

# Usefulness of the Combined Motor Evoked and Somatosensory Evoked Potentials for the Predictive Index of Functional Recovery After Primary Pontine Hemorrhage

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**Objective** To investigate the predictive index of functional recovery after primary pontine hemorrhage (PPH) using the combined motor evoked potential (MEP) and somatosensory evoked potential (SEP) in comparison to the hematoma volume and transverse diameter measured with computerized tomography.

**Methods** Patients (n=14) with PPH were divided into good- and poor-outcome groups according to the modified Rankin Score (mRS). We evaluated clinical manifestations, radiological characteristics, and the combined MEP and SEP responses. The summed MEP and SEP (EP sum) was compared to the hematoma volume and transverse diameter predictive index of global disability, gait ability, and trunk stability in sitting posture.

**Results** All measures of functional status and radiological parameters of the good-outcome group were significantly better than those of the poor-outcome group. The EP sum showed the highest value for the mRS and functional ambulatory category, and transverse diameter showed the highest value for “sitting-unsupported” of Berg Balance Scale.

**Conclusion** The combined MEP and SEP is a reliable and useful tool for functional recovery after PPH.

**Keywords** Pontine hemorrhage, Motor evoked potential, Somatosensory evoked potential, Predictive Index

Received August 27, 2013; Accepted September 13, 2013

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## INTRODUCTION

Although primary pontine hemorrhage (PPH) is rare, accounting for 5%–10% of intracranial hemorrhages [1], the mortality rate is high, ranging from approximately 40%–70% [2-5] and often leaves survivors in a severely disabled state. Currently, because of advancements in radiological tools and improvements in treatment, the

survival rate is increasing, with surviving patients often being referred to rehabilitation units. In this regard, the prevention of complications and functional recovery through accurate prognosis are important aspects of the rehabilitation strategy.

Until now, clinical characteristics or radiological parameters, such as hematoma volume or transverse diameter measured using computerized tomography (CT), have been used to determine a predictive index of functional recovery in patients with PPH [1-6]. The evoked potential (EP) is an objective neurophysiological tool to find a major neural tract, and it is widely utilized as a predictive index of functional recovery in stroke patients. The motor evoked potential (MEP) reflects the preservation of the pyramidal tracts, which play a crucial role in motor function, while a normal somatosensory evoked potential (SEP) suggests good functional recovery after stroke [7]. However, no study has yet assessed the suitability of using the combined MEP and SEP in patients with PPH to predict functional recovery. Therefore, the aim of this study was to assess the predictive index of the combined MEP and SEP in comparison to radiological parameters in patients with PPH.

## MATERIALS AND METHODS

### Subjects

Fifteen patients with PPH were recruited from the department of rehabilitation at our hospital from January 2010 to December 2012. All patient medical records were reviewed by two physicians. We excluded hemorrhages that were due to hemorrhagic transformations of an ischemic lesion, those due to arteriovenous malformation, and those that were secondary to head trauma. Patients with recurrent stroke in the pons, presence of neurologic deficits, such as peripheral polyneuropathy, and presence of contraindications to the MEP study (e.g., cardiac pacemaker, seizure history) were also excluded. All patients were treated conservatively. This study was approved by the Institutional Review Board of our institution and was performed retrospectively.

### Methods

The patients were classified into two groups: a "good" and a "poor" outcome group, according to their modified Rankin Score (mRS), measured at least 6 months from

procedure onset. mRS was classified as follows: 0, no symptoms at all; 1, no significant disability despite symptoms where patient is able to carry out all usual duties and activities; 2, slight disability where patient is unable to carry out all previous activities but is able to look out after own affairs without assistance; 3, moderate disability where patient requires some help but is able to walk without assistance; 4, moderately severe disability where patient is unable to walk without assistance and is unable to attend to own bodily needs without assistance; 5, severe disability where patient is bedridden, incontinent and requires constant nursing care and attention; and 6, deceased. The clinical features, radiological characteristics, and EP findings were compared between the two groups.

### *Clinical and radiological manifestations*

We collected data on the patients' age, sex, and presence of diabetes mellitus, hypertension, dysphagia, tracheostomy, and cranial nerve injury. Additionally, we assessed functional status, mRS for daily living activities and global disabilities, functional ambulation category (FAC, 0-5) for characterized levels of walking ability, and "sitting-unsupported" criteria of the Berg Balance Scale (SUB, 0-4) for trunk control ability [8-11].

All patients were scanned within the first 24 hours after admission. However, the largest hemorrhagic volume was measured either at the time of the initial or follow-up CT, when larger hemorrhages could be seen. We analyzed the CT manifestations as follows: first, total hematoma volume was estimated using the ellipsoid formula ( $4/3\pi \times a \times b \times c$ ) where a, b, and c represent the respective radii in three dimensions [11]. Second, the transverse diameters presenting the largest area of intraparenchymal hemorrhage were measured. Third, extension of the hemorrhage into the medulla, midbrain, and the third or fourth ventricle was noted. Fourth, the location of the hemorrhage was sorted according to the classification proposed by Chung and Park [12]: 1, massive; 2, bilateral tegmental; 3, basal-tegmental; and 4, small unilateral tegmental.

### *EP studies*

For the MEP and SEP studies, we used Nihon Kohden EMG/EP equipment (EP/EMG measuring system MEB-2200K; Nihon Kohden Corporation, Tokyo, Japan). EP

studies were performed at 62 days (range, 29–119 days) after the onset of PPH. SEPs were recorded after stimulation of the median nerve at the wrist and tibial nerve at the ankle using a stimulus frequency of 2 Hz, a pulse duration of 50 ms, and a current strong enough to cause minimal twitches of the abductor pollicis brevis and tibialis posterior muscles. Two traces of at least 500 averaged responses for each side were recorded. The cerebral responses were recorded by surface electrodes, with an active electrode over the contralateral C3 or C4 or CZ' placed according to the 10-20 system. In both cases, the reference electrode was situated at the Fz. Impedance was kept below 5 kΩ, and recordings were filtered at 10–3,000 Hz. The N20 and P38 latencies were measured for both sides [13]. MEPs were recorded from the abductor pollicis brevis and tibialis anterior muscles after stimulation of the contralateral motor cortex with a tangentially oriented figure-of-eight coil. Two sets of responses were recorded for each side. The excitatory threshold was defined as the minimum stimulus required to elicit an MEP with a peak-to-peak amplitude of 100 μV or greater in two out of four attempts [14]. The latency and amplitude of the motor response were measured for both sides. MEP and SEP responses were classified as either normal or abnormal. We defined a normal response as a score of 1, and the abnormal response as a score of 0. The sum of MEP and SEP (EP sum) was used for the assessment of the integrity of the pyramidal tract and somatosensory pathway (range, 0–8).

**Statistical analysis**

All data were analyzed using Statistical Product and Service Solutions (SPSS ver. 19; SPSS Inc., Chicago, IL, USA) and R packages (V3.0.1). The Mann-Whitney U test and Fisher exact test were used to evaluate differences in demographic data between the prognosis groups. A simple regression model was used to calculate the regression coefficient (β), p-value, and explanatory power (R<sup>2</sup>). Significance level was set at p<0.05.

**RESULTS**

The mean age of the patients was 50.14 years (range, 33–77 years). One patient was excluded because the SEP was not performed. Mean follow-up period was 23.4±11.1 months (range, 7–39 months). During the follow-up

period, one patient died 28 months after study onset. At the last time point investigated, 10 patients (71.5%) were men and 4 (28.5%) were women. Four patients (28.5%) achieved a good outcome (mRS 0, 1, 2, 3), and 10 patients (71.5%) had a poor outcome (mRS 4, 5, 6). Clinical manifestations and functional statuses according to outcome are summarized in Table 1. Age and gender frequency were not significantly different between the two groups (p=0.095 and p=0.106). The incidence of comorbidities, such as hypertension and diabetes, was also not different between the two groups. Dysphagia and tracheostomy were more common in the poor-outcome group although this finding did not reach statistical significance. In terms of functional status, mRS (p=0.002), FAC (p=0.004), and SUB (p=0.008) of the good-outcome group were significantly better compared to those of the poor-outcome group.

From the CT analysis, we found that hematoma volume (p=0.008) and transverse diameter (p=0.024) were significantly different between the two groups; 3.3±0.8 mL and 2.3±0.6 cm in the good-outcome group, and 17.4±15.2 mL

**Table 1.** Clinical manifestation and functional status

	Good outcome (n=4)	Poor outcome (n=10)	p-value <sup>a)</sup>
<b>Clinical parameter</b>			
Gender (male:female)	1:3	8:2	0.095
Age (yr)	44.8±9.3	52.3±10.8	0.106
DM	0	0	1
Hypertension	3 (75)	7 (70)	1
Dysphagia	0	7 (70)	0.070
Tracheostomy	0	6 (60)	0.085
Case of CN injury	1 (25)	4 (40)	1
<b>Functional status</b>			
mRS	1.0±1.4	5.0±0.5	0.002
FAC	3.5±1.9	0.2±0.4	0.004
SUB	4.0±0.0	0.4±1.3	0.008

Values are presented as mean±standard deviation or number (%).

CN, cranial nerve; DM, diabetes mellitus; mRS, modified Rankin Score; FAC, functional ambulatory category; SUB, “sitting-unsupported” of Berg Balance Scale.

<sup>a)</sup>p-values were calculated using the Mann-Whitney U test for continuous variables and the Fisher exact test for categorical variables.

and 3.1±0.5 cm in the poor-outcome group, respectively (Table 2). In patients, the hematoma extended into the midbrain (2 patients) or medullary area (1 patient). A further three patients showed the presence of hematomas in the ventricle. These phenomena were shown only in the poor-outcome group. Hematomas in the good-outcome group were located in the basal segmental (2 patients), small unilateral (1 patient), and small segmental areas (1 patient). Hematomas in the poor-outcome group were

mainly located in the bilateral segmental (5 patients) and basal segmental areas (3 patients). No massive hematoma type was present in the good-outcome group, and no small unilateral type was found in the poor-outcome group. Values for EP sum, MEP, and SEP were not significantly different between the two groups (Table 2).

R<sup>2</sup> values of the EP sum for mRS (R<sup>2</sup>=0.475) and FAC (R<sup>2</sup>=0.583) were higher than those for MEP (mRS, R<sup>2</sup>=0.384; FAC, R<sup>2</sup>=0.472) or SEP alone (mRS, R<sup>2</sup>=0.449; FAC, R<sup>2</sup>=0.552). All EP parameters were of low explanatory power for SUB (R<sup>2</sup>=0.212–0.312). The EP sum was negatively associated with mRS (β=-0.568, p=0.006) and positively associated with FAC (β=0.568, p=0.001) and SUB (β=0.438, p=0.045). Volume was negatively associated with SUB (β=-0.076, p=0.041) but was not associated with FAC (p=0.157) or mRS (p=0.117). Transverse diameter was positively associated with mRS (β=1.272, p=0.048) and negatively associated with SUB (β=-1.540, p=0.010) but was not associated with FAC (β=-0.737, p=0.228). R<sup>2</sup> values of the EP sum for mRS (R<sup>2</sup>=0.475) and FAC (R<sup>2</sup>=0.583) were higher than those for volume (mRS, R<sup>2</sup>=0.192; FAC, R<sup>2</sup>=0.159) and transverse diameter (mRS, R<sup>2</sup>=0.287; FAC, R<sup>2</sup>=0.287). R<sup>2</sup> values of the EP sum for SUB (R<sup>2</sup>=0.294) were slightly lower than those for volume (R<sup>2</sup>=0.305). R<sup>2</sup> values of transverse diameter (R<sup>2</sup>=0.440) for SUB were higher than those for volume and EP sum. EP sum showed the highest explanatory power for all scales except SUB, for which transverse diameter showed the highest explanatory power (Table 3).

**Table 2.** Radiological and evoked potential characteristics

	Good outcome (n= 4)	Poor outcome (n= 10)	p-value <sup>a)</sup>
<b>Radiologic finding</b>			
Volume (mL)	3.1±0.5	17.4±15.2	0.008
TD (cm <sup>2</sup> )	2.3±0.6	3.3±0.8	0.024
Extrapontine area	0	4	0.251
Location	1/2/1/0	0/3/5/2	-
<b>Evoked potential</b>			
EP sum (0-8)	5.0±2.9	2.3±1.9	0.106
MEP (0-4)	2.8±1.3	1.4±1.3	0.106
SEP (0-4)	2.3±1.7	0.9±0.9	0.142

Values are presented as mean±standard deviation.

TD, transverse hematoma; Location, location type of hematoma is given as frequencies of location (small unilateral/basal segmental/bilateral segmental/massive); MEP, motor evoked potential; SEP, somatosensory evoked potential; EP sum, the sum of MEP and SEP.

<sup>a)</sup>p-values were calculated using the Mann-Whitney U test for continuous variables and by Fisher exact test for categorical variables.

## DISCUSSION

In this study, we have confirmed the usefulness of the

**Table 3.** Comparison between EP and radiological parameters as a predictive index

	EP parameter									Radiological parameter					
	MEP			SEP			EP sum			Volume			Transverse diameter		
	β	P-value <sup>a)</sup>	R <sup>2</sup>	β	P-value <sup>a)</sup>	R <sup>2</sup>	β	P-value <sup>a)</sup>	R <sup>2</sup>	β	P-value <sup>a)</sup>	R <sup>2</sup>	β	P-value <sup>a)</sup>	R <sup>2</sup>
mRS	-0.921	0.018	0.384	-1.075	0.009	0.449	-0.568	0.006	0.475	0.062	0.117	0.192	1.272	0.048	0.287
FAC	0.921	0.007	0.472	1.075	0.002	0.552	0.568	0.001	0.583	-0.051	0.157	0.159	-0.737	0.228	0.118
SUB	0.669	0.098	0.212	0.877	0.038	0.312	0.438	0.045	0.294	-0.076	0.041	0.305	-1.540	0.010	0.440

EP, evoked potential; MEP, motor evoked potential; SEP, somatosensory evoked potential; β, regression coefficient; R<sup>2</sup>, R square; mRS, modified Rankin Scale; FAC, functional ambulatory category; SUB, “sitting-unsupported” of Berg Balance Scale.

<sup>a)</sup>p-values were calculated using simple linear regression.

combining of MEP and SEP measures for the prediction of functional recovery in patients with PPH. In addition, we found that the combined MEP and SEP was a more powerful tool than measuring either the transverse diameter or volume using CT. To the best of our knowledge, this is the first study suggesting that the combined MEP and SEP is a better indicator than volume and transverse diameter for predicting functional recovery after PPH.

The clinical symptoms of PPH include not only sensorimotor dysfunction but also dysphagia, oculomotor abnormality (dilated pupil), and respiration failure, which often lead to serious complications [3]. Previous studies on PPH have mainly focused on the factors associated with mortality [3,12,15-17]. Regarding functional recovery, the clinical parameters for a good outcome are considered to be an intact consciousness, good muscle power, and a normal pupil response [2,5]. Only a few studies have been analyzed using different parameters, such as the Glasgow Outcome Scale, activity of daily living, and mRS. In these studies, good recovery rates were considered to be 40.7%–63% using the Glasgow Outcome Scale [1-3] and 54.5% using activity of daily living [4]. In analyzing 99 survivors at 3 months post-PPH, Jang et al. [5] reported that a good recovery rate using MRS is 19.1%, whereas, in our study, it was 28.5% at 23.4 months post-PPH. However, it is difficult to directly compare good recovery rates as analyses were not conducted at the same time the selection of patients. Our results also demonstrate that clinical parameters affect the quality of life of patients, by showing that in the poor-outcome group the self-feeding rate was 30% (3/10 cases) and the de-cannulation rate was 40% (4/10 cases) (Table 1). We expect that this data will be useful in the prevention of complications and in the planning of rehabilitation therapy.

Previous studies have reported that when using CT, the following parameters are predictive of a good recovery: 1, hematoma volume less than 4–5 mL; 2, maximal transverse diameter less than 20 mm; 3, no hematoma of the ventricle or extrapontine area; and 4, hematoma located on the dorsal area [1,2,4-6]. The CT parameters in this study also demonstrated similar results to those in the good-outcome group:  $3.1 \pm 0.5$  mL hematoma volume,  $2.3 \pm 0.6$  cm transverse diameter, and no hematoma of the extrapontine area or in the ventricle (Table 2). Regardless of these beneficial effects, some limitations have been noted when using imaging parameters for the

identification and determination of pyramidal tract and somatosensory pathway functional integrity. Generally, functional impairment after stroke is influenced by motor weakness due to damage of the pyramidal tract. In addition, sensory loss is experienced by up to 65% of patients with stroke [18,19]. These two tracts play a critical role in fine motor coordination and skillful movements [20,21]. MEP and SEP have been implicated in the prediction of functional recovery as well as in assessing the integrity of the pyramidal tract and somatosensory pathway after stroke. In a previous study, an attempt was made to provide a prognosis of patients with pontine hemorrhage using brain auditory EP and SEP. However, no conclusion was drawn due to 12 cases of death amongst the 17 subjects [22]. In 2010, Lee et al. [7] reported for the first time that the assessment of the combined MEP and SEP after stroke provides a better prediction of functional recovery than do MEP or SEP alone. We also confirm that EP sum for mRS and FAC has higher explanatory power than do MEP or SEP alone. In addition to using the combined MEP and SEP in our study, we also analyzed and compared the hematoma volume and transverse diameter based on CT findings. We found that for all functional measures other than SUB, the EP showed the highest statistical significance and  $R^2$  value (mRS:  $p=0.006$ ,  $R^2=0.475$ ; FAC:  $p=0.001$ ,  $R^2=0.583$ ; SUB:  $p=0.045$ ,  $R^2=0.294$ ) (Table 3). However, SUB seems to be poorly represented in our study compared to FAC and mRS since postural stability may be further influenced by various vestibular, auditory, and visual factors. Collectively, our results have confirmed the usefulness and reliability of the predictive index of functional recovery after PPH when using the combined MEP and SEP. In summary, the combined MEP and SEP is superior in reducing individual variability and objectively delineates the pyramidal tract and somatosensory pathway. Nevertheless, the following limitations should be considered. First, this study was restricted only to patients referred to the rehabilitation department, and the sample size was relatively small. Second, it is difficult to predict early functional recovery following PPH because the time-point of the examination using the combined MEP and SEP varied. Third, this study did not reflect functions other than sensorimotor function.

In conclusion, we suggest that the combined MEP and SEP is a useful tool for the prediction of functional recovery in patients with PPH.



## CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

## ACKNOWLEDGMENTS

This research was supported by Basic Science Research Program through the National Research Foundation of Korea funded by the Ministry of Education (No. 2013R1A1A4A01013178).

## REFERENCES

1. Wessels T, Moller-Hartmann W, Noth J, Klotzsch C. CT findings and clinical features as markers for patient outcome in primary pontine hemorrhage. *AJNR Am J Neuroradiol* 2004;25:257-60.
2. Wijdicks EF, St Louis E. Clinical profiles predictive of outcome in pontine hemorrhage. *Neurology* 1997;49:1342-6.
3. Murata Y, Yamaguchi S, Kajikawa H, Yamamura K, Sumioka S, Nakamura S. Relationship between the clinical manifestations, computed tomographic findings and the outcome in 80 patients with primary pontine hemorrhage. *J Neurol Sci* 1999;167:107-11.
4. Jung DS, Jeon BC, Park YS, Oh HS, Chun TS, Kim NK. The predictors of survival and functional outcome in patients with pontine hemorrhage. *J Korean Neurosurg Soc* 2007;41:82-7.
5. Jang JH, Song YG, Kim YZ. Predictors of 30-day mortality and 90-day functional recovery after primary pontine hemorrhage. *J Korean Med Sci* 2011;26:100-7.
6. Masiyama S, Niizuma H, Suzuki J. Pontine haemorrhage: a clinical analysis of 26 cases. *J Neurol Neurosurg Psychiatry* 1985;48:658-62.
7. Lee SY, Lim JY, Kang EK, Han MK, Bae HJ, Paik NJ. Prediction of good functional recovery after stroke based on combined motor and somatosensory evoked potential findings. *J Rehabil Med* 2010;42:16-20.
8. Banks JL, Marotta CA. Outcomes validity and reliability of the modified Rankin scale: implications for stroke clinical trials: a literature review and synthesis. *Stroke* 2007;38:1091-6.
9. Oh HM, Im S, Ko YA, Ko SB, Park GY. The sitting-unsupported balance score as an early predictor of functional prognosis in stroke patients: a pilot study. *Ann Rehabil Med* 2013;37:241-6.
10. Mehrholz J, Wagner K, Rutte K, Meissner D, Pohl M. Predictive validity and responsiveness of the functional ambulation category in hemiparetic patients after stroke. *Arch Phys Med Rehabil* 2007;88:1314-9.
11. Broderick JP, Brott TG, Duldner JE, Tomsick T, Huster G. Volume of intracerebral hemorrhage: a powerful and easy-to-use predictor of 30-day mortality. *Stroke* 1993;24:987-93.
12. Chung CS, Park CH. Primary pontine hemorrhage: a new CT classification. *Neurology* 1992;42:830-4.
13. Rossini PM, Narici L, Martino G, Pasquarelli A, Peresson M, Pizzella V, et al. Analysis of interhemispheric asymmetries of somatosensory evoked magnetic fields to right and left median nerve stimulation. *Electroencephalogr Clin Neurophysiol* 1994;91:476-82.
14. Jang SH, Ahn SH, Sakong J, Byun WM, Choi BY, Chang CH, et al. Comparison of TMS and DTT for predicting motor outcome in intracerebral hemorrhage. *J Neurol Sci* 2010;290:107-11.
15. Lancman M, Norscini J, Mesropian H, Bardeci C, Bauso T, Granillo R. Tegmental pontine hemorrhages: clinical features and prognostic factors. *Can J Neurol Sci* 1992;19:236-8.
16. Dziewas R, Kremer M, Ludemann P, Nabavi DG, Dräger B, Ringelstein B. The prognostic impact of clinical and CT parameters in patients with pontine hemorrhage. *Cerebrovasc Dis* 2003;16:224-9.
17. Balci K, Asil T, Kerimoglu M, Celik Y, Utku U. Clinical and neuroradiological predictors of mortality in patients with primary pontine hemorrhage. *Clin Neurol Neurosurg* 2005;108:36-9.
18. Patel AT, Duncan PW, Lai SM, Studenski S. The relation between impairments and functional outcomes poststroke. *Arch Phys Med Rehabil* 2000;81:1357-63.
19. Carey LM, Matyas TA. Frequency of discriminative sensory loss in the hand after stroke in a rehabilitation setting. *J Rehabil Med* 2011;43:257-63.
20. Davidoff RA. The pyramidal tract. *Neurology* 1990;40:332-9.
21. Johansson RS, Cole KJ. Sensory-motor coordination during grasping and manipulative actions. *Curr Opin Neurobiol* 1992;2:815-23.
22. Ferbert A, Buchner H, Bruckmann H. Brainstem auditory evoked potentials and somatosensory evoked potentials in pontine haemorrhage: correlations with clinical and CT findings. *Brain* 1990;113(Pt 1):49-63.