reading

Oscillatory changes related to language processing are still hardly known, although we preliminarily investigated them in

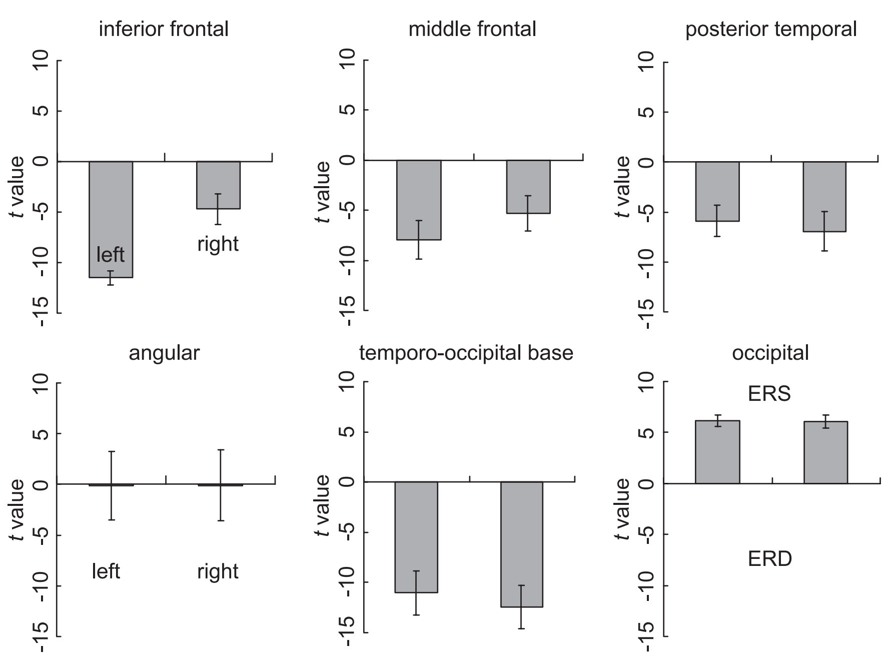

Fig. 4. Graphs showing lateralization of oscillatory changes in each analyzed area in 15 patients found to be left-dominant by the Wada test. Longitudinal axis indicates the largest t value of oscillatory changes within each area. A negative t value indicates event-related desynchronization (ERD), and a positive t value indicates event-related synchronization (ERS). The error bars represent standard errors.

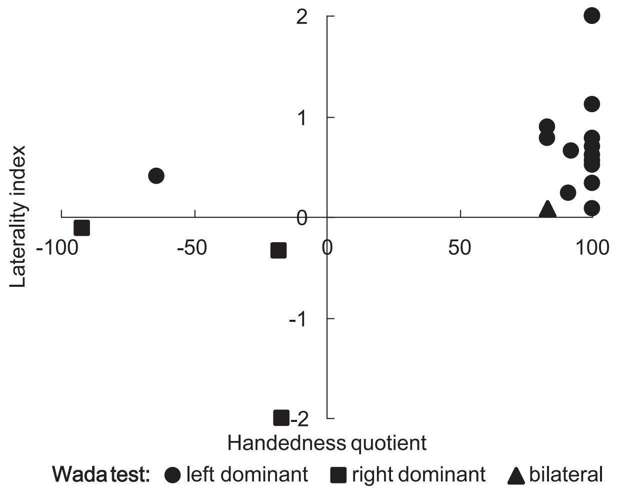

Fig. 5. Scatterplot showing the laterality index (LI) and the Edinburgh handedness quotient. Moderate correlation was found between the LI and the handedness quotient (coefficient = 0.54). Solid circles indicate the left-dominant patients found by the Wada test, squares indicate the right-dominant patients, and the triangle indicates the patient with bilateral representation.

healthy subjects using a silent reading task (Hirata et al., 2002a). Thus, in this study, we adopted the same reading task to make clear the bare oscillatory changes induced by silent word reading, although there might be more ideal tasks, taking only language lateralization into consideration. As a result, we showed that the silent reading task induced multifocal oscillatory changes in diverse language-related areas and their contralateral homologous areas, including the IFG, the MFG, the posterior part of the middle and superior temporal gyrus, the angular gyrus, and the temporo-occipital base. The areas detected are consistent with the results of many previous neuroimaging and lesion studies of reading words. Previous neuroimaging studies and reviews related these areas to various language functions. The left IFG is involved in articulatorily based phonological analysis (Fiez and Petersen, 1998) and inner speech (Fujimaki et al., 1999). The left posterior temporal regions contribute to acoustically based phonological and semantic analyses (Fiez and Petersen, 1998), and phonological transformation (Fujimaki et al., 1999). The left temporo-occipital base is involved in visual analysis specific to word-like stimuli (Fiez and Petersen, 1998), plays a role in an interface process that detects character strings to convey them from visual to language domain (Tarkiainen et al., 1999), and is the putative visual word form area (McCandliss et al., 2003), although existence of such an area is controversial (Fujimaki et al., 1999; Price and Devlin, 2003). The MFG is related to semantic processing (Petersen et al., 1988) and word generation (Frith et al., 1991), and was recently recognized as a central executive in working memory (Mesulam, 1998).

Laterality estimation based on the oscillatory change

We found that, in patients determined to be left-dominant by the Wada test, ERDs in the beta and low gamma bands were lateralized significantly to the left IFG, although left lateralization of ERD in the MFG was not significant ($P = 0.115$) and a larger study population would be needed to validate significant lateralization. These results were generally compatible with those of our preliminary studies in right-handed healthy subjects in whom we found the beta-or-low gamma ERDs in the left IFG and MFG consistently (Hirata et al., 2002a; Ihara et al., 2003a). Furthermore, several MEG investigators proposed that oscillatory changes in the gamma band reflect higher cognitive processes such as attention, perception, and language processing (Braeutigam et al., 2001; Eulitz et al., 1996; Pulvermüller et al., 1997). Another SAM study showed that silent viewing of words induced gamma band ERD in the Broca and Wernicke areas (Xiang et al., 2001). Our preliminary results and recent findings of others led to the criteria for estimating language dominance with the LI according to the priorities described in Materials and methods. Thus, we estimated language dominance by laterality of the ERD mainly in the beta or low gamma bands in the IFG or MFG. In 19 out of 20 patients (95%), language dominance estimated by SAM was in agreement with the Wada test. Our approach is reliable as a noninvasive method for evaluating language dominance.

Four patients determined to be left-dominant by the Wada test also showed left-dominant ERD in the IFG, but the most prominent ERD was observed in the alpha band. Three of these patients had

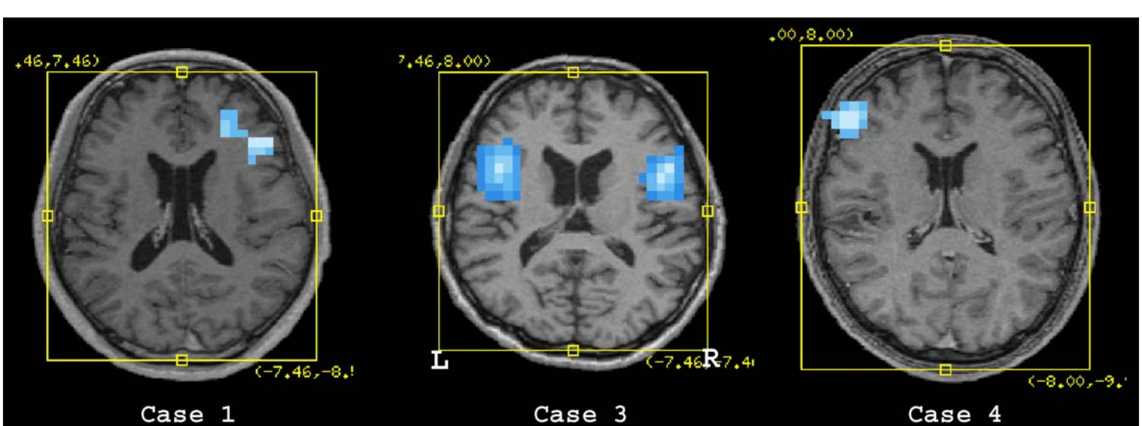

Fig. 6. SAM statistical images in left-handed patients clearly show language dominance: right dominant (case 1, left, LI = –0.33), bilateral (case 4, right, LI = 0.08) and left dominant (case 3, center, LI = 0.41). The results were congruent with the Wada test. SAM: synthetic aperture magnetometry, LI: laterality index.

frontal or perifrontal lesions. These lesions might have slowed the peak band of brain oscillations at rest, resulting in the alpha ERD in the IFG. The LI in Case 16 was 0.08, and dominance was judged to be bilateral, whereas the Wada test indicated left dominance. Functional imaging generally tends to show more or less bilateral activation, and estimated language lateralization seems to be a continuous rather than dichotomous variable (Binder et al., 1996). However, according to the aphasic symptoms after surgical treatment as well as results of the Wada test, we neurosurgeons believe that language lateralization is generally more distinct. Appropriateness of the LI threshold used to judge whether language dominance is unilateral or bilateral, and which we set empirically at 0.1 for left dominance and −0.1 for right dominance, needs to be studied further.

Until now, MEG studies have used signal intensity for evaluating the magnitude of activation, for example peak amplitude of averaged signal and dipole moment, etc. Thus, the present study used maximum t value as an index of magnitude of oscillatory change and excellent results were obtained. Volume of significant voxels is also one of alternatives as an index of language lateralization, as it is often used in fMRI and PET studies. A fMRI study demonstrated that both the magnitude of the signal change and the volume of the active region are consistent in language lateralization (Adcock et al., 2003). In the present study, we used SAM that showed the volumetric distribution of oscillatory change. In this meaning, it would be important to compare between volume estimation and intensity estimation also in our method.

In addition, the maximum t value of a single voxel might have some variance. Attention should be paid whether each maximum t value is physiologically valid or whether the maximum t value is due to mere noise variance.

Language dominance of left-handers

The most impressive finding in the present study is that SAM analysis differentiated clearly the language dominance of left-handed patients. An fMRI study reported that language dominance of left handers was left in 76%, bilateral in 14%, and right in 10% (Pujol et al., 1999). Another recent fMRI study yielded similar results (Szaflarski et al., 2002). Loring et al. (1990) reported that Wada test results for left-handed patients showed exclusive left dominance in 77%, bilateral dominance in 21% (left > right in 13%, left < right in 4%), and exclusive right dominance in 2%. Thus, the incidence of atypical language lateralization in left-handers is higher than the 4–6% in right-handers (Pujol et al., 1999; Springer et al., 1999). However, three-fourths of left-handers are left language dominant. This means language dominance in left-handers has considerable interindividual variation and handedness does not serve as an indicator of language lateralization. The rather low correlation between the LI and handedness in this study is consistent with this conclusion. Comparison with the Wada test is indispensable to validate noninvasive estimation of language lateralization. In the present study, 4 of 20 patients were left-handed, and 1 patient (case 4) converted to right-handedness but was natively left-handed. In these left-handed patients, SAM analysis found that 3 were right dominant, 1 was bilateral, and 1 was left dominant. Although our study population was small and the incidence of atypical language lateralization was different from that found in previous studies, the results of SAM analysis were congruent with those of the Wada test for the left-handers.

In conclusion, we successfully showed with SAM the multifocal regional oscillatory changes evoked by a language task and localized these oscillatory changes with a statistical estimate. Laterality of beta or low gamma ERD in the IFG or MFG is a good indicator of the side of language dominance. Language dominance estimated by the LI with these ERDs was congruent with the results of the Wada test. SAM analysis could be useful as a noninvasive alternative to the Wada test.

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