Prediction of Motor Function by Magnetic Brain Stimulation in Patients with Intracerebral Hematoma

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Abstract

Corticospinal motor pathways were monitored with motor evoked potentials (MEPs) elicited by transcranial magnetic stimulation in 13 patients with radiologically confirmed hypertensive intracerebral hemorrhage and varying degrees of hemiparesis. The electromyographic responses of the thenar muscles were recorded. The motor weakness of the upper extremity was assessed at initial monitoring and 3 months after hemorrhage, and correlated with changes in MEP. Absence of MEP in the acute stage indicated poor recovery of muscle strength. No false negative results were seen in our series. The presence of MEP in a completely hemiplegic patient predicted some recovery of motor function. The suppression of amplitude was more accurate than prolongation of latency in predicting the functional recovery. MEP monitoring of patients with hypertensive intracerebral hemorrhage in the acute stage can predict the outcome of motor function.

Key words: magnetic stimulation, motor evoked potential, corticospinal pathway, hypertensive intracerebral hemorrhage, outcome, motor function

Introduction

Functional recovery of the extremities in patients with hypertensive intracerebral hemorrhage involving motor pathways is predicted by close observation of neurological signs and radiological findings. Somatosensory evoked potentials may also be used to predict functional outcome. The recent development of percutaneous magnetic stimulation of the motor cortex allows evaluation of corticospinal pathways in awake human subjects, multiple sclerosis, motor neuron diseases, and stroke. In this study, we used magnetic stimulation to predict functional recovery of motor weakness after intracerebral hemorrhage and investigate the relationship between suppression of motor evoked potential (MEP) and degrees of recovery.

Patients and Methods

The healthy control group consisted of 15 normal volunteers who gave their informed consent to the procedure.

The 13 patients all had radiologically confirmed hypertensive intracerebral hematomas, varying degrees of hemiparesis, and a history of essential hypertension. There were seven males and six females, ranging in age from 41 to 70 years (mean 57.8 years). All patients or family gave informed consent to the study.

The motor weakness of extremities in patients was classified with the manual motor test (MMT) into six grades (0: no strength, 5: full strength) at the time of initial evoked potential testing and again 3 months after the stroke. Initial magnetic stimulation was carried out on days 0 (8 cases), 1 (3), 3 (1), and 10 (1). Follow-up MEP examination was carried out approximately 1 week and 1, 2, and 3 months later.

Computed tomography (CT) revealed hematomas in the putamen in four cases, thalamus in seven, and subcortex in two. Main hematoma involvement of the motor pathways was at the posterior limb of the internal capsule in varying degrees. Craniotomy and removal of hematoma were performed in four patients and burr hole and stereotactic drainage of hematoma in five. Four patients received medical therapy (Table 1).

The magnetic stimulator was a flat circular coil 9 cm in mean diameter placed on or very near the scalp with its center at the motor cortex, over the neck.
Capacitors charged to a maximum output of 1 kV were discharged through the coil. The magnetic field, which approached 2 Tesla at the coil center at maximum output, had a peak at about 150 μsec, and passed through the scalp and skull. The currents induced within the brain could excite the motor cortex and small hand muscles were easily activated. The magnetic stimulator could also stimulate peripheral nerves, but location of the stimulation point is less precise than with conventional electrical stimulation. Since transcranial magnetic stimulation as now used occasionally failed to evoke muscle action potentials of the lower extremity, we recorded those from hand muscles and correlated the outcome of upper extremity function.

Surface electrodes recorded the compound muscle action potential (MEP) elicited in the thenar muscles of both the affected and normal hands. The stimulating coil was positioned over the head to obtain a potential of maximal amplitude, and several responses were collected to confirm reproducibility. The procedure was easily carried out at the bedside within 30 minutes. The best MEP from a single stimulation was analyzed. The MEP latency between the stimulus and the response onset was measured and amplitude compared with the MEP recorded from a normal site. Central motor conduction time (CMCT) was calculated as the difference in onset latencies of the MEPs elicited from the neck and transcranial stimulations.

A series of single trials at each site, each of equal stimulus intensity, were recorded with the patient totally relaxed. The stimulating coil was positioned over the head to obtain a potential of maximal amplitude, and several responses were collected to confirm reproducibility. The procedure was easily carried out at the bedside within 30 minutes. The best MEP from a single stimulation was analyzed. The MEP latency between the stimulus and the response onset was measured and amplitude compared with the MEP recorded from a normal site. Central motor conduction time (CMCT) was calculated as the difference in onset latencies of the MEPs elicited from the neck and transcranial stimulations.

Table 1 Clinical features, radiographic findings, MEP, and MMT at initial testing and 3 months later

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age/ Sex</th>
<th>Hematoma localization</th>
<th>Consciousness at initial testing</th>
<th>Surgery</th>
<th>Stroke-testing interval (day)</th>
<th>MEP at initial testing*</th>
<th>MMT at initial testing**</th>
<th>Follow-up MEP*</th>
<th>MMT at 3 months**</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lco (msec)</td>
<td>Lsp (msec)</td>
<td>CMCT (msec)</td>
<td>Amp</td>
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<tr>
<td>1</td>
<td>61/M</td>
<td>rt putamen</td>
<td>semicoma</td>
<td>craniotomy</td>
<td>0</td>
<td>A</td>
<td>15.0</td>
<td>—</td>
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<td>2</td>
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<td>stupor</td>
<td>craniotomy</td>
<td>0</td>
<td>A</td>
<td>13.6</td>
<td>—</td>
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<tr>
<td>3</td>
<td>52/M</td>
<td>lt thalamus</td>
<td>alert</td>
<td>burr hole drainage</td>
<td>10</td>
<td>A</td>
<td>12.6</td>
<td>—</td>
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<tr>
<td>4</td>
<td>60/M</td>
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<td>burr hole drainage</td>
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<td>A</td>
<td>11.8</td>
<td>—</td>
<td>0</td>
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<tr>
<td>5</td>
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<td>A</td>
<td>11.2</td>
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<td>semicoma</td>
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<td>A</td>
<td>12.0</td>
<td>—</td>
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<tr>
<td>7</td>
<td>60/F</td>
<td>rt parietal</td>
<td>drowsy</td>
<td>craniotomy</td>
<td>3</td>
<td>A</td>
<td>14.0</td>
<td>—</td>
<td>0</td>
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<tr>
<td>8</td>
<td>70/F</td>
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<td>stupor</td>
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<td>1</td>
<td>A</td>
<td>13.6</td>
<td>—</td>
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<td>9</td>
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<td>burr hole drainage</td>
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<td>—</td>
<td>0</td>
<td>24.8</td>
<td>12.8</td>
<td>12.0</td>
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<tr>
<td>11</td>
<td>53/M</td>
<td>rt putamen</td>
<td>drowsy</td>
<td>—</td>
<td>0</td>
<td>22.0</td>
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<tr>
<td>12</td>
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<td>drowsy</td>
<td>—</td>
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<td>rt thalamus</td>
<td>drowsy</td>
<td>—</td>
<td>1</td>
<td>20.0</td>
<td>10.6</td>
<td>9.4</td>
<td>2</td>
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</tbody>
</table>

*Lco: latency evoked by transcranial stimulation, Lsp: latency evoked over the neck. Amp 0, 1, and 2 are absent, suppression of MEP amplitude below 50%, and more than 50% of contralateral normal MEP, respectively. A: absent, N: normal, AB: abnormal defined by significant prolongation of latency or CMCT and suppression of amplitude.
**MMT 0: no strength, 5: full strength. Poor: MMT 0–1, fair: MMT 2–3, good: MMT 4–5.

No side effects occurred in any patient or volunteer. Figure 1 shows the MEPs recorded from the thenar muscles of the right hand of one volunteer during elbow, neck, and transcranial stimulations. Normal onset latencies elicited from the elbow, neck, and motor cortex of 15 volunteers were 8.06 ± 0.97, 13.23 ± 1.55, and 21.68 ± 2.22 msec, respectively, and normal CMCT was 8.45 ± 1.48 msec (mean ± 2 SD).

Table 1 summarizes patient profiles, hematoma locations, MEPs, and hand motor tests on admission and 3 months later. The electrophysiological findings of the corticospinal pathways and the clinical data showed a good correlation between suppression of MEPs and outcome of motor function. In eight patients with paralysis of upper extremity at onset, a

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flat MEP was always associated with poor recovery of motor function after 3 months. However, in two patients with MMT 0/5 at day 0, MEP was still present to some extent and considerable recovery of motor function was achieved (Cases 9 and 10). In Case 9, marked prolongation of onset latency and CMCT, and severely suppressed amplitude still resulted in fair motor recovery. There was poor correlation between prolongation of latency and CMCT, and outcome of motor function in Cases 10 and 12. However, the MEP amplitude at onset correlated well with recovery of muscle strength in all cases.

Illustrative Cases

Case 2: A 41-year-old male was admitted with a chief complaint of rapid onset of motor disturbance in the left upper and lower extremities. He was stuporous with persistent paralyses of the left upper and lower extremities. A CT scan revealed a large putaminal hematoma with ventricular hemorrhage compressing the right internal capsule (Fig. 2). Transcranial stimulation was performed 6 hours after the onset. Right motor cortex stimulation elicited no MEP in the muscles of the paralyzed left upper extremity. Left motor cortex stimulation produced an MEP of normal latency in the right thenar muscles. He underwent craniotomy and hematoma removal through the right Sylvian fissure. Sixty days after operation, he remained paralytic and transcranial stimulation evoked no MEP.

Case 9: A 52-year-old male suddenly developed loss of consciousness and right hemiplegia. Two hours after onset, he was stuporous and completely hemiplegic in the right upper and lower extremities. A CT scan showed a left thalamic hemorrhage involving the internal capsule (Fig. 3). Transcranial stimulation produced a small MEP with a prolonged latency of 26.8 msec in the right thenar muscles, although MMT was 0/5. CMCT was significantly lengthened to 13.2 msec. Burr hole opening and stereotactic drainage of the hematoma were performed the same day. The latency became normal at 23.6 msec. Twenty days after drainage, the amplitude remained low, at less than 50% of the normal side. Muscle strength of the right upper extremity gradually improved and 3 months after onset was 3/5.

Case 10: This 66-year-old male presented with rapid impairment of consciousness and right hemiparesis secondary to left thalamic hemorrhage (Fig. 4). Four hours after the stroke, neurological examination revealed he was stuporous with paralyses of the right upper and lower extremities. MMT was 0/5. Transcranial stimulation over the left motor cortex evoked medium voltage MEP complex in the right thenar muscles with normal latency of 24.8 msec and prolonged CMCT (12.0 msec). Motor function of the right upper extremity progressively improved with medical therapy from day 1 and on day 7, MMT was 5/5. The MEP amplitude also recovered to normal range with normal latency (23.6 msec). He was subsequently discharged with normal muscle strength in the right upper extremity.

Discussion

The introduction of transcranial magnetic stimulation in 1985\textsuperscript{2,3} began extensive investigation of the electrophysiological changes in the corticospinal motor pathways in a variety of neurological diseases. The procedure is painless and no side effects have
been reported. This technique has demonstrated abnormalities of central motor conduction in multiple sclerosis\(^8,9,13\) and motor neuron disease,\(^5\) even in subclinical lesions.

Levy et al.\(^{10}\) reported that no MEP was evoked in a hemiplegic patient with hemorrhagic infarction by electrical transcranial stimulation. Electrical transcranial stimulation also demonstrated abnormal CMCT and suppressed amplitude in all patients with hemiparesis caused by a cerebrovascular lesion, regardless of the site in the corticospinal tract.\(^{15}\) Macdonell et al.\(^{12}\) reported that nine of 10 patients demonstrating MEN achieved some functional recovery after stroke and eight of nine patients without MEPs made no recovery or died. They concluded that MEPs were a slightly better predictor of functional recovery than somatosensory evoked potentials.

The exact site activated by magnetic stimulation is at present unclear. Presumably, weak magnetic fields act at the presynaptic terminals, while strong fields excite the cell body or axon of the pyramidal cell,\(^{13}\) or the level of the gray-white junction (layer VI).\(^6\) Therefore, we chose patients with intracerebral hematoma involving deep structures of the corticospinal tract without direct cortical injury. Mills et al.\(^{13}\) reported that electrical stimulation over the cervical column acts at the exit foramen of the motor roots from the spinal canal. The same site is probably excited by magnetic stimulation, and so can evaluate CMCT as the difference in latency of MEPs evoked transcranially and over the neck.\(^6\)

Our results show that absence of MEPs in the acute stage of hypertensive intracerebral hematoma indicates absolutely poor functional recovery of the upper extremity even if the hematoma is removed. We found no false negative results between MEPs and outcome of muscle strength. In contrast,
presence of MEPs in patients with complete hemiplegia (MMT 0/5) indicates some recovery of motor function with either medical and surgical treatment. The MEPs probably represent anatomical continuity of the corticospinal motor pathways in addition to preservation of electrophysiological activities. We found little correlation between changes in latencies or CMCT of the potentials and outcome of motor function, whereas amplitude reductions were associated with poor outcome. In general, slowing of conduction is associated with demyelination as in multiple sclerosis, whereas attenuation of amplitude without a pronounced latency increase indicates predominant axonal loss or conduction block in myelinated fibers. Intracerebral hematoma is thought to attenuate electrophysiological activities by destroying and/or distorting descending motor pathways. If the pathways are completely interrupted, the MEP is lost; if the interruption is less severe, the MEP amplitude may be reduced. Therefore, MEP amplitudes are superior to latencies for prediction of motor function outcome in the acute stage of intracerebral hemorrhages. Zentner also reported that intraoperative changes in amplitude of MEP were superior to latency for early detection of impending neurological complications in spinal cord operations.

This study provides encouraging evidence that MEP monitoring with magnetic stimulation in the acute stage of intracerebral hemorrhage can provide early prediction of functional recovery of motor weakness. When MEPs are present, medical or surgical treatment should be aggressively employed to achieve recovery of muscle strength in the extremities.

Fig. 3 Case 9. left: CT scan, showing a left thalamic hemorrhage. right: MEPs on the day of onset (upper traces) demonstrated moderately delayed, dispersed, and small responses on the affected side. MMT of the right upper extremity was 0/5. Twenty days after hemorrhage (lower traces), there was a considerable normalization of MEP and MMT (3/5).

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Fig. 4 Case 10. left: CT scan, showing a left thalamic hemorrhage. right: Medium voltage MEP complex was recorded with MMT 0/5 on the affected side on the day of onset (upper traces). In 7 days after hemorrhage (lower traces), muscle strength of the right upper extremity became 5/5.

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