

Correlation of the Motor Evoked Potentials Amplitude and Hand Function of the Affected Side in Stroke

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Objective To investigate the correlation between the motor evoked potentials (MEPs) amplitude of 1st dorsal interosseus in affected limbs and affected hand function after stroke.

Method We enrolled 109 patients with acute and subacute 1st attack stroke. Transcranial magnetic stimulation (TMS) was applied to the motor cortex and MEP was recorded at the 1st dorsal interossei (DI) muscle. MEP parameters were latency of the affected side, latency ratio (latency of affected side/latency of unaffected side), amplitude of affected side and amplitude ratio (amplitude of affected side/latency of unaffected side). Hand function tests (HFT) including hand power measures and a nine hole peg test (NHPT) were conducted and the ratios of the value of the affected hand to unaffected hand were used for the analysis. The Korean version of the modified Barthel index (K-MBI) and the manual muscle test (MMT) of finger flexion were also evaluated. Correlation between MEP parameters and the clinical variables such as HFT, K-MBI and MMT grades were analyzed.

Results While MEPs in the affected 1st DI were recorded in fifty six patients, MEPs were not recorded in forty nine patients. The responsiveness of MEPs was significantly correlated with the HFT, K-MBI and MMT grades. The amplitude ratio had the most significant correlation with the HFT and MMT grade in this MEP study. Also, the amplitude ratio had more significant correlations with the K-MBI score compared with other MEP parameters.

Conclusion We concluded that the amplitude ratio may be a useful MEPs parameter for indicating hand function.

Key Words Motor evoked potential, Amplitude, Hand function, Stroke

INTRODUCTION

Dysfunction of the upper extremity after stroke is caused by various factors, including muscle weakness and paralysis, muscle strength imbalance, dystonia and sensory disturbance. For the objective assessment of those dysfunctions, various clinical standards and tests

employing diverse tools have been in use. Among others, motor evoked potentials (MEPs) obtained by transcranial magnetic brain stimulation (TMS) are widely used in studying central nervous system diseases.¹ This electrodiagnostic test, which allows for the quantitative assessment of functional recovery after stroke, has been widely used to study central nervous system disorders

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because it is safe and easy to perform and guarantees quick responsiveness. Important, the test is usually taken as a follow-up to evaluate the motor function of stroke patients and to establish their prognoses, as there have been numerous reports that a good prognosis is expected for functional recovery when motor potentials are constantly evoked at stroke onset while prognosis is bad when MEPs are absent.²⁻⁷ Some studies have shown that MEP amplitudes could be considered effective parameters because amplitudes hold strong correlations within or between MEP tests,⁸⁻¹⁰ and motor threshold and MEP amplitude make standards for assessing motor functions and measuring the level of functional recovery because the recovery of motor function is linked to a decrease of the motor threshold and an increase of the MEP amplitude.¹¹⁻¹³ The amplitude of MEPs, however, has rarely been taken into account in analyzing the results of MEP tests. This is because some studies have argued that the amplitude value varies depending on test environments and in healthy subjects its range is huge and lacks consistency.¹⁴⁻¹⁶ Moreover, most studies conducted in Korea to date have focused on the correlation between functional recovery and muscle strengths by observing onset latency, central motor conduction time or the presence of MEPs, and few has pay attention to the correlation of MEP amplitudes with the upper limb functions.¹⁷⁻²⁰ This study was conducted to help establish a comprehensive approach to stroke patients as well as treatment plans. To this end, the MEP amplitude ratio was calculated by comparing MEP amplitudes obtained by stimulating both unaffected and affected hemispheres. The writers examined correlations of the ratio with hand function test results, Modified Barthel Index (MBI) scores and manual muscle test (MMT) grades in addition to investigating MEP latencies and presence of MEP responses. As such, the clinical value of the amplitude-related MEP parameters in the affected side was evaluated.

MATERIALS AND METHODS

Subjects

A retrospective study was conducted by analyzing medical records of stroke patients hospitalized from January 2008 to August 2010, who received TMS-MEP tests, MBI evaluation procedures and hand function tests. The subject group consisted of stroke patients

with first-attack stroke at acute and subacute phases. Their lesions were limited to one side of the brain. Patients whose lesions were not localized due to subarachnoid hemorrhage, arteriovenous malformation and others reasons were excluded from the subject group along with those who had traumatic brain injury, brain tumor and bilateral stroke. Patients with ulnar or peripheral neuropathy were not included as well as those who were unable to perform hand function tests because of compromised cognitive function (those who earn less than 20 points in the Korean mini-mental state examination).

Methods

MEP tests were conducted in a standardized way using the Keypoint[®] (Medtronic Inc, Copenhagen, Denmark) electromyography tester. MEPs were obtained by transcranial magnetic brain stimulation, for which 70 mm-radius butterfly-shaped coils connected to the Magpro×100 MagOption (Medtronic Inc, Copenhagen, Denmark) simulator were used. The stimulating point was set where to see the lowest resting motor threshold (RMT), which is defined as the percentage of stimulator output necessary to obtain an MEP response greater than 50 μ V in five of 10 trials in the relaxed muscle, while the surface electrode was attached to the 1st dorsal interosseus. Four stimulations were performed each time with intensity set at 120% of RMT value. If MEPs appeared during the four stimulations, the shortest latencies and maximal amplitudes were noted and their average values were taken. TMS was done for both the affected and unaffected hemispheres. If MEPs appeared from both sides, latency and amplitude ratios were calculated, which were used as MEP parameters along with average latency and amplitude from the affected hemisphere.

The hand function test was conducted in patients sitting on a chair with their shoulders neither adducted nor rotated in a neutral position. Their elbows were bent 90 degrees, and forearms and wrists were in neutral positions. In hand functioning tests, grip strength, lateral pinch power, palmar pinch power and tip pinch power were observed and the Nine Hole Peg Test (NHPT) was done. Grip strength was recorded using the JAMAR hand dynamometer (JAMAR[®], Chicago, USA), and pinch power was assessed by drawing an average three test results gained from the Hydraulic pinch gauge (Jamar[®], Chicago, USA). The NHPT is a timed test where the subject places 9 dowels in 9 holes and

removes them using one upper limb. Subjects were scored on the amount of time it takes to place and remove all the nine pegs. The ratios of the affected side results to the unaffected side were calculated and used as a variable for hand functions, not their absolute values, in order to exclude other factors affecting hand functions.

The level of daily activity performance was evaluated by using the Korean version of the Modified Barthel Index (K-MBI). Five items in the K-MBI, which are related to the upper extremity (personal hygiene, bathing self, feeding, toilet and dressing), were evaluated, and total scores and scores of each item were noted. At the time of evaluation, manual muscle grades for finger flexion were also determined.

MEP tests were conducted at 20.1 ± 14.5 days post-stroke, and 1.9 ± 2.7 days later hand function tests were performed. Hand function tests and K-MBI evaluation were carried out in the same day (Table 1).

Statistics

All statistical analyses were performed using the Statistical Package for the Social Sciences Ver. 16.0 for Windows. Pearson correlation analysis was used to see the relationship of MEP parameters with hand function test results, while Spearman correlation analysis was applied to relating MEP parameters to scores of upper-extremity-related items in the K-MBI, total K-MBI scores, and MMT grades. Independent t-test was done for comparisons of MEP presence, lesion location, causes of stroke, and sex with MEP parameters, hand function test results, K-MBI scores and MMT grades. Values of $p < 0.05$ were considered significant.

RESULTS

Subject Group

Out of 105 patients in total, no response was captured in 56 subjects when their affected side was magnetically stimulated, while the other 49 produced MEPs in response to the stimulation of both sides (Table 1). All patients were right handedness.

In a group where MEPs were detected, MEP parameters, K-MBI scores, MMT grades, and hand functioning test results appeared to have no significant relations to the location of brain lesion, (i.e., which hemisphere the lesion is located on or whether it invades cerebral cortex), sex and cause of stroke. In subjects as a whole

Table 1. Patients Characteristics and Demographics

Characteristics	Numbers	
	MEPs (-)	MEPs (+)
Lesion side		
Right hemisphere	30	23
Left hemisphere	26	26
Lesion site		
Cortical involved	25	13
Subcortical involved	31	36
Etiology		
Infarction	42	40
Hemorrhage	14	9
Sex (Male/Female)	35/21	28/21
Age (years)	60.6 ± 12.6	62.1 ± 14.5
Days from onset to MEPs	20.0 ± 13.1	21.2 ± 15.8
Days from MEPs to HFT	1.4 ± 1.9	2.4 ± 3.2

MEPs: Motor evoked potentials, MEPs (-): The absence of MEPs, MEPs (+): The presence of MEPs

Table 2. Comparison between Cortical and Subcortical Lesion

	Cortical lesion	Subcortical lesion
HFT		
Grip strength ratio	0.39 ± 0.32	0.60 ± 0.30
Lateral pinch power ratio	$0.45 \pm 0.27^*$	$0.71 \pm 0.27^*$
Palmar pinch power ratio	0.49 ± 0.29	0.63 ± 0.29
Tip pinch power ratio	0.49 ± 0.27	0.66 ± 0.28
NHPT ratio	1.64 ± 0.75	2.24 ± 1.75
K-MBI		
Hygiene	$2.48 \pm 1.32^*$	$3.33 \pm 1.13^*$
Bathing	$1.66 \pm 1.24^*$	$2.63 \pm 1.36^*$
Feeding	$5.51 \pm 2.87^*$	$6.86 \pm 2.39^*$
Toileting	$4.33 \pm 2.97^*$	$5.63 \pm 2.82^*$
Dressing	$4.18 \pm 2.28^*$	$5.38 \pm 2.47^*$
Total score	$46.69 \pm 21.91^*$	$58.24 \pm 20.51^*$
MMT grades	$2.03 \pm 1.31^*$	$2.63 \pm 1.37^*$

Values are mean \pm SD.

HFT: Hand function test, NHPT: Nine hole peg test, K-MBI: The Korean version Modified Barthel Index, MMT: Manual muscle test, Hand functions ratio: The ratio of the value of the affected hand to the unaffected hand

* $p < 0.05$

(105), compared with patients with cerebral cortex lesions, patients whose lesion is located in the sub-cortical region show statistically significant differences in lateral pinch power, K-MBI scores and MMT grades (Table 2). Other factors seemed to bring no differences.

Group with the Absence of MEPs on the Affected Side

In the group with the absence of MEPs, 50 patients (or 89%) were not able to perform any of hand functioning test processes, while six patients (or 11%) could carry out part or all of test items. The higher MMT grade a patient had, the more hand function test items he or she could perform. The patient group with absence of MEPs to stimulation of the affected hemisphere showed a statistically significant reduced in MMT grades and K-MBI scores related to the functioning of the upper extremity as well as its total scores, compared to those with MEPs (Table 3).

Group with the presence of MEPs

MEP Parameters: The average of latencies gained by

Table 3. Values of K-MBI and MMT Grades in MEPs (-) and MEPs (+) Patients

	MEPs (-)	MEPs (+)	P
MMT grades	1.28±0.54	3.5±0.9	<0.001
K-MBI			
Hygiene	2.42±1.20	3.68±0.97	<0.001
Bathing	1.65±1.01	2.96±1.41	<0.001
Feeding	5.59±2.64	7.24±2.34	0.001
Toileting	3.81±2.52	6.60±2.64	<0.001
Dressing	3.59±1.94	6.40±2.12	<0.001
Total score	42.63±16.85	66.48±19.43	<0.001

Values are mean±SD.

MEPs: Motor evoked potentials, MEPs (-): The absence of MEPs, MEPs (+): The presence of MEPs, MMT: Manual muscle test, K-MBI: The Korean version Modified Barthel Index

stimulating the affected side was 22.66±2.20 msec, showing a significant delay compared to the unaffected-side latency of 21.67±1.61 msec ($p>0.05$). The average amplitude from the affected side stood at 1.84±2.60 mV, significantly lower than the value of 4.48±3.19 mV gained from the counterpart ($p>0.05$). The latency ratio was 1.04±0.08, while the amplitude ratio stood at 0.38±0.32 (Table 4).

Relations of MEP Parameters with Hand Function Test Results and MMT Grades: After TMS of the affected hemisphere, MEPs were elicited in 49 patients, and 35 (or 71%) of them were able to perform all of the five hand function tests with the affected limbs. Eight (or 16%) of them could carry out all items except the NHPT, and two patients (4%) failed to undertake tests except grip strength and lateral pinch power tests. Four (8%) failed to carry out any of the tests although MEPs were present in their affected side (Table 4).

The amplitude ratio of the affected hemisphere to the unaffected was found significantly correlated to the hand strength ratios in four categories (grip strength, lateral pinch power, palmar pinch power and tip pinch power), while no correlation was observed with regard to the NHPT ratio. The MEP amplitude of the affected side showed significant correlations with grip strength, lateral pinch power and palmar pinch power, and no other entries were related to it. The latency of the affected hemisphere and latency ratio appeared to have no statistically significant relations to results of hand function tests. MMT grades for finger flexion in the affected side showed significant positive correlations with the amplitude ratio ($r=0.550$) and the affected-side am-

Table 4. Values of MEP and HFT Parameters in MEPs (+) Patients

	Affected side	Unaffected side	Ratio (Aff/Unaff)
MEP parameters			
Latency (msec)	22.66±2.20	21.67±1.61	1.04±0.08
Amplitude (mV)	1.84±2.60	4.48±3.19	0.38±0.32
HFT			
Grip strength (kg)	12.65±10.97	23.83±11.07	0.55±0.31
Lateral pinch power (kg)	5.49±6.29	7.86±3.72	0.64±0.29
Palmar pinch power (kg)	3.94±3.31	7.05±3.57	0.59±0.29
Tip pinch power (kg)	3.26±2.72	5.59±3.34	0.61±0.28
NHPT (sec)	39.23±37.01	36.23±32.78	2.18±1.63

Values are mean±SD.

MEP: Motor evoked potential, HFT: Hand function test, NHPT: Nine hole peg test, MEPs (+): The presence of MEPs, Aff/Unaff: The value of the affected side/the value of the unaffected side.

plitude ($r=0.540$). The latency of the affected side exhibited negative correlations to MMT grades although the correlation coefficient was relatively small. The latency ratio was found to have no correlation with any factors (Table 5).

MEP Parameters and K-MBI scores: The findings of this study show that the amplitude ratio is correlated with personal hygiene ($r=0.292$) and feeding ($r=0.347$)

scores in the K-MBI more than other MEP parameters are (Table 6).

DISCUSSION

To date there have been numerous studies on MEPs elicited by TMS, which allows for assessing the hand

Table 5. Correlations of MEP and HFT Parameters and MMT Grades in MEPs (+) Patients

	Grip strength ratio (n=45)	Pinch power ratio			NHPT ratio (n=35)	MMT grade (n=49)
		Lateral (n=45)	Palmar (n=43)	Tip (n=43)		
Latency	$r=-0.129$ $p=0.398$	$r=-0.174$ $p=0.253$	$r=-0.048$ $p=0.761$	$r=0.085$ $p=0.589$	$r=-0.195$ $p=0.263$	$r=-0.332$ $p=0.020$
Latency ratio	$r=-0.286$ $p=0.052$	$r=-0.237$ $p=0.117$	$r=0.119$ $p=0.446$	$r=0.134$ $p=0.390$	$r=-0.201$ $p=0.248$	$r=-0.276$ $p=0.055$
Amplitude	$r=0.310$ $p=0.038$	$r=0.446$ $p=0.002$	$r=0.347$ $p=0.023$	$r=0.213$ $p=0.171$	$r=0.116$ $p=0.505$	$r=0.540$ $p<0.001$
Amplitude ratio	$r=0.515$ $p=0.001$	$r=0.574$ $p<0.001$	$r=0.422$ $p=0.012$	$r=0.524$ $p=0.001$	$r=-0.010$ $p=0.952$	$r=0.550$ $p<0.001$

Values are correlation coefficient and p value.

MEP: Motor evoked potential, HFT: Hand function test, NHPT: Nine hole peg test, MMT: Manual muscle test, MEPs (+): The presence of MEPs, Hand functions ratio: The ratio of the value of the affected hand to the unaffected hand, Latency: Latency of the affected side, Latency ratio: Latency of the affected side/amplitude of the unaffected side, Amplitude: Amplitude of the affected side, Amplitude ratio: Amplitude of the affected side/amplitude of the unaffected side.

Table 6. Correlations of MEP Parameters and K-MBI in MEPs (+) Patients

	Hygiene	Bathing	Feeding	Toileting	Dressing	Total score
Latency	$r=-0.023$ $p=0.874$	$r=-0.031$ $p=0.835$	$r=-0.172$ $p=0.236$	$r=-0.062$ $p=0.671$	$r=-0.043$ $p=0.771$	$r=0.012$ $p=0.935$
Latency ratio	$r=-0.110$ $p=0.453$	$r=-0.047$ $p=0.750$	$r=-0.168$ $p=0.250$	$r=-0.055$ $p=0.709$	$r=-0.076$ $p=0.606$	$r=-0.036$ $p=0.807$
Amplitude	$r=0.112$ $p=0.443$	$r=-0.006$ $p=0.969$	$r=0.145$ $p=0.320$	$r=0.040$ $p=0.785$	$r=0.027$ $p=0.854$	$r=0.010$ $p=0.943$
Amplitude ratio	$r=0.292$ $p=0.042$	$r=0.194$ $p=0.181$	$r=0.347$ $p=0.015$	$r=0.246$ $p=0.089$	$r=0.243$ $p=0.092$	$r=0.174$ $p=0.233$

Values are correlation coefficient and p value.

MEP: Motor evoked potential, K-MBI: The Korean version Modified Barthel Index, MEPs (+): The presence of MEPs, Latency: Latency of the affected side, Latency ratio: Latency of the affected side/amplitude of the unaffected side, Amplitude: Amplitude of the affected side, Amplitude ratio: Amplitude of the affected side/amplitude of the unaffected side.

function of stroke patients quantitatively and objectively and establishing prognosis in the follow-up stage. However, the MEP amplitude has been in limited use in these studies. It has been known that MEP amplitude is not suitable for assessing patient's neurophysiological status because MEP amplitude varies widely depending on the patient's sex, age, level of muscle contraction and other factors and because normal ranges are set at different levels according to clinical laboratories. However, this study used the ratio of the amplitude of the affected side to that of the unaffected side as a variable, not absolute values. Then the writers examined the ratio's correlation with hand function, ability to perform day-to-day activities and MMT grades. As a result, the amplitude ratio was the most relevant factor compared with other MEP parameters and the amplitude was proven to have correlations with some of hand functions, while the latency ratio and latency were not showing correlations with hand function and daily activity performance. In addition, the amplitude ratio and amplitude appeared to be related to MMT grades, demonstrating that amplitude parameters well reflect hand strengths among MEP parameters. Lee et al.²¹ reported that there is a significant correlation between MMT grades and evoked potentials, and that the ratio of MEP amplitudes from the affected side to the unaffected has a moderate correlation with MMT grades. The implication of this study lies in the fact that the amplitude ratio shows a significant correlation not just with strength grades, but also with hand functions, therefore demonstrating the need to observe amplitude ratios in MEP tests.

Study findings show that the presence of MEP responses is likely to accompany significant differences in ability to perform daily activities and MMT grades in comparison to patients without MEPs. Seventy-one percent of patients with MEPs elicited by TMS were able to perform all of the five hand function tests, while 89 percent of patients without MEPs could not perform any of the tests. These findings are similar to the conclusions of many preceding studies that confirm the prognostic value of MEP appearance for predicting functional recovery in hemiplegia patients.^{1,17-19} When MEPs appear during the test, among all MEP parameters the amplitude ratio showed the strongest positive correlation with hand strengths, i.e., grip strength ratio, pinch power ratios and MMT grades, proving that the amplitude ratio well reflects the level of hand strengths. Grip strength ratio, pinch power and other hand strength

parameters are now in wide use as clinical standards to evaluate hand functions of patients objectively and to determine the effectiveness of treatment. However, it is hard to apply this approach to patients who have trouble performing tests because of declines in concentration and cognitive functions. Manual muscle tests are easy to carry out but the understanding and cooperation of patients are required, and MMT grades are widely spaced so that it cannot grasp the changes of functions sensitively. Due to these obstacles, it is difficult to evaluate the hand strengths accurately and to conduct the MMT in acute stroke patients, while the MEP test has advantages that it requires relatively less cooperation from patients and that test results could be quantified easily and quickly. Therefore, the clinical value of the MEP test could be emphasized as an objective tool to supplement the MMT and hand function tests. The presence of MEPs and the amplitude ratio, when available, could be clinically used as indices to assess hand functions and predict their return.

Moreover, findings show that the amplitude ratio is correlated to personal hygiene and feeding activities in the K-MBI than other MEP parameters are. Han et al.²² reported that an increase in lateral pinch power on the unaffected side has a positive correlation with total scores of the K-MBI by studying hand functions of the unaffected side in hemiplegic stroke patients. In this study, the strongest correlation was found between the amplitude ratio and lateral pinch power among all hand-strength factors because evoked potentials were recorded from the 1st dorsal interossei (Fig. 1). It is

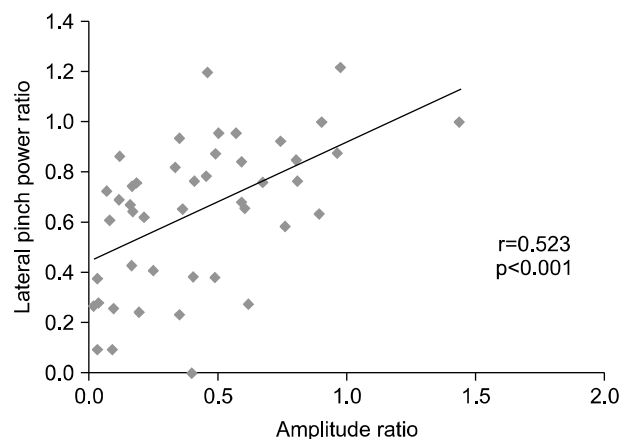


Fig. 1. Correlation of amplitude ratio (amplitude of the affected side to the unaffected side) and lateral pinch power ratio (lateral pinch power of the affected side to the unaffected side).

considered that the daily activity performance showed similar results to the study of Han et al.²² because the performance is largely influenced by the impairment level of the affected side. However, it is hard to conclude that the findings of this study confirm a significant correlation between the amplitude ratio and K-MBI scores. Further studies remain to be conducted to investigate such a correlation.

MEPs represent the activity of the motor nerve system as a whole, which includes cerebral cortex and cerebrospinal tract, and are closely linked to the excitability of the cerebral cortex.^{23,24} This study also observed that MEP appearance is significantly related to daily activity performance and MMT grades. Compared with the cortical lesion, the sub-cortical lesion has statistically significant differences in lateral pinch power, total scores and upper-extremity-related scores in the K-MBI, and MMT grades, meaning relatively less degradation of motor functions. However, these differences are not considered clinically significant, and there was no significant difference in MEP parameters depending on the lesion location. Eight percent of patients with elicited MEPs failed to perform any of hand function tests, and eleven percent of patients without MEP responses could carry out the tests, showing that the level of neurophysiological recovery is not necessarily in step with clinical recovery. Therefore, such inconsistency must be taken into account when applying MEP tests for clinical purposes, and further studies on various types of brain-damage patients are needed in the future.

MEP amplitude ratio was found to have positive correlations with hand strengths and MMT grades, while no significant correlation was noticed between the ratio and NHPT results. This is probably because the surface electrode was attached only to the 1st dorsal interossei and the results of the NHPT, a test designed to evaluate hand dexterity, are influenced not just by hand strengths but by sensory-motor coordination and the ability to control the contraction and relaxation of other muscles. It seems that the MEP amplitude ratio reflects strength-related hand motor functions but does not well present the general function of the upper extremity and its dexterity. Further studies are needed to investigate the relationship between potentials recorded from various sites and general functions of hands and upper limbs comprehensively by attaching electrodes to other muscles than the 1st dorsal interossei and by relating MEP amplitudes to other factors of hand functions than strengths. In this process the amplitude ratio will be a more

accurate index reflecting hand motor functions.

The limitation of this study is the lack of follow-up to track the changes of MEP amplitudes and functional recovery over time. This study was designed to draw a sectional view on the relationship of MEP parameters with hand motor functions, daily activity functions and MMT grades at a point of time. Subsequent systematic follow-up studies in more patients on the relationship between the changes of the amplitude ratio and the level of hand function recovery will help to make the amplitude ratio a more reliable index for predicting the return of hand function.

CONCLUSION

The findings of this study proved that compared to other MEP parameters, the MEP amplitude ratio of the affected hemisphere to the unaffected side shows the strongest correlations with hand strengths, daily activity performance and MMT grades. This means that calculation of the ratio is of clinical value in evaluating hand functions of stroke patients in addition to seeing MEP responses. The MEP amplitude ratio needs to be emphasized and adopted as an objective and quantified index to represent the level of hand function in rehabilitation treatment. To confirm this, further studies remain to be performed.

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