Relationship between somatosensory event-related potential N140 aberrations and hemispatial agnosia in patients with stroke: a preliminary study

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Relationship between somatosensory event-related potential N140 aberrations and hemispatial agnosia in patients with stroke: a preliminary study

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Abstract

Purpose: The somatosensory event-related potential N140 is thought to be related to selective attention. This study aimed to compare the somatosensory event-related potential N140 in healthy subjects to that in patients with stroke to determine whether N140 and attentiveness are associated in patients with stroke with or without hemispatial agnosia. ***Materials and Methods:*** Normal somatosensory event-related potential N140 values were determined using data from ten healthy subjects. Fifteen patients with stroke were divided into two groups based on the presence of hemispatial neglect. Somatosensory event-related potential N140 components were compared between the two groups. ***Results:*** Stimulation of the affected limb in the hemispatial agnosia group resulted in significantly longer N140 latency at the contralateral vs. the ipsilateral electrode. This was the inverse of the relationship observed in normal subjects, with stimulation of the intact side in patients with hemispatial agnosia, and with stimulation of both the intact and affected sides in patients without agnosia. In the hemispatial agnosia group, the peak latency of N140 following stimulation of the affected side was significantly longer than it was following stimulation of the intact side and when compared to that in patients without agnosia. In addition, abnormal N140 peak latencies were observed at the Cz and ipsilateral electrodes in patients with hemispatial agnosia following stimulation of the intact side. ***Conclusions:*** These findings suggest that somatosensory

event-related potential N140 is independently generated in each hemisphere and may reflect cognitive attention.

Keywords

Somatosensory evoked potentials, event-related potential, stroke, hemispatial agnosia, N140

Introduction

Somatosensory event-related potential (S-ERP) N140, a negative wave with a peak latency around 140 ms, is thought to be involved in processing negativity［1］ and is related to selective attention. In fact, the amplitude of S-ERP N140 varies depending on the type of cognitive task［2-6］, task conditions［7］, and the degree of difficulty of the task［8,9］. The use of long inter-stimulus intervals and the absence of habituation to repeated stimuli lead to larger N140 amplitudes［10］. These findings strongly support the idea that S-ERP N140 is an endogenous component. The amplitude of S-ERP N140 also increases as a function of stimulus intensity. Therefore, N140 is thought to consist of not only endogenous, but also exogenous, components［11］. Most earlier studies on N140 have been carried out in healthy subjects ［1,2,8,10,13-17］. Studies of long-latency S-ERP components in neurologically impaired

patients are relatively scarce［18］, although S-ERP N140 latency was found to be prolonged in patients with vascular dementia［5］.

The parietal lobe contains somatosensory and visual bimodal neurons ［19-21］, and is activated during a tactile-visual discrimination task, as indicated by a positron emission tomography study ［22］. Hemispatial agnosia, which is not uncommon in patients with stroke, may be related to difficulties in recognition［23］. In other words, somatosensory and visual signal processing may have a common signal in their recognition pathways. We postulated that somatosensory and visual information have a common final recognition pathway, and that S-ERP N140 may be affected when there is difficulty in processing sensory information. We thus studied the behavior of S-ERP N140 in healthy subjects and patients with stroke to determine whether there are any differences among normal subjects, patients with stroke with hemispatial agnosia (HSA), and patients with stroke without agnosia (no agnosia, NA).

Subjects and methods

This study was conducted in accordance with the tenets of the Declaration of Helsinki. Informed consent was obtained orally from all subjects before the experiments. There were no significant differences in age or sex between the healthy subjects and the patients. Ten healthy

volunteers (all right-handed; 7 men and 3 women; aged 42–76 years, [mean, 55 ± 10.6 years]) and 15 patients with stroke (all right-handed; 9 men and 6 women; 9 with cerebral infarction and 6 with cerebral hemorrhage, 6 with right hemispheric lesions and 9 with lesions on the left side; aged 20–73 years [mean, 58.3 ± 4.9 years]) participated in this study. Handedness was determined using the Edinburgh Handedness Inventory［24］. All patients had various degrees of motor deficits with or without sensory deficits, and all had strokes within six months of the study. No patients had brainstem or thalamic lesions, or impaired consciousness or aphasia. The Mini Mental State Examination was administered to all patients before the study to verify that they had sufficient cognitive function to understand the tasks.

The line cross-out test［25］is a simple test and is useful for evaluating hemispatial neglect. All patients with stroke performed this test, which was used to assess the presence of hemispatial agnosia. In a silent room, the subject was asked to complete the test with both eyes open using the non-affected hand. The result is considered to be normal if the subject crosses out all lines and abnormal if the subject fails to cross out one or more lines.

Electrical stimulations (200-μs square pulses) were alternately delivered at irregular rates of 0.1 to 0.3 Hz (inter-train interval, 3.3–10 ms) to the right and left median nerves at the wrist. The subject lay on a bed in the supine position with eyes closed and was asked to keep

track of the number of stimuli. Stimulation intensity was set to a minimum of twice the motor threshold, but was adjusted slightly until the subject perceived equal intensities with stimulations on the left and right sides. In patients with stroke, stimulus intensity was also set to twice the motor threshold at first. However, all patients with stroke had less feeling on the affected side than on the intact side following the stimulation. The stimulus intensity was then adjusted by increasing the intensity to higher than twice the motor threshold until the patient subjectively felt equal stimulus intensity on both hands. This was done to avoid discrimination between the two hands. Except for patients with severe sensory loss (one patient each from the HSA and NA groups, Table 2), the intensity of the stimulus on the affected side was increased to up to 3 times the motor threshold so that the stimulus was subjectively perceived to be equal on the left and right sides. Stimulus delivery was stopped at every 16th to 24th stimulus, the subject was provided with a brief rest, and was asked to indicate the total number of stimuli delivered to verify attentiveness to the stimuli. This also minimized habituation to repeated stimuli. One-hundred responses per side were averaged. We found that greater than 100 stimuli tended to lead to deterioration of the N140 amplitude in some subjects. This may have been due to habituation, fatigue, or an inability to maintain focus.

The linked-earlobe electrodes were used as reference, and potentials were recorded from C3, C4, and Cz (midline) according to the ten-twenty international system. The ground electrode was placed on the right forearm. Oculomotor potential was recorded from the electrode placed at FPz. Potentials greater than 50 μV were rejected. The band pass was set at 0.5 Hz to 1.5 kHz. The analysis time was 500 ms and the sampling rate was 2 kHz. Neuropack 8 (Nihon Kohden, Tokyo, Japan) was used to carry out the stimulations and to average the responses.

S-ERP N140 data were analyzed in both healthy subjects and patients with stroke. The parameters studied were 1) peak latency of N140, 2) differences in the peak latency of N140 between central electrodes contralateral (Contra) and ipsilateral (Ipsi) to the side of stimulation, and 3) differences in the peak latency of N140 following stimulation on the left vs. right side at the Contra, Cz, and Ipsi electrodes. Latencies for any of the above parameters greater than 3 standard deviations (SDs) away from those of healthy subjects were considered to be abnormal. Based on the normative data, abnormality was determined using absolute latencies of N140 at Ipsi, Cz, and Contra, N140 latency differences between Contra and Ipsi, and latency differences following stimulation on the affected vs. the intact side.

Motor disturbances in patients with stroke were classified based on the Brunnstrom scale (stages 1 to 6, most severe at stage 1 and minimal at stage 6). Pain sensation was evaluated by

pricking the tip of the index finger (3 times on each side) gently using a pin. Superficial sensation was considered normal if the pin-prick was subjectively felt to be equal between the affected and intact limbs, mildly impaired if the difference between the two sides was less than two-fold, moderate if this difference was greater than two-fold, and severe if the patient had no sensation. Deep sensory deficits were examined by passively moving the finger up or down 10 times. When finger positions were correctly identified in all trials, position sense was considered normal. Position sense was considered mildly impaired if the patient answered correctly 6–9 times out of ten, and severely impaired if the patient had no response.

Two-group paired *t*-tests were used to analyze normal N140 peak latency data, Welch's *t*-tests were used to compare mean age and N140 latency to those of normal subjects, Fisher's exact probability tests were used to analyze basic information in patients with stroke, and Mann-Whitney's U tests were used to analyze sensorimotor disturbances in the stroke group and to compare N140 factors between the HSA and NA groups. Statistical analysis was performed using IBM® SPSS® Statistics 24（IBM, Tokyo, Japan）, and p values < 0.05 were considered statistically significant.

Results

Intensity of stimulus delivered to median nerve

Stimulus intensity was 9.6 ± 1.7 mA at the right median nerve and 9.4 ± 1.9 mA at the left median nerve in healthy subjects. There were no statistical differences between the right and left stimuli. In patients with stroke, the stimulus intensity was 9.9 ± 2.1 mA on the intact side and 12.6 ± 2.6 mA on the affected side. There was a significant difference between the affected and intact sides ($p < 0.001$, two-group paired t-test).

N140 in healthy subjects

Peak latency of S-ERP N140 following stimulation of the right median nerve was 129.4 ± 10.0 ms at C3 (Contra), 130.9 ± 10.2 ms at Cz, and 134.1 ± 8.4 ms at C4 (Ipsi), and 129.5 ± 11.4 ms, 132.0 ± 9.4 ms, and 134.3 ± 8.2 ms, respectively, following stimulation of the left median nerve. The latency at Contra was significantly shorter than that at Ipsi with stimulation on both sides (**Fig. 1**, $p < 0.01$, two-group paired t-test). Data from all 10 normal subjects were combined to create grand-averaged data for the Contra, Cz, and Ipsi electrodes (**Fig.** 2). The normal latency range was considered to be the mean ± 3 SDs (**Table 1**).

Characteristics of the patients with stroke

Patients with stroke were divided into two groups: the HSA group, and the NA group, based on performance on the line cross-out test (**Table 2).** Five patients had HSA and 10 patients were in the NA group. Although no significant demographic differences were observed between the two groups, there were significantly more patients with right hemisphere lesions in the HSA group**,** while left hemisphere lesions were more common in the NA group. Clear N140 waves were not evoked following stimulation of the affected side in two patients. One of these patients was in the HSA group and one was in the NA group.

N140 in patients with stroke

Peak latency of N140

N140 peak latency was more prolonged in the HSA group than in the NA group at every electrode position, although there were no significant differences. There was greater prolongation of the latency following stimulation of the affected side vs. that of the intact side (Table 3A).

Differences in N140 peak latency between Contra and Ipsi

Similar to the trend observed in normal subjects, N140 latency at the Contra electrode was shorter than that at the Ipsi electrode following stimulation of either the intact or the

affected limb in the NA group. In the HSA group, however, N140 latency at the Contra electrode was longer than that at the Ipsi electrode when the affected limb was stimulated. However, the relationship between latency at the Contra electrode and that at the Ipsi electrode was the same as that observed in normal subjects and patients with NA when the intact limb was stimulated (**Fig. 3,** Table 3B).

Differences in N140 peak latency following stimulation on the affected vs. intact side

Significantly larger N140 peak latencies were observed in the HSA group ($p < 0.05$, Mann-Whitney's U test, Table 3C) at the Contra following stimulation of the affected side vs. the intact side.

Peak to peak amplitude of N140

No significant differences in N140 amplitude were observed between the HSA and NA groups (Table 3D).

Statistical comparison of N140 latencies in patients with stroke vs. values obtained from normal subjects

We observed significant differences between normal subjects and patients in the NA group following stimulation of the affected side at all electrodes. However, in the HSA group, these abnormalities were noted following stimulation of both the affected and intact sides. The

only exception was observed at the Contra electrode following stimulation of the intact side (Table 4).

Number of patients in the abnormal category

Peak latency of N140

There were generally more abnormalities in the HSA group than in the NA group. In the HSA group, the abnormalities were found following stimulation of both the intact and affected sides. However, in the NA group, the abnormalities were noted only following stimulation of the affected side. Three of five patients in the HSA group had abnormal peak latencies following stimulation of the intact side at the Cz and Ipsi, while no patients had abnormal peak latencies in the NA group ($p < 0.05$, Fisher's exact probability test) (Table 5A).

Differences in N140 peak latency between Contra and Ipsi

Two of five patients in the HSA group had abnormal differences in peak latencies at the Contra and Ipsi electrodes following stimulation of the intact side, while no patients in the NA group had such abnormal differences in peak latency. One of four patients in the HSA group and no patients in the NA group had abnormal latency differences following stimulation of the affected side (Table 5B).

Differences in N140 peak latency at Contra, Cz, and Ipsi following stimulation of the affected side vs. the intact side

While abnormalities in differences in N140 peak latencies following stimulation of the affected and intact sides were found in both groups, these differences were more prevalent at the Contra electrode. Most notably, all 4 patients had abnormalities at the Contra electrode in the HSA group. However, there were no significant differences between the HSA and the NA groups (Table 5C).

Short latency SEP components ahead of N140

In normal subjects, components of shorter latency ahead of N140, such as N20, P40, N60, and P100 were stably observed (Fig. 2). In patients with stroke, the association between N140 and those early components is very unstable. One patient with stroke from the HAS group showed no remarkable delay of short latency SEP components, but remarkable delay of N140 peak latency following stimulation of the affected side (Fig.3). In another patient with stroke from the HSA group, no short latency SEP components were clearly evoked, but clear and delayed P100 and N140 were evoked following stimulation of the affected side (Fig. 4). Finally, a patient with stroke from the NA group showed clear delay of N20, P40, and N60, but no remarkable delay of N140 at Contra following stimulation of the affected side (Fig.5).

Discussion

We studied the behavior of S-ERP N140 in healthy subjects and in patients with stroke to determine whether there are any differences among normal subjects and patients with stroke with or without hemispatial agnosia. We found differences in some N140 abnormalities between patients in the NA and HSA groups. Overall N140 latency following stimulation of either the affected side or the intact side was prolonged in the patient groups when compared to the normal group. This prolongation was especially prominent in the HSA group. Compared to the NA group, the HSA group had a significantly larger S-ERP N140 peak latency difference between the Contra and Ipsi electrodes. The most striking difference was the longer latency of N140 at the Contra electrode compared to the Ipsi electrode only following stimulation of the affected side. This was in contrast to the normally observed relationship between N140 at the Ipsi vs. Contra electrodes (i.e., shorter latency at the Contra electrode compared to the Ipsi electrode). This was true in normal subjects, in patients with NA, and in patients with HSA following stimulation of the intact side. There was also a significantly greater N140 peak latency difference between the Contra and Ipsi electrodes following stimulation of the affected vs. the intact side in the HSA group compared to the NA group. An overall greater incidence of

abnormal N140 was found in the HSA group than in the NA group. Furthermore, abnormalities were detected following stimulation of both the affected side and the intact side in the HSA group, but only following stimulation of the affected side in the NA group.

SEP and S-ERP components may be exogenous or endogenous. The P40, N60, P100, N140, and P300 components are thought to be endogenous components affected by cognitive tasks, while P14, N20, and P22 are exogenous components that are little influenced by cognitive function［12］. In experiments using the somatosensory oddball paradigm, the N140 component may be evoked by both target and non-target stimuli, while P300 is observed only following target stimuli［8］.

The peak latency of S-ERP N140 varies with stimulus intensity, stimulus frequency, and the nature of the cognitive task used. N140 latency is reduced with increasing stimulus intensity until the intensity reaches twice the sensory threshold. It then plateaus at stimulus intensities greater than twice the sensory threshold［9］. Since the intensity used in the study was two to three times the motor threshold, the latency of N140 was not dependent on stimulus intensity in our experimental paradigm.

As seen in Figs. 3–5, the relationship between N140 and the early SEP components is very unstable. We assumed that there is no direct correlation between N140 and those early SEP

components, and we did not measure the latencies and amplitudes of shorter latency SEP components ahead of N140 in this study.

The aberrations in S-ERP N140 observed in our study were therefore, probably not caused by exogenous factors, but were related to sensory perception disturbances secondary to stroke or purely endogenous factors. Since no significant differences were found in the degree of sensory impairment between the HSA and NA groups, the aberrations of S-ERP N140 in this study primarily reflect endogenous factors rather than perception differences.

S-ERP N140 appears in the contralateral hemisphere at first ［8］ and appears to spread toward the Cz and the ipsilateral hemisphere later［13,16］. Our study seemingly supports this notion. It is more likely that there are different generators for N140 in both hemispheres. This is consistent with the view of Forss et al. ［26］, who propose that the mesial cortex activation source (M-source) of the somatosensory evoked magnetic field (SEF), which is thought to be equivalent to S-ERP N140, leads to opposing currents in the two hemispheres on the mesial wall, which cancel each other at midline. However, in the case of SEP, N140 at the Cz electrode is probably an amalgam of the N140s from both hemispheres. This normally results in the highest amplitude of N140 at Cz.

Desmedt and Tomberg［13］ hypothesized that the N140 reflects the activation of area 46 and complex reciprocal interactions among the posterior and prefrontal cortices and subcortical structures. In addition, activation of the contralateral S1, the contralateral and ipsilateral S2, the posterior parietal cortex, and the mesial cortex is observed following somatosensory stimulation ［26］**.** In this type of activation, the M-source, which appears at approximately 100–130 ms, is distributed over the scalp. It is dominant in the center, but is slightly shifted contralaterally. This mesial cortex source activation has similar features to S-ERP N140. Both are attention-dependent components specific to somatosensory stimuli and are not observed during auditory cognitive tasks. Thus, it seems that both S2s are strongly activated during the generation of S-ERP N140.

SEP and S-ERP studies in patients with different types of dementia indicate that central conduction time and S-ERP N140 latency are prolonged in patients with vascular dementia, but not in those with dementia of the Alzheimer type or dementia secondary to Parkinson’s disease［18］. After stroke, N140 may recover following selective attention training using tactile stimulation［27］. Our study was limited by the small sample size. Nevertheless, our results suggest that further studies of the middle to long components of S-ERP, including N140,

may be important for discriminating between various cognitive dysfunctions seen in patients with stroke and dementia.

Conclusions

We found S-ERP N140 aberrations, especially alterations in peak latency, in patients with stroke with HSA. In the HSA group of patients with stroke, 1) stimulation of the affected limb resulted in significantly longer N140 latency at the Contra vs. the Ipsi electrode. This was in contrast to the relationship observed following left- and right-side stimulations in normal subjects, following stimulation of both the intact and affected sides in patients with NA and in those with HSA following stimulation of the intact side. 2) The peak latency of N140 following stimulation of the affected side was significantly more prolonged than that following stimulation of the intact side in patients with HSA compared to patients with NA. 3) Even following stimulation of the intact side, abnormal N140 peak latencies were observed at Cz and Ipsi electrodes in patients with HSA. These findings suggest that S-ERP N140 is independently generated in each hemisphere and may reflect cognitive attention.

Declaration of conflicting interests

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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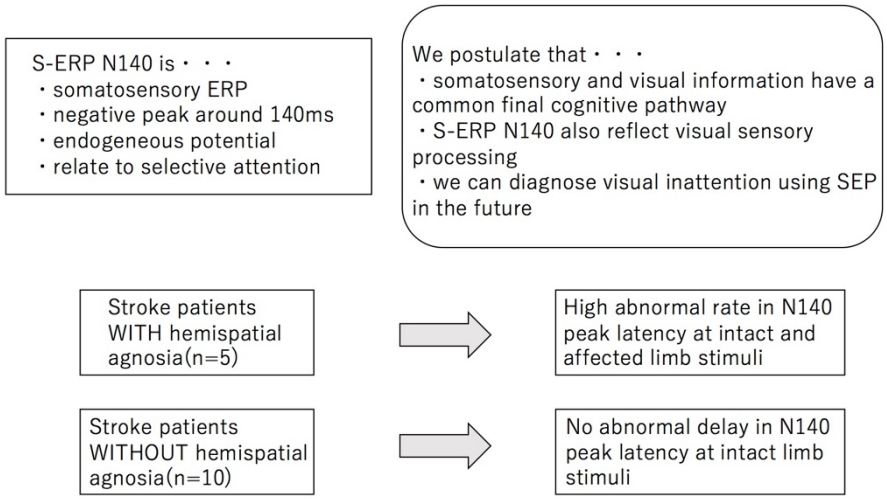
Graphical Abstract



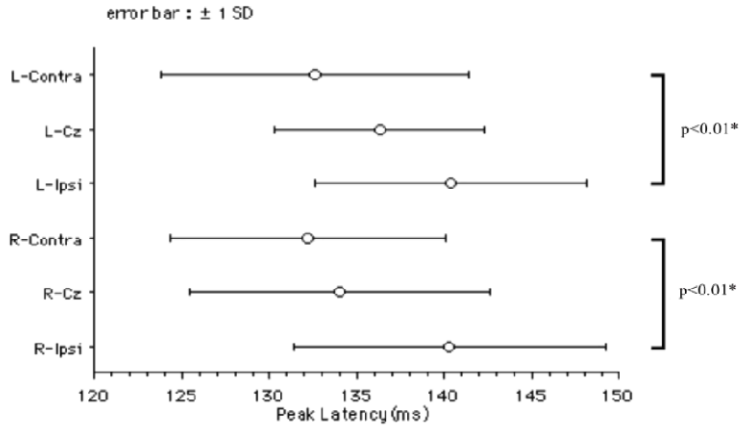


Fig. 1. Average ± 1 SD of N140 peak latency in normal subjects (n = 10).

The peak latency of Contra is shorter than that of Ipsi.

L- : left median nerve stimulus at wrist. R- : right median nerve stimulus at wrist.

* Two-group paired t-test .

No statistical differences were observed between L-Contra and R-Contra, L-Cz and R-Cz, or L-Ipsi and R-Ipsi.

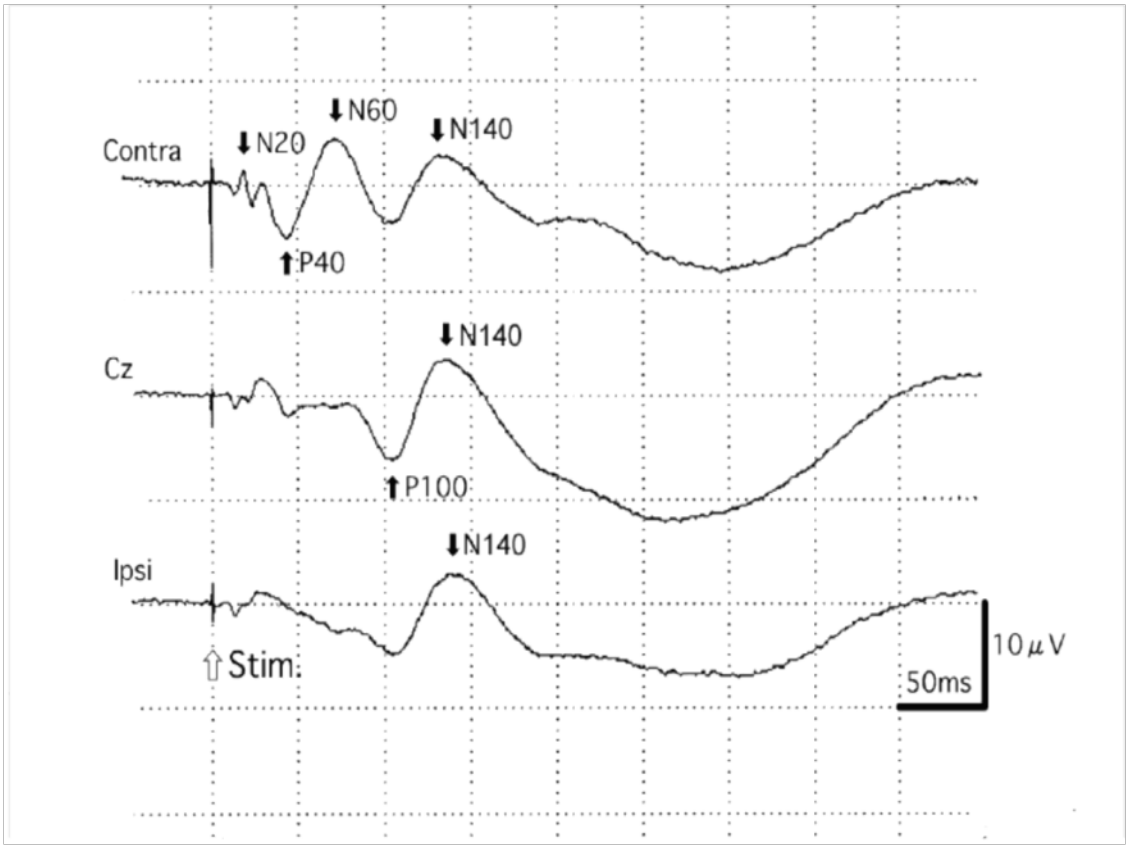


Fig. 2. Grand averaged S-ERPs following left and right median nerve stimulations (normal subjects, n = 10, grand average of 20 limbs, total of 2,000 averages). No statistical differences in latency were observed following right vs. left median nerve stimulation at Contra, Cz, and Ipsi. All data was combined to create the grand averaged data for the Contra, Cz, and Ipsi electrodes. N20 and the P40/N60 component are maximum at Contra, and the P100/N140 component is at a maximum at the Cz electrode.

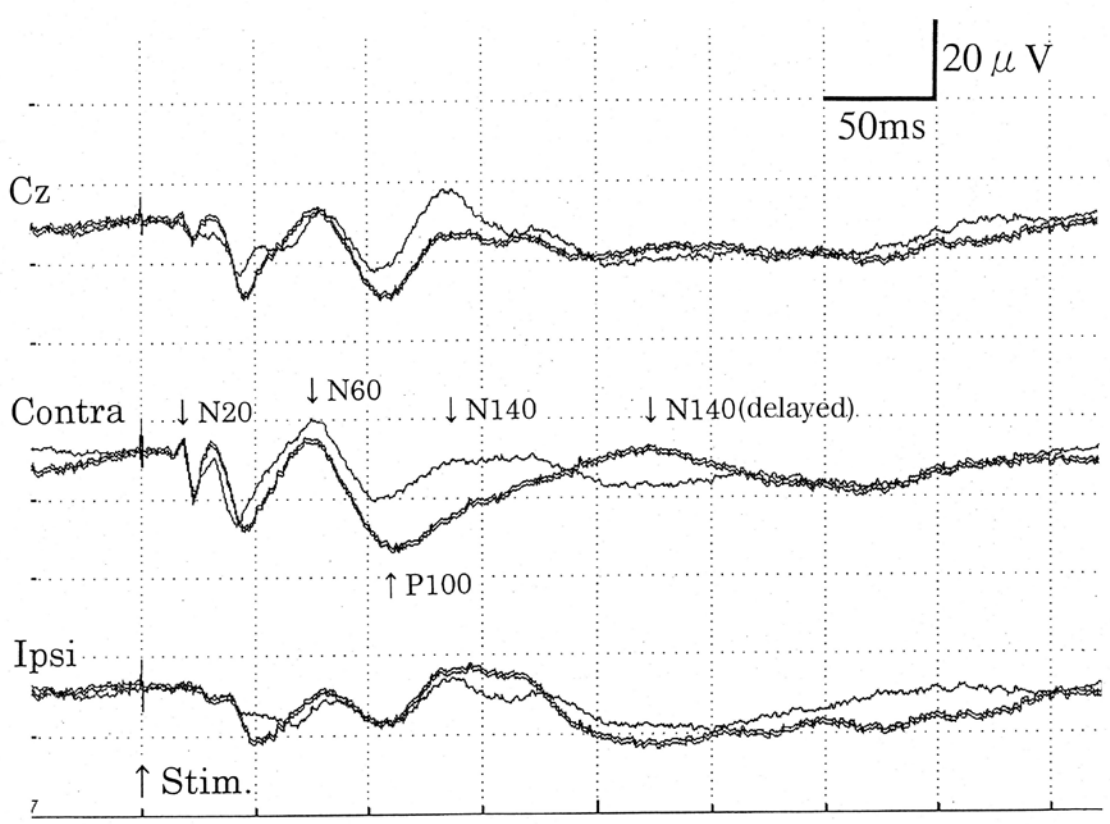


Fig. 3. Subject from the HSA group. Following stimulation of the affected side, no clear delay of short latency SEP components, but remarkably delayed N140 was observed at Contra, and an almost identical N140, in terms of shape and latency, was observed at Cz and Ipsi. There is no remarkable delay of short latency SEP components.

Double line : affected side stimulation
Single line : non-affected side stimulation

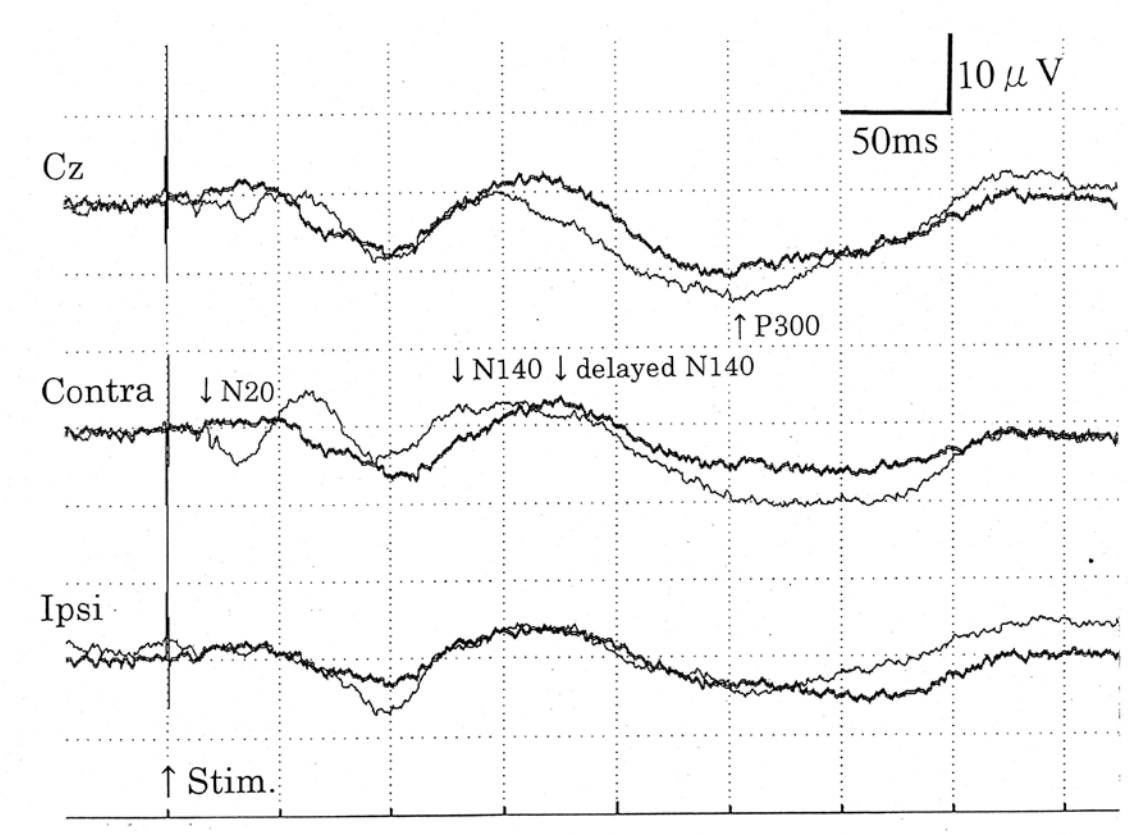


Fig.4. Subject from the HSA group. No clear short latency SEP components after N20 were observed at Contra, but clear and delayed P100 and N140 were evoked following stimulation of the affected side. Averaged 100 times each.

Double line : affected side stimulation

Single line : non-affected side stimulation

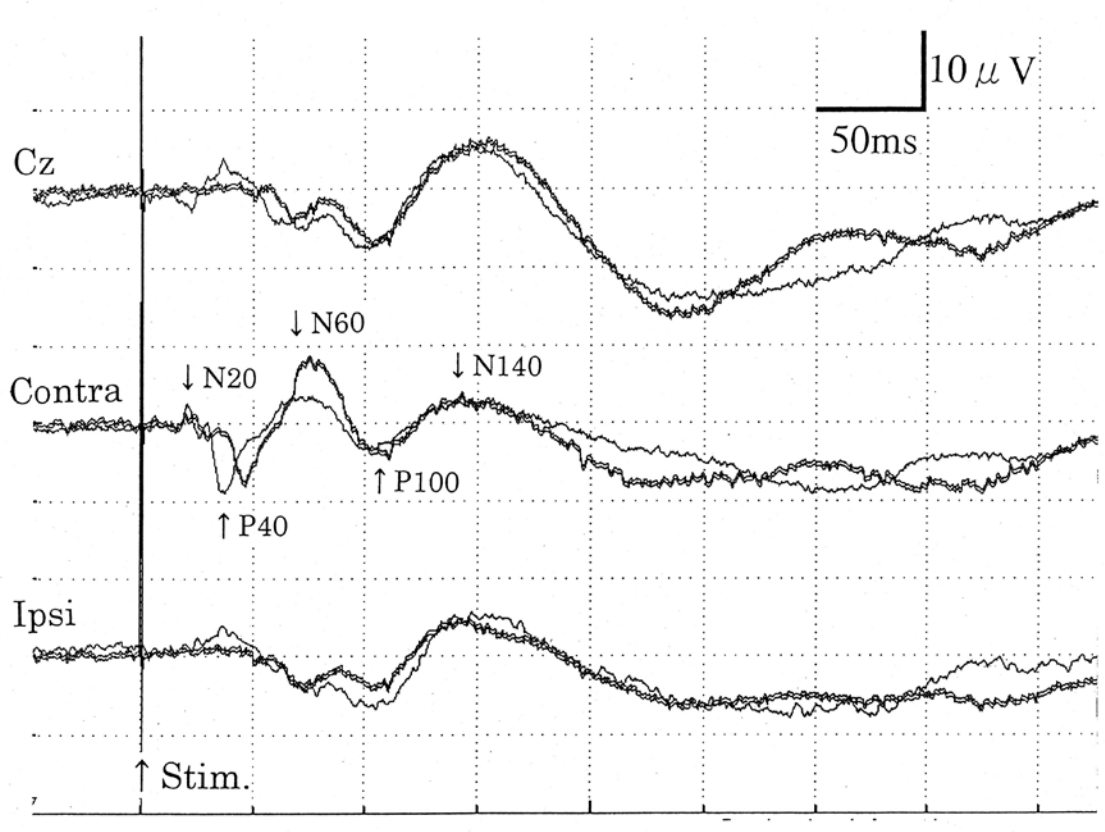


Fig. 5. Subject from the NA group. Delay of P40 and N60 was observed, but no remarkable delay of N140 at Contra following stimulation of the affected side.

Averaged 100 times each.

Double line : affected side stimulation

Single line : non-affected side stimulation

Table 1.

S-ERP N140 component peak latencies in normal subjects (n = 10).

SEP N140 component		**Mean ± 1 SD**	**Normal range** [a]
N140 peak latency			
	Contra	132.4 ± 8.1 ms	108.1-156.8 ms
	Cz	135.2 ± 7.3 ms	113.3-157.1ms
	Ipsi	140.4 ± 8.1 ms	116.0-164.8 ms
Difference in N140 peak latency between Contra and Ipsi (Ipsi-Contra)			
		8.0 ± 4.4 ms	0-21.2 ms [b]
Difference in N140 peak latency following stimulation of the right vs. the left side			
	Contra	3.5 ± 1.8 ms	0-8.9 ms [b]
	Cz	4.6 ± 4.5 ms	0-18.1ms [b]
	Ipsi	3.3 ± 2.9 ms	0-12.0 ms [b]

[a] : The "normal range" was determined using mean ± 3 SD.

Table 2. Demographic findings in the HSA and NA groups

	HSA	NA	p
Mean age (yr)	67.6 ± 4.3	58.7 ± 14.4	NS [a]
Male/female	4/1	5/5	NS [b]
Affected side (R/L) [b]	1/4	8/2	p = 0.025
Hand dominance (R/L)	5/0	10/0	NS [b]
Infarction/Hemorrhage	3/2	6/4	NS [b]
Brunnstrom stage： arm			
1/2/3/4/5/6	0/1/3/0/1/0	0/2/1/2/5/0	NS [c]
Brunnstrom stage： finger			
1/2/3/4/5/6	2/1/1/0/1/0	1/1/2/3/3/0	NS [c]
Brunnstrom stage： leg			
1/2/3/4/5/6	0/0/3/0/1/1	0/1/2/3/3/1	NS [c]
Sensory disorder			
Superficial			
Normal/Mild/Moderate/Severe	0/3/1/1	0/7/2/1	NS [c]
Deep			
Normal/Mild/Moderate/Severe	0/1/3/1	0/4/4/2	NS [c]

[a]： Welch's t-test

[b]： Fisher's exact probability test

[c]： Mann-Whitney's U test

Table 3. Comparison of N140 factors between the HSA and NA groups

SEP N140 component	HSA Group (mean ± 1 SD)	NA Group (mean ± 1 SD)	p [b]
A) **N140 peak latency**			
Stimulus to intact side			
Contra	142.5 ± 18.0 ms	137.2 ± 5.7 ms	NS
Cz	154.8 ± 14.9 ms	140.3 ± 5.9 ms	NS
Ipsi	153.7 ± 13.7 ms	142.7 ± 7.3 ms	NS
Stimulus to affected side			
Contra	200.2 ± 48.6 ms [a]	151.2 ± 16.3 ms [a]	NS
Cz	174.6 ± 50.1 ms [a]	152.8 ± 14.9 ms [a]	NS
Ipsi	174.6 ± 50.1 ms [a]	153.7 ± 13.8 ms [a]	NS
B) **Differences in N140 peak latency between Contra and Ipsi (Ipsi-Contra)**			
Stimulus to intact side	11.2 ± 15.2 ms	5.5 ± 5.6 ms	NS
Stimulus to affected side	-25.5 ± 44.0 ms [a]	2.4 ± 5.5 ms [a]	$p < 0.05$
C) **Differences in N140 peak latency between the affected side and the intact side**			
Contra	58.2 ± 32.6 ms [a]	13.5 ± 14.9 ms [a]	$p < 0.05$
Cz	20.5 ± 37.1 ms [a]	11.8 ± 12.9 ms [a]	NS
Ipsi	18.6 ± 38.6 ms [a]	9.9 ± 11.7 ms [a]	NS
D) N140 amplitude (peak to peak)			
Stimulus to intact side			
Contra	14.9 ± 5.1 μV	15.6 ± 5.5 μV	NS
Cz	17.7 ± 6.3 μV	18.8 ± 9.2 μV	NS
Ipsi	15.1 ± 6.5 μV	14.7 ± 6.0 μV	NS
Stimulus to affected side			
Contra	15.4 ± 4.6 μV [a]	13.9 ± 3.5 μV [a]	NS
Cz	15.9 ± 5.0 μV [a]	14.6 ± 4.9 μV [a]	NS
Ipsi	14.7 ± 4.5 μV [a]	13.6 ± 4.3 μV [a]	NS

[a] : N140 was not evoked clearly in one subject.

[b] : Statistical analysis performed using Mann-Whitney's U test

Table 4. Statistical comparison of N140 peak latency in normal subjects

	Contra	**Cz**	**Ipsi**
vs. NA (intact)	NS	NS	NS
vs. NA (affected)	$p < 0.0005$	$p < 0.0005$	$p < 0.005$
vs. HSA (intact)	NS	$p < 0.0005$	$p < 0.01$
vs. HSA (affected)	$p < 0.0001$	$p < 0.005$	$p < 0.005$

Intact： intact side median nerve stimulation.

Affected： affected side median nerve stimulation.

Statistical analysis was performed using Welch's t-test.

Table 5.

Comparison of numbers of normal (≦3 SD) and abnormal (＞3 SD) subjects between the HSA and NA groups.

SEP N140 component	HSA Group numbers of subjects (normal /abnormal)	No agnosia Group numbers of subjects (normal /abnormal)	p [b]
A) **N140 peak latency**			
Stimulus to intact side			
Contra	4/1	10/0	NS
Cz	2/3	10/0	$p < 0.05$
Ipsi	2/3	10/0	$p < 0.05$
Stimulus to affected side			
Contra	1/3 [a]	6/3 [a]	NS
Cz	2/2 [a]	6/3 [a]	NS
Ipsi	2/2 [a]	6/3 [a]	NS
B) **Difference in N140 peak latency between Contra and Ipsi**			
Stimulus to intact side	3/2	10/0	NS
Stimulus to affected side	3/1 [a]	9/0 [a]	NS
C) **Difference in N140 peak latency between the affected side and the intact side**			
Contra	0/4 [a]	3/6 [a]	NS
Cz	3/1 [a]	7/2 [a]	NS
Ipsi	2/2 [a]	5/4 [a]	NS

[a] : N140 was not evoked clearly in one subject.

[b] : Statistical analysis was carried out using Fisher's exact probability test.