Motor symptom is a major manifestation of ischemic cerebrovascular disease and transient ischemic attacks (TIAs). By definition, the episodes of TIAs last less than 24 hours and do not leave a persistent deficit. However, functional studies by single photon emission computed tomogram or infarction on brain computerized tomogram and magnetic resonance imaging. Here, we applied transcranial magnetic stimulation (TMS) to study whether TIA could produce persistent subclinical dysfunction for more than 24 hours.

Methods. The study included 23 TIA patients who had the criteria of hand weakness as one of their clinical manifestations. TMS was done twice in each TIA patient. The first time was during the period of 24-48 hours after onset and the second 7 days after onset. We studied the cortical motor threshold, the latencies and the amplitudes of the motor evoked potentials, the central motor conduction time, and the cortical silent period at the intensity of 1.5 times motor threshold with maximal voluntary isometric contraction. The recording was at the first dorsal interosseous muscle.

Results. There was no significant difference between the whole group of TIA patients and normal control. However, in the subgroup of TIA patients who had hand weakness more than 1 hour, they had increased motor threshold and prolonged cortical silent period during the first test. Both improved 1 week after onset. On the contrary, in TIA patients who had hand weakness less than 1 hour, their data were all within normal limits during the first and the second studies.

Conclusions. Our results indicate that the motor function of TMS study will recover to full if the motor symptoms subside within 1 hour in TIA patients. Subclinical motor deficits may persist in TIA patients who have motor symptoms more than 1 hour.

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Original Article

Transcranial Magnetic Stimulation in Patients with Transient Ischemic Attacks

Background. By definition, transient ischemic attacks (TIAs) do not leave a neurological deficit beyond 24 hours after onset. However, a subgroup of TIA patients is characterized by persistent perfusion defect on single photon emission computed tomogram or infarction on brain computerized tomogram and magnetic resonance imaging. Here, we applied transcranial magnetic stimulation (TMS) to study whether TIA could produce persistent subclinical dysfunction for more than 24 hours.

Methods. The study included 23 TIA patients who had the criteria of hand weakness as one of their clinical manifestations. TMS was done twice in each TIA patient. The first time was during the period of 24-48 hours after onset and the second 7 days after onset. We studied the cortical motor threshold, the latencies and the amplitudes of the motor evoked potentials, the central motor conduction time, and the cortical silent period at the intensity of 1.5 times motor threshold with maximal voluntary isometric contraction. The recording was at the first dorsal interosseous muscle.

Results. There was no significant difference between the whole group of TIA patients and normal control. However, in the subgroup of TIA patients who had hand weakness more than 1 hour, they had increased motor threshold and prolonged cortical silent period during the first test. Both improved 1 week after onset. On the contrary, in TIA patients who had hand weakness less than 1 hour, their data were all within normal limits during the first and the second studies.

Conclusions. Our results indicate that the motor function of TMS study will recover to full if the motor symptoms subside within 1 hour in TIA patients. Subclinical motor deficits may persist in TIA patients who have motor symptoms more than 1 hour.
for more than 24 hours.

**METHODS**

**Subjects**

According to the definition of the National Institute of Neurological Disorders and Stroke classification,19 we studied 23 patients (15 male, 8 female, aged 47 to 80 years, mean 65.4 ± 4.1 years) with hand motor dysfunction due to carotid system TIAs. Barthel index was used to assess motor function. In the study, all the patients had fully recovered to have score of 100. When patients were noted to have minor deficits or relative weakness in the dominant hand, they were excluded. In these 23 TIA patients, brain computerized tomogram or magnetic resonance imaging showed small infarct in the thalamus (1/23), internal capsule (1/23), corona radiata (1/23), and globus pallidus (2/23). We excluded TIA patients with a history of stroke, questionable TIAs, isolated amaurosis fugax, pure sensory symptoms, monoplegia of lower limb, and manifestations with posterior circulation. We also excluded patients with head injury history, peripheral neuropathy, diabetes mellitus and uremia. Brain computerized tomogram was done in each TIA patient to screen out brain tumor or intracranial hemorrhage and to prove the diagnosis. TMS was done twice in each TIA subject after informed consent. The first time was usually done in the period of 24-48 hours after onset and the second time 7 days after onset. Twenty-nine normal subjects were included as control (19 male and 10 female; age 62.4 ± 3.8 years).

**Threshold of motor evoked potentials**

The study was done with a magnetic stimulator (Magstim 200, Novametrix Medical Systems, Wallingford, CT, U.K.). The brain stimuli were applied with a circular coil (90 mm). The coil was aligned to produce a stimulating current that flowed from posterior to anterior in the brain approximately perpendicular to the line of the central sulcus. First of all, we had to find the most appropriate point on the scalp. The point was the most effective for the coil to evoke EMG responses in the first dorsal interosseous muscle (FDI). Then, the magnetic intensity was progressively reduced in 5% steps until a level was reached below which reliable EMG responses disappeared. The interval between consecutive stimuli was more than 15 s. Motor threshold (MT) was usually estimated at complete rest and was defined as a reliable motor-evoked potentials (MEP) response with a minimal 50-100 μV in 5 of 10 consecutive trials.20 When there were active muscle activities in the background, the MT was defined as a minimal response size around 200-300 μV.20

All subjects sat comfortably on a chair with their forearm lying on a horizontal plane. Two self-adhesive recording surface electrodes were placed 3 cm apart over the FDI belly. The MEPs were recorded with an EMG machine (Nihon Kodhen, Neuropack 8, Tokyo, Japan), with filters set between 20 Hz and 3 kHz, and the sweep was 300 ms.

**MEP amplitude and the central motor conduction time**

The spinal magnetic stimulation was done in order to measure the central motor conduction time. We measured the onset latency and the peak-to-peak amplitude of the maximal MEPs to TMS in each subject by manual selection.

**Cortical SP**

The magnetic stimuli were delivered over the optimal motor cortex hand area at maximal voluntary isometric contraction. The magnetic stimulation was performed at the intensity of 1.5 times MT.17,21 During the test, the subject was instructed to maintain a steady muscle contraction. At least 2 successive responses were superimposed. SP duration was defined as the duration (ms) between the end point of the MEP and the restoration of the EMG activity. In the affected hand of TIA patients, the magnetic stimulation was applied not only at 1.5 MT but also at the same intensity as the normal hand.

**H/M ratio**

Electrical stimulation (1-ms duration) was applied in the median nerve over the elbow. The maximal amplitude of H reflex (Hmax) and the maximal motor response (Mmax) of the flexor carpi radialis muscle were mea-
sured. The amplitude of the H reflex and M wave was measured from negative peak to the following positive trough. The H max/M max ratio was expressed as a percentage. This ratio was considered as an index of spinal excitability of motor neurons.\textsuperscript{22}

**Statistical analysis**

All values were expressed as mean ± SD. Nonparametric comparisons among groups were performed using the Kruskal-Wallis test. A \( p \) value less than 0.05 was defined as statistically significant. For side-to-side comparison, the Wilcoxon rank-sum test was used. Bonferroni correction was applied for multiple comparisons to ensure that the overall type I error rate was controlled to not greater than 0.05.

**RESULTS**

The normal values were established from 58 upper limbs of 29 healthy subjects aged 62.4 ± 3.8 years (Table 1). As most TIAs lasting more than 1 hour may actually correspond to cerebral infarction with transient signs or TIA due to lacunar infarction,\textsuperscript{23} the TIA patients were classified into 2 groups by symptoms lasting less than 1 hour (group I, GI, \( n = 14 \)) and more than 1 hour (group II, GII, \( n = 9 \)).

Before patients were divided into groups, all of the data of TIA patients did not have any significant difference from that of the normal subjects. In GI patients (14/23), all the data were all within normal limits during the first and the second tests. However, in the GII patients (9/23), there were increased MT (\( p = 0.0363 \)) and prolonged cortical SP (\( p = 0.0214 \)) during the first test. The cortical SP was also shorter at the sound hand than at the affected hand when the stimulation was of the same intensity (1.5 times MT of affected hand) during the first test. The side difference of MT (\( p = 0.0254 \)) and cortical SP (\( p = 0.001 \)) was also increased during the first test in GII patients (Fig. 1). In the follow-up of 1 week after onset, all the data of GII patients did not show significant difference from that of controls. Throughout the study, there was no significant difference in the following data: the peak amplitude and the onset latencies of MEPs, central motor conduction time, and forearm H/M ratio study in GI and GII patients.

**Table 1. Transcranial magnetic stimulation of TIA patients**

<table>
<thead>
<tr>
<th></th>
<th>TIA group I (&lt; 1 hour) (n = 14)</th>
<th>TIA group II (&gt; 1 hour) (n = 9)</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1st</td>
<td>2nd</td>
<td></td>
</tr>
<tr>
<td><strong>Threshold (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sound</td>
<td>41.8 ± 4.2</td>
<td>41.4 ± 4.6</td>
<td>38.1 ± 3.9</td>
</tr>
<tr>
<td>Affected</td>
<td>42.2 ± 5.4</td>
<td>40.4 ± 4.1</td>
<td>53.9 ± 4.2*</td>
</tr>
<tr>
<td>Side difference</td>
<td>1.4 ± 4.2</td>
<td>1.1 ± 3.5</td>
<td>6.9 ± 6.3*</td>
</tr>
<tr>
<td><strong>Amplitude/maximal intensity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sound</td>
<td>5.9 ± 1.9</td>
<td>6.1 ± 2.6</td>
<td>5.3 ± 1.8</td>
</tr>
<tr>
<td>Affected</td>
<td>5.8 ± 2.4</td>
<td>5.9 ± 2.9</td>
<td>5.3 ± 2.2</td>
</tr>
<tr>
<td>Side difference</td>
<td>0.8 ± 0.8</td>
<td>0.7 ± 1.2</td>
<td>0.6 ± 0.9</td>
</tr>
<tr>
<td><strong>Latency</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sound</td>
<td>18.8 ± 1.6</td>
<td>18.6 ± 1.6</td>
<td>18.4 ± 1.4</td>
</tr>
<tr>
<td>Affected</td>
<td>18.7 ± 1.8</td>
<td>18.6 ± 1.5</td>
<td>19.2 ± 1.5</td>
</tr>
<tr>
<td>Side difference</td>
<td>0.4 ± 0.6</td>
<td>0.2 ± 0.8</td>
<td>0.4 ± 0.5</td>
</tr>
<tr>
<td><strong>Silent period</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sound</td>
<td>148.7 ± 15.8</td>
<td>149.4 ± 13.8</td>
<td>149.1 ± 18.5</td>
</tr>
<tr>
<td>Affected</td>
<td>146.5 ± 16.7</td>
<td>150.9 ± 14.3</td>
<td>193.6 ± 13.7*</td>
</tr>
<tr>
<td>Side difference</td>
<td>18.2 ± 10.7</td>
<td>19.0 ± 12.6</td>
<td>44.4 ± 13.2*</td>
</tr>
<tr>
<td><strong>CMCT</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sound</td>
<td>7.2 ± 0.5</td>
<td>6.9 ± 0.6</td>
<td>7.3 ± 0.5</td>
</tr>
<tr>
<td>Affected</td>
<td>7.0 ± 0.9</td>
<td>7.1 ± 0.7</td>
<td>7.4 ± 0.6</td>
</tr>
</tbody>
</table>

\* \( p < 0.05 \); 1st = during the period of 24-48 hours after onset; 2nd = one week after onset; CMCT = central motor conduction time.
DISCUSSION

In the study of SP of patients with ischemic stroke, Braune and Fritz noted that SPs were significantly prolonged in the affected hand of a patient with right hemispheric TIA 4 days after onset.24 Our study confirmed their findings and clearly showed that duration of attack had an important role. It further pointed out that the technique of magnetic stimulation could show persistent brain dysfunction in a subgroup of TIA patients, similar with studies of imaging and SPECT. In the study of CT or MRI, the longer the episode of TIA, the greater is the possibility of finding a cerebral infarct.19 In SPECT studies, patients with attacks lasting more than 120 minutes had regional hypoperfusion more frequently,25 though the statistical significance was not reached in their conclusion. The MT and SP improved in our GII patients 1 week later. None of them had prolonged cortical SP or increased MT more than 2 SD above normal values 1 week later. In SPECT studies, a number of patients may have persistent flow abnormalities as late as 90 days after onset. Our TMS studies also showed that it was not unusual to find persistent motor dysfunction in TIA patients. Though the diagnosis of GI and GII patients would satisfy the TIA criteria, it seemed that the pathogenesis of the cerebral insult was not identical in these 2 patient groups.

The cortical SP was longer in the affected hand of GII patients, even at the same intensity as the normal side. Because the H/M ratio of forearm did not show side difference in GII patients, it indicated the findings of increased MT and prolonged SP should be due to supraspinal mechanism. A significantly prolonged SP was usually noted in lesions outside the primary motor cortex,21 consistent with the imaging findings of our TIA patients, such as internal capsule and thalamus. As a stimulus at intensity below MT is able to produce SP without apparent preceding MEP,16,17,26 it suggests that the SP and MEP arise from different mechanism.16 The mechanism of SP has spinal and cortical components. The initial part of the SP is of spinal components and comes through multiple mechanisms including Renshaw and Golgi tendon organ activation.13,27 The later part of the SP reflects primarily cortical inhibition.13,28 The inhibitory mechanism of cortical components does not arise from a direct inhibitory output but comes through inhibitory processes within the cortical network, causing a reduction in the excitatory corticospinal tract output.27,29

The MT of GII patients showed higher than that of normal control values in the first assessment. The MT of GII patients improved a lot 1 week after onset. This was similar to a stroke finding that the MT was uniformly reduced 1 week later.9 Mechanism of increased MT may be due to: (1) partial block and increased time dispersion of the impulse propagation due to demyelination of the cortical tracts; (2) loss of corticospinal fibers due to a lesion in the motor cortex and/or in the spinal cord; (3) abnormal activity of spinal interneurons regulating the im-

Fig. 1 The silent period to transcranial magnetic stimulation of a GII TIA patient. The silent period was longer in the affected hand initially and shortened 1 week later.
pulse transmission between cortical and spinal motor-neurons; (4) resting membrane potential changes of the cortical and/or spinal motoneurons. Because the central conduction time was normal and imaging studies did not show significant findings in all subjects, the mechanism of increased threshold should be due to changes of membrane potential.

In GII patients, there was finding of increased MT but without significant decreased amplitude of MEPs. MT is usually of relatively lower stimulation intensity and would have minimal current spread. Therefore, MT usually provides corresponding information about a central core region of the neurons. The maximal MEP is usually provoked by a higher intensity. With intensity above threshold, the stimulation usually involves neurons in addition to the core region activated at threshold. These neurons are intrinsically less excitable or they are spatially further from the center of activation by the magnetic stimulus. As the intensity increases, the D waves would be directly activated and would help assess post-synaptic function and/or synaptic function. That could be the reason why the amplitude of maximal MEP did not show any significant difference in the GI or GII patients.

In the study of excitability, significant difference was shown in MT but not in the amplitude of MEPs or central conduction time. It further proved that threshold measurement was a useful adjunct for the clinical assessment of questionable motor dysfunction and could be a probe to earlier detect subclinical motor involvement.

**ACKNOWLEDGEMENT**

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**REFERENCES**


