Assessment of Median Nerve Somatosensory Evoked Potentials in Cerebral Ischemia

Peggy S. Gott, PhD, Dean S. Karnaze, MD, and Mark Fisher, MD

Seventy patients with cerebral ischemia (21 with transient ischemic attack and 49 with stroke) were studied with short-latency median nerve somatosensory evoked potentials to characterize the evoked potentials in all ischemic patients and to investigate their efficacy for prognosis in stroke. Within 72 hours of symptom onset, all 70 patients received a scaled neurologic function score, with a maximum of 50 points. Somatosensory evoked potential abnormalities were found in 10% (2/19), 42% (15/36), and 93% (14/15) of all patients with initial neurologic examinations who had normal (50 points), mild-moderate (30–49 points), and severe deficits (≤29 points), respectively. Thirty-seven of the 49 stroke patients were available for a follow-up neurologic assessment. Eighty-nine percent (8/9) of the stroke patients with poor outcome had somatosensory evoked potential abnormalities; 82% (9/11) of the stroke patients with severe neurologic deficits at onset had poor outcome. Results demonstrate that somatosensory evoked potential abnormalities are common in patients with cerebral ischemia but that somatosensory evoked potential findings are not significantly better than a detailed neurologic examination in predicting outcome from stroke. (Stroke 1990;21:1167–1171)

Subjects and Methods

Seventy patients, 36 men and 34 women aged 25–82 years (mean ± SD 53.8 ± 11.9 years), with signs and/or symptoms of cerebral ischemia were examined and given a neurologic function score (NFS), with a maximum of 50 points, within 72 hours of the event (NFS1). Of the 70 patients, 49 had stroke and the remaining 21 transient ischemic attacks. Thirty-seven of the 49 patients with stroke were available for an outcome NFS at approximately 2 months (mean ± SD 70 ± 41 days) after the acute event (NFS2). This was done in accordance with guidelines of the institutional review committee. Initial deficit was categorized by NFS1 totals as follows: normal, 50 points; mild to moderate, 30–49 points; and severe, ≤29 points. Outcome was defined by NFS2 totals as follows: good, 50 points; fair, 30–49 points; and poor, ≤29 points. Scoring for the NFS was as follows: 1) level of consciousness: alert, 12 points; lethargy, 8 points; stupor, 4 points; coma, 0 points; 2) conjugate eye movements: normal, 3 points; nystagmus, 2 points; mild gaze palsy, 1 point; moderate to severe gaze palsy, 0 points; 3) visual fields: normal, 5 points; quadrantanopsia, 3 points; hemianopsia, 0 points; 4) speech, language, facial movement, light touch, pinprick, joint position, stereognosis, extinction, finger-nose, and heel-knee-shin examinations: 2 points maximum for each; 1 point for mild impairment; 0 points for moderate to severe impairment; 5) upper extremity strength and lower extremity strength with a maximum of 5 points for each, using a standard

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ssessment in the acute state and prediction of outcome after cerebral ischemia have been evaluated primarily by clinical examination. Numerous scoring systems with varying degrees of accuracy have been developed to evaluate the functional severity of acute stroke and to determine prognosis.1–8 More recently, evaluation by median nerve somatosensory evoked potentials (SEPs) has been applied in the prediction of stroke outcome.9–12 The reports indicate significant association between SEP abnormalities and various outcome measurements primarily classified on a functional level. In this study, we characterized the SEPs in both transient ischemic attack and stroke and investigated efficacy of SEPs versus the neurologic examination in prediction of outcome in the stroke patients. The initial neurologic evaluation and outcome determination were quantified from a scaled neurologic examination. This is the first study to address the question of whether SEPs have better predictive power than the clinical exam for stroke prognosis.

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**Table 1. Measurements of Somatosensory Evoked Potentials From 68 Age-Matched Control Subjects**

<table>
<thead>
<tr>
<th>Wave measurements</th>
<th>Age group (yr)</th>
<th>18–39 (n=30)</th>
<th>40–59 (n=18)</th>
<th>60–85 (n=20)</th>
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<tbody>
<tr>
<td>Latency (msec)</td>
<td></td>
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<tr>
<td>N9</td>
<td>9.94±0.75</td>
<td>10.00±1.11</td>
<td>10.73±1.05</td>
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<tr>
<td>N9–N13</td>
<td>3.58±0.39</td>
<td>3.74±0.54</td>
<td>3.75±0.68</td>
<td></td>
</tr>
<tr>
<td>N13–N19</td>
<td>5.64±0.37</td>
<td>5.72±0.49</td>
<td>6.05±0.76</td>
<td></td>
</tr>
<tr>
<td>P22</td>
<td>22.00±0.96</td>
<td>22.33±1.55</td>
<td>23.77±1.70</td>
<td></td>
</tr>
<tr>
<td>Amplitude (μV)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N19–P22</td>
<td>0.94–6.27</td>
<td>0.79–6.01</td>
<td>0.64–4.75</td>
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<tr>
<td>P22 ratio</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.03–2.54</td>
<td>1.05–2.32</td>
<td>1.00–2.61</td>
<td></td>
</tr>
<tr>
<td>interhemispheric</td>
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Values are mean±SD for latency data; amplitude is presented as a range of values.

5-point strength grading system: normal, 5 points; mild weakness, 4 points; moderate weakness but able to overcome gravity, 3 points; cannot overcome gravity, 2 points; flicker, 1 point; no movement, 0 points. With bilateral involvement, scoring was performed on the side of greater involvement.

Patients were characterized as having a transient ischemic attack or stroke based on the duration of the ischemic event. Duration of symptoms greater than 24 hours were classified as stroke rather than transient ischemic attack. Clinical, computed tomographic, and, when available, arteriographic information was used to classify the patients with regard to underlying etiology. The four basic disease classifications were 1) large vessel atherosclerotic occlusive, 2) cardiogenic, 3) lacunar, and 4) undetermined. Criteria for large vessel disease consisted of symptoms of internal carotid, anterocerebral, middle cerebral, posterocerebral, or vertebrobasilar insufficiency, without evidence of vasculitis or cardiac embolic source and with confirmatory details provided by computed tomography and, when available, arteriography. Criteria for cardiogenic processes consisted of the presence of an embolicigenic cardiac arrhythmia or valvular disease, electrocardiographic evidence of myocardial infarction with echocardiographic demonstration of an embolic source, or myocardial infarction in a patient with large vessel symptoms and normal cerebral arteriography. Criteria for lacunar disease consisted of clinical evidence for any of the four classic lacunar syndromes, that is, pure motor hemiparesis, pure sensory stroke, ataxic hemipareses, and dysarthria-clumsy hand syndrome, with either normal computed tomogram or one demonstrating small deep infarcts. Patients who did not fit into any of the three etiologic syndromes were placed into the undetermined category.

Short-latency SEPs were performed on all 70 patients within 3.93±2.44 (mean±SD) days of the event. Tests were performed with a Nicolet Pathfinder II (Nicolet Instrument Corp., Madison, Wis.). Each median nerve was stimulated independently with a 0.1-msec constant current pulse at a rate of 5.1 Hz. Stimulus intensity was just sufficient enough to elicit a twitch of the thenar muscles. One thousand stimuli were averaged for a 50-msec epoch with 512 points.

Montage for recording the SEP was at electrode positions Fz–EP, Fz–C2, and Fz–C3' or C4' (EP, Erb's point; C2, second cervical vertebra; C3' or C4', 2 cm posterior to the standard C3 or C4 positions on the hemisphere contralateral to the nerve stimulated). Amplification was 200,000, and bandpass was 30–1,500 Hz.

Somatosensory evoked potential measurements were made for the following peak and interpeak latencies: N9 (from EP), N13, N19, P22, N13–N19 (central conduction time), N13–P22, N9–N13. The P22 amplitude (peak-to-peak N19 to P22) was determined, and an interhemispheric P22 ratio was calculated (larger divided by smaller).

For SEP analysis, each patient's results were compared with the appropriate age-matched normative data, which was grouped into three age ranges: 18–39 years (n=30, mean±SD 28.4±4.0 years), 40–59 years (n=18, mean±SD 51.1±5.5 years), and ≥60 years (n=20, mean±SD 70.4±6.4 years). Normal upper limits for latencies of each age group were calculated by using the mean±3 SDs (Table 1). For measurements that were not normally distributed such as the P22 amplitude and interhemispheric amplitude ratio, a 95% tolerance limit was defined. Peaks were also considered abnormal when absent.

Somatosensory evoked potentials were read as normal or abnormal before neurologic examination results were known to the interpreter. Subsequently, associations between the SEP, NFS1, NFS2, and related clinical data were evaluated by χ² or Fisher's exact test.

**Results**

Somatosensory evoked potential abnormalities were found in 44% (31/70) of the patients. The types and number of primary abnormalities are shown in Table 2. Two patients had more than one primary abnormality that could not be attributed to a more caudal disturbance (e.g., N9–N13 and N13–N19), and three patients had bilateral abnormalities.
Somatosensory evoked potential abnormalities in patients with cerebral ischemia were compared with specific clinical findings. History of a previous event or etiology were not significantly associated with the SEP results. There was no difference in the number of patients with hemispheric as compared with nonhemispheric events for frequency of abnormal SEPs and poor outcome. Sensory loss and motor deficit were both significantly associated with SEP results \((p \leq 0.004 \text{ and } p \leq 0.001, \text{ respectively})\). Most patients had more than one type of sensory involvement (e.g., joint position and light touch). Eighty percent (16/20) of patients with a disturbance in joint position had abnormal SEPs whereas 31% (4/13) with sensory deficits other than proprioception had an SEP abnormality. Twenty patients had both sensory and motor abnormalities; 16 of these 20 patients (80%) had abnormal SEPs. Five of nine (55%) with only a motor deficit also had abnormal SEPs.

TABLE 2. Somatosensory Evoked Potential Abnormalities in Patients With Cerebral Ischemia

<table>
<thead>
<tr>
<th>Wave measurements</th>
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<tbody>
<tr>
<td>N9–N13 prolonged</td>
<td>2*</td>
</tr>
<tr>
<td>N13–N19 prolonged</td>
<td>9</td>
</tr>
<tr>
<td>N13 absent</td>
<td>3</td>
</tr>
<tr>
<td>P22 latency prolonged</td>
<td>3</td>
</tr>
<tr>
<td>P22 amplitude ratio reduced</td>
<td>4</td>
</tr>
<tr>
<td>N19 and P22 reduced or absent</td>
<td>12t</td>
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</tbody>
</table>

*These patients also had prolonged N13–N19 latencies.
†Nine patients had absent N19 and P22 responses; three had reduced P22 amplitude.

Somatosensory evoked potential results were compared with specific clinical findings. History of a previous event or etiology were not significantly associated with the SEP results. There was no difference in the number of patients with hemispheric as compared with nonhemispheric events for frequency of abnormal SEPs and poor outcome. Sensory loss and motor deficit were both significantly associated with SEP results \((p \leq 0.004 \text{ and } p \leq 0.001, \text{ respectively})\). Most patients had more than one type of sensory involvement (e.g., joint position and light touch). Eighty percent (16/20) of patients with a disturbance in joint position had abnormal SEPs whereas 31% (4/13) with sensory deficits other than proprioception had an SEP abnormality. Twenty patients had both sensory and motor abnormalities; 16 of these 20 patients (80%) had abnormal SEPs. Five of nine (55%) with only a motor deficit also had abnormal SEPs.

Comparison of SEPs and NFS1s for prognosis following stroke in 49 patients (21 patients with transient ischemic attacks were eliminated) showed that each was significantly associated with outcome (Table 3). None of the stroke patients had an NFS1 of 50 (normal). Therefore, for NFS2, the 50-point (good) and 30–49-point (fair) outcome categories were combined to provide a comparable number of groups in NFS1 and NFS2 for statistical analysis. Somatosensory evoked potential findings were significantly associated with initial deficit NFS1 \((p \leq 0.001)\) and with outcome NFS2 \((p \leq 0.030)\) (Figure 1). Somatosensory evoked potentials from a patient with a severe deficit and poor outcome are shown in Figure 2.

Somatosensory evoked potential abnormalities were present in 89% (8/9) of patients with poor outcome. Five patients had latency delays, and three had amplitude abnormalities of N19 and/or P22. Prognosis was associated significantly with an SEP abnormality of conduction delay \((p \leq 0.003 \text{ versus EP-N13, N13–N19, and P22 latency})\) but not with amplitude abnormalities \((p \leq 0.199 \text{ versus N14, N19, P22, and P22 ratio})\). Eighty-two percent (9/11) of patients with severe deficits at onset had poor outcome, including three deaths, all secondary to their strokes. Of the three patients who later died, one had bilateral latencies, one had unilateral prolonged N13–N19 latencies, and one had normal SEPs; NFS1s were 27, 29, and 15, respectively.

Discussion

We have found that SEP abnormalities after cerebral ischemia are significantly associated with the severity of acute neurologic deficit and with neurologic outcome. This study demonstrates that stroke outcome is predicted more accurately by a quantified scaled neurologic examination than by SEP \((p \leq 0.001 \text{ versus } p \leq 0.030)\).

These results tend to confirm and extend previous studies of the prognostic value of SEPs in cerebral ischemia.

TABLE 3. Comparison of Somatosensory Evoked Potentials and Neurologic Function Scores for Prognosis in Stroke Patients

<table>
<thead>
<tr>
<th></th>
<th>NFS1 (n=49)</th>
<th>NFS2 (n=37)</th>
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<tbody>
<tr>
<td></td>
<td>Mild to moderate deficit* (30–49 points)</td>
<td>Severe deficit (0–29 points)</td>
</tr>
<tr>
<td>SEPs</td>
<td>38.8 (19)</td>
<td>2.0 (1)</td>
</tr>
<tr>
<td>Normal (%)</td>
<td>30.6 (15)†</td>
<td>28.6 (14)</td>
</tr>
<tr>
<td>Abnormal (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(p)</td>
<td>(\leq 0.001)</td>
<td></td>
</tr>
<tr>
<td>NFS1</td>
<td>Mild to moderate deficit (%)</td>
<td>...</td>
</tr>
<tr>
<td></td>
<td>Severe deficit (%)</td>
<td>...</td>
</tr>
<tr>
<td>(p)</td>
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</table>

NFS1, neurologic function score (0–50 point range, with 50 points indicating normal function) assessed within 72 hours of stroke; NFS2, neurologic function score assessed ~2 months after stroke; SEPs, somatosensory evoked potentials. Values in parentheses indicate number of patients. SEPs were performed within an average of 4.0 days of the NFS1.

*None of the stroke patients had an NFS1 of 50. Therefore, for a comparable number of groups in NFS1 and NFS2 in the statistical analysis, the good and fair outcome groups were combined.
†SEPs significantly associated with initial deficit NFS1 by Fisher's exact test.
‡SEPs significantly associated with outcome NFS2 by Fisher's exact test.
§NFS1 significantly associated with outcome NFS2 by Fisher's exact test.
FIGURE 1. Bar graph showing percent of abnormal somatosensory evoked potentials (SEPs) for neurologic function scores (NFSs) in stroke patients. NFSs range from 0 to 50 points, with a score of 50 indicating normal function. NFS1 indicates NFS assessed within 72 hours of acute event; 30–50 points represents mild to moderate deficit (no stroke patient had an NFS1 of 50), and ≤29 points represents severe deficit. NFS2 indicates outcome NFS assessed at ~2 months after acute event; 30–50 points represents good to fair outcome, and ≤29 points represents poor outcome. SEPs were significantly associated with NFS1 (p<0.001) and NFS2 (p<0.030).

La Joie et al found that 98% of patients with absent SEPs and nonfunction of the right upper extremity did not gain functional return of the extremity. Similarly, Pavot et al showed that SEP results divided into four grades were significantly correlated with functional outcome. The grade of SEP abnormality was determined solely by interhemispheric comparison; amplitude asymmetry was the predominant abnormality. Zeman and Yiannikas demonstrated that both SEPs and sensory examination were statistically significant in predicting functional outcome measured by placement, length of stay, and Barthel Index. Macdonell et al reported that SEPs predicted functional recovery after stroke but that motor evoked potentials were slightly more accurate. SEPs were described as either normal or absent, with no cases demonstrating conduction delays or interhemispheric asymmetries.

Results from our study showed both conduction delays and amplitude abnormalities, including absent peaks and interhemispheric asymmetry. Poor outcome occurred with either a conduction or amplitude abnormality. All patients had SEP abnormalities at or above the lower medullary area as evidenced by involvement of N13 or subsequent peaks. Two patients with N9–N13 prolonged also had N13–N19 delayed. Prolonged N14 (N13) has been reported in diffuse vascular encephalopathy, but the Erb’s point potentials were also significantly increased. None of our patients had prolonged N9 latencies, which suggests that conduction up to the brachial plexus was normal.

As in previous investigations, patients without clinically detectable sensory loss had abnormal SEPs. One possible explanation is that the SEP is more sensitive than the clinical examination in detecting decreased sensation. However, five of the 11 patients without sensory loss had motor deficits. Greenberg et al also found abnormal SEPs in patients with pyramidal signs with or without sensory impairment. In fact, the clinical signs that best correlated with abnormal SEPs were those of pyramidal tract dysfunction.

Lower extremity SEPs were not performed in this study since none of our patients had predominant lower extremity involvement. If the lower extremities were primarily involved, then posterior tibial nerve
SEPs would be the appropriate evoked potential test rather than the median nerve SEPs. In addition, we have used outcome at approximately 2 months after stroke as our clinical end point. We cannot rule out the possibility that significant clinical changes might have occurred after this time period. However, previous investigations have not demonstrated that such late changes are common. More than 80% of stroke patients achieve maximal functional improvement by 1 month after stroke.

The NFS1 score predicted that 11 of the stroke patients would have a poor outcome and the remaining 26 a good to fair outcome. According to NFS2 scores, 9/11 (82%) did in fact have a poor outcome and 26/26 (100%) a good to fair outcome, giving an overall accuracy of 91%. In development of a similar prognostic index, Fullerton et al found six significant and independent factors present during the first 48 hours after stroke that were related to outcome 6 months later, with an overall accuracy of 67%. In another recent study, Tupper and Henley identified 22 variables 2 weeks after stroke that were significant in predicting outcome 1 year later. Higher cerebral function was described as the most important factor.

In our study, both SEPs and the neurologic examination were accurate in predicting stroke outcome. The data should be interpreted cautiously, since evaluation in the acute state and outcome were assessed using the same scale. Nevertheless, there was no clear benefit of SEPs over the clinical examination.

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We wish to thank Elaine O’Connor for recording the SEP tests, Haydee Rudholm for assistance with patients and subjects, and Alice Sharp for typing the manuscript.

References


Key Words • cerebral ischemia • evoked potentials • prognosis
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