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Study of Short Latency Somatosensory and Brain Stem Auditory Evoked Potentials Patients with Acute Ischemic Stroke Involving Middle Cerebral Artery Territory

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Abstract

Background The precise timings of evoked potentials in evaluating the functional outcome of stroke have remained indistinct. Few studies in the Indian context have studied the outcome of early prognosis of stroke utilizing evoked potentials.

Objective The aim of this study was to determine somatosensory evoked potentials (SSEPs) and brain stem auditory evoked potentials (BAEPs), their timing and abnormalities in acute ischemic stroke involving the middle cerebral artery (MCA) territory and to correlate SSEP and BAEP with the functional outcome (National Institutes of Health Stroke Scale (NIHSS), modified Rankin scale (mRS) and Barthel's index) at 3 months.

Methods MCA territory involved acute ischemic stroke patients (n = 30) presenting consecutively to the hospital within 3 days of symptoms onset were included. Details about clinical symptoms, neurological examination, treatment, NIHSS score, mRS scores were collected at the time of admission. All patients underwent imaging of the brain and were subjected to SSEP and BAEP on two occasions, first at 1 to 3 days and second at 4 to 7 days from the onset of stroke. At 3 months of follow-up, NIHSS, mRS, and Barthel's index were recorded.

Results P37 and N20 amplitude had a strong negative correlation (at 1–3 and 4–7 days) with NIHSS at admission, NIHSS at 3 months, mRS at admission, and mRS at 3 months and a significant positive correlation with Barthel's index ($p < 0.0001$). BAEP wave V had a negative correlation (at 1–3 and 4–7 days) with NIHSS at admission, NIHSS at 3 months, mRS at admission, and mRS at 3 months and a positive correlation with Barthel's index ($p < 0.0001$).

Conclusion SSEP abnormalities recorded on days 4 to 7 from onset of stroke are more significant than those recorded within 1 to 3 days of onset of stroke; hence, the timing of 4 to 7 days after stroke onset can be considered as better for predicting functional outcome.

Keywords
- somatosensory evoked potentials
- stroke
- middle cerebral artery
- neurologic examination
- prognosis

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Introduction

Globally, stroke is the second most common disabling neurological disorder leading to 5 million deaths every year.[1] Middle cerebral artery (MCA) is the most affected blood vessel in stroke.[2] Computed tomography (CT) and magnetic resonance imaging (MRI) are the currently employed neuroimaging techniques in the prognosis of stroke.[3] However, evoked potentials have the advantage of being objective and more sensitive in evaluating the consequences of lesions in stroke over detailed neurological examinations.[1]

The infarction of MCA territory is often associated with poor functional outcome.[4] The functional outcome in MCA territory infarction can be predicted using various clinical and nonclinical parameters. Clinical assessment can be done by scoring systems like National Institutes of Health Stroke Scale (NIHSS), and 90 days modified Rankin Scale (mRS).[4] Radiological assessment can be done by scoring systems like the Alberta stroke program early CT score (ASPECTS) that provide nonclinical parameters predicting the outcome of the stroke.[5]

Measurement of evoked potentials is the standard noninvasive neurophysiological technique to demonstrate abnormal sensory potential when the history or clinical examination is equivocal in revealing an unsuspected clinical abnormality in the sensory system.[6] Literature describes early prognosis may also improve the treatment strategies of stroke.[7] Somatosensory evoked potentials (SSEPs) and brain stem auditory evoked potentials (BAEPs) are the useful, noninvasive means of assessing somatosensory and auditory system functioning.[2,8] Previous studies also reported that short-latency SSEPs N20 and BAEP wave V within 7 days of stroke were highly consistent with the patient outcome.[7,9,10] However, few studies from the Indian context have studied the outcome of early prognostication of stroke utilizing evoked potentials. Hence, this study intended to determine SSEP and BAEP timing and abnormalities in acute ischemic stroke involving the MCA territory and its correlation with the functional outcome (modified Rankin scale and Barthel's index) at 3 months.

Methods

MCA territory involved acute ischemic stroke patients presenting consecutively to the hospital within 3 days of symptoms onset were included. Details about clinical symptoms, neurological examination treatment, NIHSS score,[11] and mRS scores[12] as per the proforma were collected admission. All patients underwent imaging of the brain and subjected to SSEPs and BAEPs.

Magnetic resonance imaging (MRI) was performed by a 1.5-Tesla scanner on the day of admission after symptom onset. Infarct volume was assessed using diffusion-weighted imaging (DWI) sequence of MRI. Absolute volumes measured by planimetry were compared with estimates of ellipsoid ABC/2 for DWI volume.[13] At 3 months of follow-up, NIHSS, mRS, and Barthel's index[14] were collected.

Recording of the evoked potentials was done using a Nihon Kohden Neuropack EMG/EP Measuring System. SSEPs were obtained by applying an electric stimulus up to 100 mA at the wrist with a frequency of 2.1 Hz for a duration of 30 seconds. N20 latency, N20 amplitude, P37 amplitude, and P37 latency were the different parameters assessed. Under similar settings as SSEP, BAEP was performed by placing surface electrodes with conducting jelly and impedance below 5k ohms. BAEP recording was done on Vertex using amplification of 2, 00,000 to 5, 00, 000 with a filter set at 100 to 3000 HZ for a duration of 10 milliseconds.

Statistical Analysis

Data were analyzed using statistical software R v 3.6.3. Categorical variables were represented in the form of frequency distribution. Continuous variables were represented by mean ± standard deviation and analyzed using paired-*t* test. Correlation of evoked potential with NIHSS, mRS, and Barthel's index was done using Pearson's correlation coefficient and Spearman's rank correlation. A p-value ≤ 0.05 indicates statistical significance.

Results

The mean age of patients was 64.1 ± 10.5 years. Most patients were within the age range of 61 to 70 years (46.67%) and predominantly male (66.67%). Most patients presented with dysarthria (60%) and weakness (right: 43.33%; left: 50%). The most common clinical deficit was hemiparesis (90%; ►**Table 1**). Wave V of BAEP was abnormal only in large volume infarcts, with mean infarct volume measuring 150.3 cm^3. The mean volume of infarct with abnormal SSEP in this study was 41.77 cm^3.

P37 latency and N20 amplitude were significantly less at 1 to 3 days post-admission compared with 4 to 7 days post-admission. However, P37 amplitude, N20 latency, and wave V of BAEP were significantly more in 1 to 3 days compared with 4 to 7 days (►**Table 2**).

No correlation was found between P37 latency and NIHSS, mRS, and Barthel's index at 3 months. A strong negative correlation was found between P37 amplitude (at 1–3 days and 4–7 days) and NIHSS at admission, NIHSS at 3 months, mRS at admission, and mRS at 3 months. However, a strong positive correlation was found between P37 amplitude (1–3 days and 4–7 days) and Barthel's index ($p < 0.001$). A strong negative correlation was found between N20 amplitude (at 1–3 days and 4–7 days) and NIHSS at admission, NIHSS at 3 months, mRS at admission, and mRS at 3 months, while a strong positive correlation was observed with Barthel's index ($p < 0.001$). A moderate significant negative correlation was found between BAEP wave V (at 1–3 days and 4–7 days) with NIHSS at admission, NIHSS at 3 months, mRS at admission, and mRS at 3 months and a moderate positive correlation was observed with Barthel's index ($p < 0.001$; ►**Table 3**).

Table 1 Baseline characteristics of the study participants

Variables	Number of subjects (%)
Age (y)	
40–50	3 (10%)
51–60	6 (20%)
61–70	14 (46.67%)
71–80	6 (20%)
≥ 81	1 (3.33%)
Gender	
Male	20 (66.67%)
Female	10 (33.33%)
Symptoms	
Altered mental state	
Present	1 (3.33%)
Absent	29 (96.67%)
Aphasia	
Present	14 (46.67%)
Absent	16 (53.33%)
Dysarthria	
Present	18 (60%)
Absent	12 (40%)
Weakness	
Right hemiparesis	13 (43.33%)
Left hemiparesis	15 (50%)
Absent	2 (6.67%)
Sensory loss	
Present	14 (46.67%)
Absent	16 (53.33%)
Mean size of infarct (cm^3)	
N20 Latency	42.94286
N20 amplitude	46.4
P37 Latency	43.92308
P37 amplitude	40.58125
Wave V of BAEP	150.36583

Abbreviation: BAEP, brain stem auditory evoked potential.

Discussion

Numerous pathological mechanisms that include ischemia, spinal cord compression, tumor, and demyelination may influence somatosensory conduction and evoke abnormalities in SSEP testing and its results.[15] The absence of certain SSEPs waveforms can signify brain death. Median nerve SSEPs are often used in combination with lower-extremity SSEPs to gain more prognostic information.[16] Hence, SSEPs theoretically resemble BAEPs and correlate well with electrophysiological changes and cortical blood flow has been used to assess cerebral function and ischemic stroke.[17-19]

Although evoked potentials have been widely used in the prediction of stroke outcomes, the precise timing in the emergence of SSEP and BAEP in the early detection of stroke is not clear. Previous research has reported that early prediction, that is, within < 7 days of onset of stroke with the use of evoked potentials may ease the management of stroke through appropriate planning and organization. The study also stated late diagnosis may lead to development of potential complications such as edema and remains a longer period.[19] Hence, in this study, SSEP and BAEP were performed within 1 to 3 days and 4 to 7 days after onset of stroke affecting the MCA territory to demonstrate the ideal timing of SSEP and BAEP in the evaluation of stroke.

We found that there was a worsening of the SSEP waveform abnormalities on 4 to 7 days after onset of stroke compared with SSEP done 1 to 3 days after the onset of stroke. The pathogenic mechanisms for recording of abnormal potentials include cortical depression and diaschisis.[20,21] Zhang et al[7] also reported that N20 of SSEP and wave V of BAEP after 4 to 7 days of stroke onset better predict the stroke outcome. Tzvetanov and Rousseff[22] found that median nerve SSEP had an independent predictive value in the functional recovery, while the combined assessment of median nerve SSEP and Medical Research Council scale improved the prognosis in acute stroke.

Apart from N20 of the median nerve, we also noted an abnormal lower limb SSEP. The amplitude of P37 of the tibial nerve also had a strong negative correlation with the NIHSS, mRS, and with Barthel's index, both at 1 to 3 days and 4 to 7 days. The territory innervating the lower limb in the brain is supplied mainly by the anterior cerebral artery, but the pathways to the cortical areas generating lower limb SSEP are situated in zones of subcortical

Table 2 Comparison of waveforms at 1 to 3 days and 4 to 7 days post-admission

Variable	Days		*p*-Value
	1–3	4–7	
P37 latency	31.13 ± 15.88	33.8 ± 17.59	0.0003
P37 amplitude	1.75 ± 1.03	1.35 ± 1.05	0.0001
N20 latency	19.77 ± 10.37	21.19 ± 11.75	0.011
N20 amplitude	1.57 ± 1.01	1.29 ± 1.09	0.001
Wave V of BAEP	4.33 ± 2.22	4.15 ± 2.12	<0.0001

Abbreviation: BAEP, brain stem auditory evoked potential.

Table 3 Correlation of SSEP and BAEP with NIHSS, mRS, and Barthel's index at admission and at 3-month follow-up

Variables		NIHSS at admission	NIHSS 3 months	mRS at admission	mRS 3 months	Barthel's index at 3 months
P37 latency	1–3 days	ρ = 0.2421 0.1973	ρ = 0.3171 0.08779	ρ = 0.2451 0.1918	ρ = 0.3061 0.1	ρ = 0.2748 0.1417
	4–7 days	ρ = 0.1024 0.5901	ρ = 0.1113 0.5579	ρ = 0.0871 0.647	ρ = 0.1234 0.5159	ρ = 0.13192 0.4871
P37 amplitude	1–3 days	*r* = 0.8616 < 0.0001[a]	*r* = 0.8643 < 0.0001[a]	*r* = 0.6510 < 0.0001[a]	*r* = 0.8353 < 0.0001[a]	ρ = 0.8331 < 0.0001[a]
	4–7 days	*r* = 0.8465 < 0.0001[a]	*r* = 0.7576 < 0.0001[a]	*r* = 0.8527 < 0.0001[a]	*r* = 0.8388 < 0.0001[a]	ρ = 0.6591 < 0.0001[a]
N20 latency	1–3 days	ρ = 0.0458 0.8099	ρ = 0.0734 0.6998	ρ = 0.0027 0.9885	ρ = 0.0592 0.7557	ρ = 0.06317 0.7401
	4–7 days	ρ = 0.03579 0.8511	ρ = 0.1111 0.5589	ρ = 0.05631 0.7676	ρ = 0.1185 0.5329	ρ = 0.1270 0.5033
N20 amplitude	1–3 days	*r* = 0.8738 < 0.0001[a]	*r* = 0.82019 < 0.0001[a]	*r* = 0.79854 < 0.0001[a]	*r* = 0.8584 < 0.0001[a]	ρ = 0.7200 < 0.0001[a]
	4–7 days	*r* = 0.7623 < 0.0001[a]	*r* = 0.6835 < 0.0001[a]	*r* = 0.79732 < 0.0001[a]	*r* = 0.7460 < 0.0001[a]	ρ = 0.7025 < 0.0001[a]
Wave V of BAEP	1–3 days	ρ = 0.51502 0.004[a]	ρ = 0.50993 0.004[a]	ρ = 0.50718 0.004[a]	ρ = 0.54037 0.002[a]	ρ = 0.56508 0.0011[a]
	4–7 days	ρ = 0.52875 0.0026[a]	ρ = 0.49141 0.0058[a]	ρ = 0.50210 0.0046[a]	ρ = 0.53349 0.0023[a]	ρ = 0.52105 0.0032[a]

Abbreviations: BAEP, brain stem auditory evoked potential; mRS, modified Rankin scale; NIHSS, National Institutes of Health Stroke Scale; SSEP, somatosensory evoked potential; *r*, Pearson's correlation coefficient; *ρ*, Spearman's rank correlation coefficient.
[a]Significant

supply of MCA. Therefore, it correlates with the subcortical white matter ischemia.[23] Most studies emphasize median nerve SSEP prognostic value in regard to both motor and functional in stroke outcome.[8,24,25] However, changes in tibial SSEPs have been reported in a few papers.[25,26] Tzvetanov et al reported that tibial SSEP investigation early in the stroke, that is, within 3 to 19 days of stroke onset independently or in combination with muscle power assessment significantly increases the prognostic capability.[26] Kovala who studied SSEP in 3 to 19 days after stroke onset reported a greater prognostic value for the tibial nerve SSEP than the median nerve.[16] Eksantivongs et al reported that although both median and tibial SSEPs abnormalities have high positive predictive value and are very sensitive in the assessment of neurological disability, they failed to exclude severe neurological deficits.[27] Another interesting study by Lee et al[28] reported that the preserved lower limb SSEP significantly improves the balance in subacute hemiparetic stroke.

The wave V of BAEP is a robust predictor of brain stem function. The impairment of brain stem function in any disease or complication of supratentorial region affects the generation of wave V of BAEP from the inferior colliculus.[10] Hence, the abnormalities of wave V of BAEP are generally found in brain stem lesions caused by stroke, demyelination, or mass lesions. In this study, wave V was absent in six patients who had poor recovery at 3 months of follow-up. A similar study by Burghaus et al[2] reported that wave V of BAEP has significant prognostic value in predicting the outcome and management strategies. Another study that performed SSEP and BAEP within 1 week of onset of stroke in patients with spontaneous putaminal hemorrhage found that patients with absent SSEP and wave V of BAEP were severely disabled after 6 months of follow-up.[19]

Certainly, the study has a few limitations. First, the study has a low sample size, therefore, further large scale multicentric studies need to be implemented to validate the current study findings. Second, the study did not exclude asymptomatic underlying small vessel diseases.

Conclusion

SSEP abnormalities recorded on days 4 to 7 from the onset of stroke are more significant than those recorded within 1 to 3 days of onset of stroke for assessing the functional outcome. Hence, 4 to 7 days after stroke onset can be considered as better timing for predicting functional outcome. Abnormal N20 of the median nerve and P37 of the tibial nerve are useful in assessing the functional outcome. Overall, it can be concluded that SSEP and BAEP can be helpful in the evaluation of prognosis in patients suffering from acute MCA territory infarcts within 1 week of onset of stroke.

Authors' Contributions

A.M: concept/design/literature search/data analysis/manuscript preparation and editing; M.J.: concept/design/manuscript preparation, editing and review; A.M.: design and literature search; P.R.: manuscript review; PA: design/manuscript review; R.S.: manuscript review.

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Conflict of Interest
None declared.

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