Noninvasive Determination of Speech Dominance by Single Magnetic Stimulation of the Bilateral Hand Motor Cortex

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Abstract

Magnetic stimulation of the hand area of the motor cortex in both hemispheres was performed at rest and during reading aloud to observe modulated facilitation of hand muscle motor potentials in 6 right-handed patients, with supratentorial lesions but no motor impairment or aphasia, who had undergone the Wada test to determine speech dominance, showing that 5 were left hemisphere dominant and one was bilateral hemisphere dominant. Motor potentials were facilitated during reading aloud in only the right hand in 3 patients, all left hemisphere dominant, greater in the right hand in one, left hemisphere dominant, and greater in the left hand in one patient, bilateral hemisphere dominant. Based on these results we defined a laterality index which was consistent with the Wada test results. Magnetic stimulation may prove useful for determining cerebral dominance, as our method correlates well with the Wada test, and is safe, convenient, and inexpensive.

Key words: magnetic stimulation, speech, amytal test, cerebral dominance, handedness

Introduction

Intracarotid injection of sodium amytal for lateralization of cerebral speech dominance (Wada test) is a standard diagnostic procedure for the preoperative evaluation of patients with epilepsy and supratentorial lesions such as arteriovenous malformation and tumors.25,27) The Wada test has been considered essential for determination of speech dominance, but the possibilities of amobarbital cross-flow to the contralateral hemisphere10) and adverse effects on blood vessels20) have raised concerns. The Wada test remains invasive despite the development of a selective injection method9) and the use of nonirritating pharmacological agents to mitigate these complications.20)

Noninvasive replacements for or additions to the Wada test have been proposed, such as positron emission tomography (PET),19) functional magnetic resonance (fMR) imaging,2) functional Doppler sonography,12) and the recording of event-related brain potentials.8) PET studies yield information on hemisphere lateralization and pin-point the area of interest,4,19) but are also invasive, expose the patient to radiation, and are expensive. fMR imaging is a new non-invasive method which detects activated areas of the brain, but requires that individuals not move during the test, and is also expensive.2) Event-related potential measurements can detect hemispheric asymmetries, but require that the subject concentrate on the task.8) Functional transcranial Doppler sonography is convenient and requires minimal cooperation from the subject,12) but depends on acoustic penetration of the temporal bone, whereas 4 of 19 patients did not present with the necessary “window.”12) We previously showed that single magnetic stimuli delivered at intensities safe for use with normal subjects could be used to detect lateralized effects on brain function.23) Electromyographic (EMG) responses in the relaxed hand muscles evoked by transcranial stimulation of the motor cortex of the dominant hemisphere were enhanced if stimuli were delivered while subjects read aloud. This effect clearly depended on lateral dominance in normal subjects.

The present study compared our technique with the Wada test in patients with supratentorial lesions to try to establish a useful noninvasive test of cerebral dominance.
**Materials and Methods**

This study included 6 patients admitted to Kagoshima University Hospital between April 1, 2006 and May 31, 2008, all men aged from 19 to 67 years (mean ± standard error of the mean 39.0 ± 7.24 years). All patients had supratentorial lesions; 3 with glioma, 2 with arteriovenous malformations, and 1 with meningioma. Four of the 6 lesions were in the left and 2 in the right hemisphere; 2 each in the frontal, temporal, and occipital regions. The patients’ motor functions and speech were normal, and intelligence was high enough to understand all procedures. Prior informed consent was obtained from all patients; the ethics committee of our university approved the procedures.

Bilateral surface EMGs were recorded from the first dorsal interosseous (FDI) muscles using silver/silver chloride surface electrodes (diameter 0.9 cm) with the patient seated in a comfortable chair. The active electrode was placed over the motor point and the reference electrode over the interphalangeal joint. Responses were recorded with an MEB4204 apparatus (Nihon Kohden Corp., Tokyo) using two channels with high and low gains, and filtered with a time constant of 3 msec through a high-pass filter set at 3000 Hz.

Transcranial magnetic stimulation (TMS) used 2 high-power magnetic stimulators (Magstim Model 200; Magstim Company Ltd., Whitland, Dyfed, UK), each connected to a figure-eight coil with external and internal wing diameters of 74 mm and 34 mm, respectively, and peak magnetic field of 3.0 T (Fig. 1). The stimulating coils were positioned with a mechanical holder on a stand over each hemisphere above the optimal site for eliciting responses in the target muscles (bilateral FDI) and oriented, so that the current in the brain flowed in the lateroposterior to medioanterior direction through these sites. The stimulation threshold for eliciting responses in the FDI muscles was determined with the subjects relaxed; the threshold tended to vary by less than 5% from the stimulator output. Stimuli of about 5–10% above the relaxed threshold were applied to produce EMG responses with a peak-to-peak amplitude of about 500 mV.

Amobarbital sodium, 100 mg in 5 ml saline, was injected at 1 ml/sec through a transfemoral catheter into the internal carotid artery. All patients received left and right carotid injections at an interval of not less than 30 minutes. Stimuli were applied when contralateral hemiparesis or counting errors occurred. Hemispheric language dominance was assessed by errors in tasks such as naming 5 items, reporting name, age, and date of birth, and reproducing 3 words memorized before injection.

Handedness was determined using the Edinburgh Inventory\(^\text{17}\) of 12 items. Scores were calculated with the formula:

\[
H = 100 \cdot \frac{\Sigma X(i,R) - \Sigma X(i,L)}{\Sigma X(i,R) + \Sigma X(i,L)}, \quad -100 \leq H \leq +100
\]

where \(X(i,R)\) and \(X(i,L)\) are the number of plus signs for the \(i\)th item in the right and left columns, respectively.

Each set of experiments consisted of stimuli to the left and right hemispheres which were randomly intermixed and applied at 5-second intervals. Each patient underwent 2 blocks of trials. In each block, the patient was instructed to remain seated and relaxed while reading aloud in Japanese. The reading material was an easy Japanese story written in hiragana and kanji characters, the former provide phonetic and the latter semantic information. In the first block, the first 20 stimuli (10 to each hemisphere) were delivered with the patient at complete rest. Another 20 were applied while the patient read the story. In the second block, the order was opposite. The peak-to-peak size was measured for each single response in all trials. The effect of the task was assessed by comparing the size of the responses evoked during task performance. Mann-Whitney U analysis used a commercially-available computer.
Table 1 Clinical characteristics and test findings

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age, yrs/</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Speech dominance*</th>
<th>Handedness (laterality quotient**)</th>
<th>Mean peak-to-peak amplitude (read/rest), μV</th>
<th>Laterality index***</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>52/M</td>
<td>lt temporal lobe AVM</td>
<td>lt</td>
<td>rt (100)</td>
<td>411/328</td>
<td>78/336</td>
<td>68.7</td>
</tr>
<tr>
<td>2</td>
<td>39/M</td>
<td>lt frontal lobe glioma</td>
<td>lt</td>
<td>rt (83.3)</td>
<td>895/476</td>
<td>331/500</td>
<td>47.9</td>
</tr>
<tr>
<td>3</td>
<td>19/M</td>
<td>rt occipital lobe ependymoma</td>
<td>lt</td>
<td>rt (75)</td>
<td>1339/440</td>
<td>440/366</td>
<td>43.4</td>
</tr>
<tr>
<td>4</td>
<td>67/M</td>
<td>lt occipital lobe meningioma</td>
<td>lt</td>
<td>rt (100)</td>
<td>3034/553</td>
<td>486/560</td>
<td>72.7</td>
</tr>
<tr>
<td>5</td>
<td>28/M</td>
<td>rt frontal lobe glioma</td>
<td>bil</td>
<td>rt (100)</td>
<td>387/262</td>
<td>596/157</td>
<td>44.0</td>
</tr>
<tr>
<td>6</td>
<td>29/M</td>
<td>lt temporal lobe AVM</td>
<td>lt</td>
<td>rt (100)</td>
<td>3165/1111</td>
<td>1342/600</td>
<td>12.0</td>
</tr>
</tbody>
</table>

*According to Wada test. **Edinburgh Inventory score.17) ***Calculated from the ratios of the mean read/rest amplitudes in the right and left hands (see text). AVM: arteriovenous malformation, M: male.

Results

Table 1 describes the patient characteristics. All patients were right-handed, with Edinburgh Inventory handedness scores ranging from +75 to +100 (mean 93.1 ± 4.52). Based on the Wada test results, 5 of the 6 patients were left hemisphere dominant. The other patient had a +100 handedness score and was bilateral dominant. Peak-to-peak amplitudes of the EMG responses for the FDI muscles in the control trials were 528.3 ± 124.0 μV on the right and 419.8 ± 67.7 μV on the left. Our principal findings in our 6 right-handed patients are illustrated by the raw data presented in Fig. 2. EMG responses evoked in the right hand were larger when reading aloud than at rest; whereas EMG responses in the left hand were of the same amplitude under both conditions.

Figure 3 shows the facilitation of the motor potential from the FDI muscles produced by magnetic stimulation. The EMG amplitude from the FDI muscles was increased by reading aloud only in the right hand in 3 of the 6 patients, and increased in both hands in 2 patients. No significant facilitation was observed while reading aloud in the right hand, whereas significant inhibition occurred in the left hand in Case 1. Greater facilitation was observed in the right hand and greater facilitation in the left hand in one each of the 2 patients with bilateral facilitation. Based on the Wada test results, the patient with greater left hand facilitation was bilateral hemisphere dominant.

The laterality index ranged from 12.1 to 72.7 (mean 48.94 ± 10.8) in the 5 patients who were left hemisphere dominant according to the Wada test.

![Figure 2](image-url) Representative Case 4. Serial peak-to-peak amplitude of electromyographic response from the right (upper) and left (lower) first dorsal interosseous muscles during control trials (dotted lines) and during reading aloud (solid lines). Reading aloud increased the magnitude of the responses in the right but not the left hand.
Fig. 3 Bar graphs showing the peak-to-peak amplitudes of the left and right first dorsal interosseous (FDI) muscles (column = mean, error bar = standard error of the mean). White and gray columns indicate the amplitudes at rest and when reading aloud, respectively. Significant facilitation is present only in the right FDI muscle in Cases 2, 3, and 4. Significant facilitation is bilateral in Cases 5 and 6. Note the greater facilitation in the left FDI in Case 5 with bilateral speech dominance according to the Wada test. *p < 0.05, **p < 0.01. ns: not significant.

results, and was −44.0 in the patient with bilateral hemisphere dominance. Therefore, the findings of the magnetic stimulation test and Wada test were consistent.

Discussion

TMS was first applied in speech studies in 1991.18) Rapid-rate TMS was used to identify language areas, but led to transient loss of speech function. Other investigations showed that speech localization with rapid-rate TMS was highly correlated with the findings of the Wada test.11) However, rapid-rate TMS was not as sensitive for determining hemispheric language dominance as had been reported and could elicit undesirable side effects,15) and speech arrest with rapid-rate TMS did not replicate the results of the Wada test.7) In a 1996 workshop on safety, rapid-rate TMS guidelines were developed for its use.26) In contrast, single TMS is considered simple and safe.6) Speech processing investigations revealed a significant improvement in performance in the oral word association test.31) Verbal tasks were accelerated with 0.5-Hz stimulus because TMS activated attentional networks in the frontal lobes.21) Focal effects were identified in the digit span test but only for left hemisphere stimulation in patients with seizures of left temporal origin,5) and focal magnetic stimulation delivered over Wernicke’s area facilitated lexical processes because of general preactivation of language-related neuronal networks.24) These investigations focused on facilitation of language-related processes by TMS. Our method measures the facilitation of motor potentials that occur during speech, so only requires that the study subject read aloud from a simple text. On the other hand, our method can be used only in subjects with intact speech and motor function.

We previously showed that the mechanism(s) underlying the facilitation of motor potentials during speech are located in the cortex,23) as confirmed by later studies.13,14,22) Recent studies demonstrated that the specific involvement of hand motor circuits in counting,1) and observation of speech-related lip movements or listening to speech increases the excitability of the corresponding motor cortex.10) These studies suggest that speech and the motor cortex have close functional connections. At present, the specific mechanism(s) involved remain unclear, but time course analysis may yield
more information. The TMS of Wernicke’s area was found to decrease by 500 to 1000 msec during a picture-naming presentation. This long latency effect suggests that the types of excitability changes in language-related processes detected by TMS can be produced by the nonspecific preactivation of cortical networks.

Basically, the Wada test acts through inhibition, and simulates or predicts postoperative neurological deficits. Theoretically, the Wada test is the ideal method for neurosurgeons. However, activation studies using the TMS method can detect live brain function, whereas the Wada test detects only right, left, or bilateral dominance. Even left hemisphere dominance diagnosed by the Wada test is associated with definite activity in the contralateral hemisphere; this finding may be confirmed by future fMR imaging studies. Moreover, the activities of the two hemispheres were not equal in bilateral dominant subjects.

The findings of our method correlate well with the Wada test results. Our method is safe, convenient, and inexpensive. All subjects in the current study were right-handed, so studies on left-handed patients are underway in our laboratory to confirm that our method is useful for determining cerebral dominance in all patients.

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References


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