Intensive Care Med (2001) 27: 1305–1311
DOI 10.1007/s001340101008

ORIGINAL

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Time-dependency of sensory evoked potentials in comatose cardiac arrest survivors

Received: 1 November 2000
Final revision received: 16 May 2001
Accepted: 17 May 2001
Published online: 5 July 2001

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Abstract *Objective*: To assess the validity of early sensory evoked potential (SEP) recording for reliable outcome prediction in comatose cardiac arrest survivors within 48 h after restoration of spontaneous circulation (ROSC).
Design and setting: Prospective cohort study in a medical intensive care unit of a university hospital.
Patients: Twenty-five comatose, mechanically ventilated patients following cardiopulmonary resuscitation
Measurements and results: Median nerve short- and long-latency SEP were recorded 4, 12, 24, and 48 h after ROSC. Cortical N20 peak latency and cervicomedullary conduction time decreased (improved) significantly between 4, 12, and 24 h after resuscitation in 22 of the enrolled patients. There was no further change in short-latency SEP at 48 h. The cortical N70 peak was initially detectable in seven patients. The number of patients with increased N70 peak increased to 11 at 12 h and 14 at 24 h; there was no further change at 48 h. Specificity of the N70 peak latency (critical cutoff 130 ms) increased from 0.43 at 4 h to 1.0 at 24 h after ROSC. Sensitivity decreased from 1.0 at 4 h to 0.83 at 24 h after ROSC.
Conclusion: Within 24 h after ROSC there was a significant improvement in SEP. Therefore we recommend allowing a period of at least 24 h after cardiopulmonary resuscitation for obtaining a reliable prognosis based on SEP.

Keywords Sensory evoked potentials · Cardiopulmonary resuscitation · Postischemic metabolic and circulatory derangements · Outcome prediction

Introduction

Mortality in patients following cardiopulmonary resuscitation (CPR) is high, and the survival rate without brain damage still ranges from 10 % to 20 % [1]. The severity of cerebral anoxia is the major factor limiting the success of CPR. Approximately 80 % of patients after cardiac arrest remain in coma some time, and 1-year mortality exceeds 80 % [2, 3].

Intensivists are often confronted with the question of whether it is justified to continue expensive ICU treatment in comatose survivors of cardiac arrest. Several clinical, biochemical, electrophysiological, and imaging techniques have been studied comprehensively as predictors of individual outcome [4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14]. We have previously reported that early recording of somatosensory evoked potentials (SEP), a reproducible and noninvasive measure of cortical function, has a high prognostic reliability in comatose cardiac arrest survivors [15]. Short-latency SEP reflect the functional status of the central sensory pathway between the cervicomedullary junction and the sensory cortex, whereas long-latency SEP are generated by complex thalamocortical and corticocortical interactions [16]. SEP are useful to quantify cerebral impairment [17, 18, 19, 20, 21] and have been found to be the most reliable

method for predicting death and persistent vegetative state in patients with anoxic-ischemic coma [22]. Depending on the extent of cerebral anoxia, SEP peaks are delayed or absent [15]. It is unknown, however, whether impaired microvascular cerebral perfusion and reperfusion damage occurring in the initial hours after cardiac arrest adversely affect SEP findings and thus limit the validity of SEP early after CPR. We hypothesized that early SEP recordings are not sufficiently reliable for prediction of cerebral outcome due to substantial cerebral metabolic changes during the first hours following CPR.

Materials and methods

The study was carried out at medical intensive care units of the General Hospital of Vienna and enrolled 25 consecutive patients who were comatose (Glasgow Coma Scale 3) and mechanically ventilated following CPR (5 women, 20 men; median age 59 years, range 42–87). Patient data are reported according to the Utstein-style recommendations [23]. Excluded were patients with a history of stroke, insulin-dependent diabetes, or chronic renal failure, patients with hypoxic asystole or ventricular fibrillation following intoxication with central depressant drugs, and patients in whom cerebral hypoperfusion was evident (mean arterial blood pressure < 50 mmHg despite inotropic support). Treatment and management followed the guidelines of the American Heart Association for cardiopulmonary resuscitation [24]. To prevent postischemic hyperexcitatory brain damage, all patients received standardized sedation (9–21 mg/h midazolam and 0.15–0.30 mg/h fentanyl) to achieve a score on the Ramsay et al. [25] scale of 6. All patients enrolled were kept normothermic.

The final outcome was assessed within 6 months after cardiac arrest using the Glasgow-Pittsburgh outcome categories of the Utstein recommendations [23]. A cerebral performance category (CPC) of 1 or 2 represents good outcome, while one of 3–5 indicates poor outcome. The best score achieved within 6 months after resuscitation was used for analysis. A critical cutoff of 130 ms for the N70 peak latency has recently been shown to have the highest sensitivity and specificity for outcome prediction [1]. Therefore this cutoff was used for statistical analysis in the present study. A total of 45 healthy control subjects were recruited over a period of 5 years among the inhabitants of Vienna (age range 18–72 years) in order to generate a SEP reference data base.

The study was conducted according to the principles established in Helsinki. Recording of SEP after CPR was approved by and the need for informed consent was waived by the Ethics Committee.

Sensory evoked potentials

Short- and long-latency SEP were recorded on an electrodiagnostic system (Nicolet Spirit, Nicolet, Madison, Wis., USA) 4, 12, and 24 h after restoration of spontaneous circulation (ROSC). In 10 of the 25 patients additional recording was performed 48 h after ROSC. Each SEP measurement was carried out within 30 min of the required time.

Ag/AgCl-sintered electrodes (Picker International, Munich, Germany) were placed using adhesive electrolyte gel (Grass, Quincy, Mass., USA) according to the international 10/20 system at C2 (cervical N13) and C3′ and C4′ (3 cm behind C3 or C4, N20, N35, N70 peaks) contralateral to the site of stimulation, and referenced to both midfrontal and linked-earlobe electrodes, which were recorded simultaneously. The ground electrode was placed on the forearm 10 cm proximal to the stimulation electrode. Stimulation was delivered by means of a bipolar surface electrode with 3.3 stimuli/s (short-latency) and 1.3 stimuli/s (long-latency) of electrical pulses of 0.2 ms duration on the right and left median nerve. The intensity of stimulation was adjusted between 5 and 15 mA to produce a minimal thumb twitch.

In each recording two sets of 700 (short-latency) and 200 (long-latency) evoked responses were obtained for reliable averages. Means of left-sided and right-sided stimulation were used for calculation. In healthy subjects short-latency recording results in cervical N13 peak and first negative cortical N20 peak allowing the calculation of the cervicocortical N13 to N20 conduction time; long-latency SEP consist of two negative and two positive cortical peaks labeled N35, P45, N70, and P95, respectively.

Statistical analysis

Data are presented as means ± SD. Serial SEP measurements were compared by one-way repeated measurement analysis of variance or one-way repeated measurement analysis of variance on ranks as appropriate. The Student-Newman-Keuls multiple comparison procedure was used for calculating levels of significance between measurements; p values less than 0.05 were considered statistically significant. Sensitivity was defined as the proportion of patients with poor outcome who were classified correctly by SEP criteria, specificity was defined as the proportion of patients with favorable outcome who were classified correctly, positive predictive value was defined as the proportion of patients predicted to have a poor outcome who actually had a poor outcome, and negative predictive value was defined as the proportion of patients with favorable outcome who actually had a favorable outcome.

Results

Clinical data

Initial electrocardiography showed ventricular fibrillation in 15, asystole in 9 patients, and electromechanical dissociation in one patient. Collapse was witnessed in 22 patients. Basic life support was provided in 13 patients and advanced life support in all 25 patients. ROSC was achieved after a median of 22 min (range 5–77 min). Catecholamine therapy consisted of dopamine ($n = 18$; 1.6–6.9 μg kg^{-1} min^{-1}), dobutamine ($n = 7$; 2.5–11.1 μg kg^{-1} min^{-1}), epinephrine ($n = 6$; 0.03–2.2 μg kg^{-1} min^{-1}) and norepinephrine ($n = 1$; 0.1 μg kg^{-1} min^{-1}). Three of the 25 patients required no catecholamines. All patients were normothermic at the time of SEP measurement. Clinical outcome was favorable (CPC 1) in seven of the enrolled patients. Fourteen patients died, and four remained in a persistent vegetative state within 6 months of follow-up.

Table 1 Sensory evoked potentials 4, 12, and 24 h after ROSC (the decrease in numbers of patients is caused by an absence of the corresponding peaks)

	4 h		12 h		24 h	
	n	SEP	*n*	SEP	*n*	SEP
Short latency						
N 13 (ms)	25	14.1 ± 2.3	25	13.1 ± 2.5	25	12.9 ± 2.7
N20 (ms)	24	22.8 ± 2.5	22	21.4 ± 2.0*	22	20.8 ± 2.4*
AmpN20 (uV)	24	2.2 ± 1.8	22	2.0 ± 1.6	22	2.3 ± 1.5
CCT (ms)	24	7.21 ± 0.9	22	6.24 ± 0.8*	22	5.92 ± 0.9*
Long latency						
N35 (ms)	13	44.0 ± 8.3	15	42.7 ± 6.3	17	40.6 ± 5.1
N70 (ms)	7	133.4 ± 17.8	11	127.0 ± 14.4	14	122.0 ± 14.9
AmpN70 (uV)	7	0.9 ± 0.7	11	1.4 ± 0.8	14	1.9 ± 1.3

*$p < 0.01$ vs. 4 h

Table 2 Sensory evoked potentials 24 and 48 h after ROSC (the decrease in numbers of patients is caused by an absence of the corresponding peaks)

	24 h		48 h	
	n	SEP	*n*	SEP
Short latency				
N13 (ms)	10	13.9 ± 1.2	10	13.8 ± 1.1
N20 (ms)	7	19.4 ± 1.1	7	19.9 ± 1.3
AmpN20 (uV)	7	2.3 ± 1.9	7	2.6 ± 1.7
CCT (ms)	7	5.4 ± 0.8	7	5.7 ± 0.5
Long latency				
N35 (ms)	7	38.3 ± 4.8	7	39.1 ± 4.2
N70 (ms)	5	112.9 ± 17.7	5	121.4 ± 18.2
AmpN70 (uV)	5	2.2 ± 0.9	5	2.8 ± 3.1

Early SEP

The cervical N13 peak was detectable in all 25 patients. There was no significant change in the N13 peak latency within the initial 24 h after ROSC (Table 1). One patient had no detectable negative cortical N20 peak throughout study and died without awakening. In two patients the N20 peak was detectable only at 4 h after ROSC; one of these patients remained in a persistent vegetative state, and the other remained comatose and died from circulatory failure 7 days after CPR. In the remaining 22 patients the N20 peak was detectable, but its latency 4 h after ROSC was significantly longer than in healthy subjects (22.8 ± 2.5 vs. 19.3 ± 1.1 ms, $p < 0.01$). N20 peak latency shortened (improved) between 4, 12, and 24 h after ROSC ($p < 0.01$, Table 1). The sensitivity of the N20 peak latency was 0.06 [95 % confidence interval (CI) 0.04–0.07] 4 h and 0.17 (95 % CI 0.13–0.2) 24 h after ROSC, and the specificity (1.0; 95 % CI 0.80–1.0) was equal 4 and 24 h after ROSC. The positive predictive value was 1.0 (95 % CI 0.8–1.0) 4 and 24 h after ROSC, and the negative predictive value was 0.29 (95 % CI 0.23–0.35) 4 h and 0.32 (95 % CI 0.26–0.38) 24 h after ROSC. Cervicomedullary conduction time improved similarly ($p < 0.01$, Table 1). There was no further statistically significant change between 24 and 48 h (Table 2).

Late SEP

An increasing number of the patients showed a detectable negative cortical N35 peak within 24 h after ROSC. There was no statistically significant decrease in peak latencies throughout the study period ($p = 0.189$). The number of patients in whom the negative cortical N70 peak was detectable increased from 7 at 4 h to 11 at 12 h, and 14 at 24 h (Table 1). The N70 peak latency tended to decrease, i.e., improve, but probably due to the small sample size there was no statistically significant change in N70 peak latency throughout the study. No patient with an initially detectable N70 peak developed a loss of this cortical peak during the overall whole study (Table 1).

To determine whether further changes in N70 peak latencies occur between 24 and 48 h after CPR, SEP were additionally recorded in 10 of the 25 patients studied 48 h after ROSC. Peak latencies showed no further statistically significant improvement compared to the prior measurements at 24 h (Tables 2; Fig. 1). The sensitivity of the N70 peak latency 48 h after ROSC was 1.0 (95 % CI 0.80–1.0), the specificity was 0.75 (95 % CI 0.60–0.90), the positive predictive value 0.86 (95 % CI 0.69–1.0), and the negative predictive value 1.0 (95 % CI 0.8–1.0) (Table 3).

The prognostic value of the N70 peak at 4 and 24 h was calculated accordingly to the above criteria. Only three of seven patients with good outcome had an N70 peak of less than 130 ms 4 h after ROSC, but the N70 peak was detectable below this cutoff in all seven patients at 24 h. Specificity increased from 0.43 (95 % CI 0.34–0.51) at 4 h to 1.0 (95 % CI 0.8–1.0) at 24 h. Three patients with favorable and 2 with unfavorable outcome showed a N70 peak latency between 122 and 128 ms 24 h after ROSC. Both patients with a N70 peak latency higher than 130 ms died.

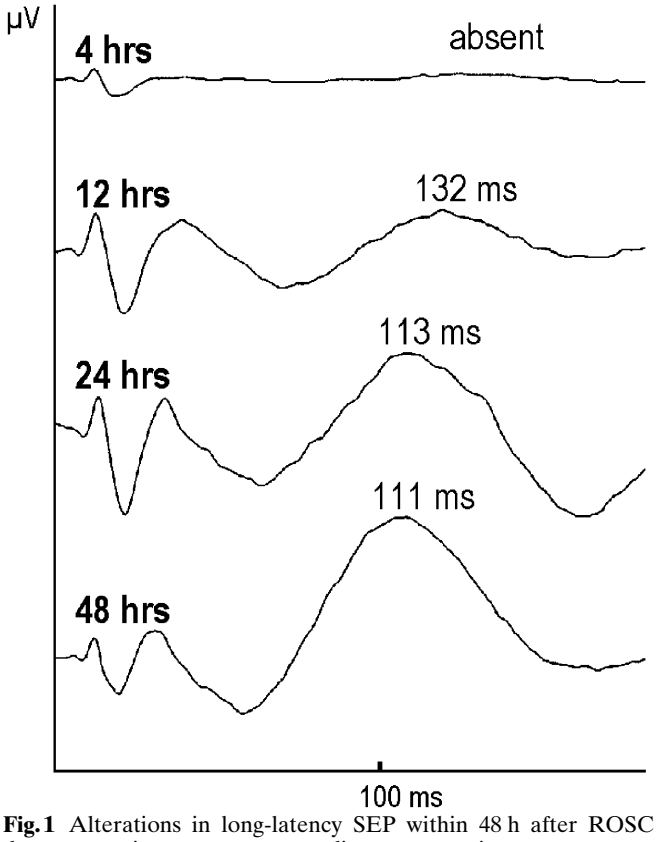

Fig. 1 Alterations in long-latency SEP within 48 h after ROSC demonstrate in one comatose cardiac arrest survivor

All 18 patients with poor outcome had an N70 peak latency greater than 130 ms or an absent N70 peak 4 h after ROSC. After 24 h 3 of these 18 patients with ultimately poor outcome regained an N70 peak less than 130 ms. Thus sensitivity decreased from 1.0 (95 % CI 0.8–1.0) at 4 h to 0.83 (95 % CI 0.67–1.0) 24 h after ROSC. The positive predictive value increased from 0.82 (95 % CI 0.66–0.98) at 4 h to 1.0 (95 % CI 0.8–1.0) 24 h after ROSC, while the negative predictive value decreased from 1.0 (95 % CI 0.8–1.0) at 4 h to 0.70 (95 % CI 0.56–0.84) 24 h after ROSC (Table 4).

Discussion

The recording of SEP is a noninvasive and reproducible bedside technique that can accurately predict outcome in comatose cardiac arrest survivors [1, 15]. The present study demonstrates that determination of prognosis in such patients based on this method is time dependent. Within 24 h after cardiac arrest we noticed a statistically significant improvement in SEP in the majority of the enrolled patients, while SEP peak latencies showed no further statistically significant change between 24 and 48 h after ROSC.

Table 3 Prediction of outcome in 10 comatose cardiac arrest survivors 4, 24, and 48 h after ROSC

	4 h	24 h	48 h
Sensitivity	0.83	0.83	1.0
Specificity	0.50	1.0	0.75
Positive predictive value	0.71	1.0	0.86
Negative predictive value	0.67	0.80	1.0

Table 4 Prediction of outcome in 25 comatose cardiac arrest survivors 4 and 24 h after ROSC

	4 h	24 h
Sensitivity	1.0	0.80
Specificity	0.43	1.0
Positive predictive value	0.82	1.0
Negative predictive values	1.0	0.70

The neurological prognosis in comatose cardiac arrest survivors often remains uncertain. Fewer than 40 % of patients in anoxic-ischemic coma for more than 12 h make a meaningful recovery [26], and most patients end up in a persistent vegetative state or death. A variety of clinical, biochemical, electrophysiological, and neuroimaging parameters has been proposed for prognostic evaluation [4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14]. Among these predictors a recent meta-analysis identified SEP as the method with the highest prognostic reliability [22]. This method is useful to quantify functional brain impairment. In the case of severe cerebral hypoxia the negative cortical N70 peak is delayed or absent. According to our previous experience, a critical cutoff between favorable and unfavorable cerebral outcome of 130 ms, measured within 24 h and 7 days after CPR, had a specificity of 1.0 and a sensitivity of 0.83 [1]. As for short-latency SEP serial studies have emphasized poor outcome from coma associated with bilateral absent cortical responses [27, 28]. The current study was designed to clarify whether SEP results are reliable at an early stage after ROSC.

Many postischemic metabolic and circulatory disorders occur immediately and delayed after successful CPR. These include postischemic hypoperfusion and dysregulation of blood flow, permeability changes in the blood-brain barrier, and even secondary depression of previously recovered metabolic activities [29]. The effect of these postischemic disturbances on the validity of SEP results is unknown.

Our data demonstrate a marked change to the better in SEP between 4 and 24 h following CPR in 76 % of the enrolled patients. Until now there has been no sufficient explanation for this improvement between 4 and 24 h after restored circulation, since all existing studies concerning hypoxic-ischemic brain damage due to cardiac

arrest describe a deterioration in cerebral circulatory, metabolic, and histopathological conditions in the 1st h of postischemic recirculation. Thus all attempts at explanation for detected improvement remain speculative. Causes of secondary deterioration may be a decline in cerebral blood flow during the first 6 h of the postresuscitation period followed by hyperemia which heralds delayed-onset CNS cell death [30], and abnormally high cerebral arteriovenous O_2 gradients for at least 24 h, indicating a mismatching of O_2 delivery to O_2 uptake [31]. Cerebral hypoxia may lead to a biphasic pattern of brain edema [32]. The initial transient edema resolved within several hours of recirculation. After 24 h of recirculation edema recurred, particularly in the sensorimotor cortex, the area from where SEP are derived by stimulating the contralateral median nerve [1, 15, 32]. The latter findings would be compatible with the statistically significant improvement in our SEP results between 4 and 12 h after ROSC, but they fail to explain the further improvement after 24 h of postischemic recovery.

Our results are supported by neurological findings obtained in a rhesus monkey model of 16 min global brain ischemia. The observed neurological deficit was initially 100 %, 70 % at 6 h, and improved to 50 % 24 h after ischemia, along with a recovery in the electroencephalography [33]. In our study we found an improvement in SEP in 76 % of patients during a similar time period.

Various confounding variables not related to cerebral ischemia may have affected our SEP results. However, confounding is unlikely as all of the patients received standardized medical treatment and were kept normoglycemic during the observation period. Furthermore, cerebral perfusion was maintained after initial CPR by keeping a mean arterial pressure of 70 mmHg.

The obligatory sedation in our patients may be a limiting factor in the validity of these SEP findings. On the one hand, both short- neither long-latency SEP are markedly affected by sedation, as previous work has shown [15], and on the other, sedation was standardized with midazolam and fentanyl being administered throughout the study period of 48 h. Despite continuous sedation we observed statistically significant improvement in SEP peak latencies. Furthermore, according to our previous study, continuous sedation does not affect the prognostic value of SEP in cardiac arrest survivors [15].

Another possible confounding variable is the patient's body temperature. A number of studies have demonstrated that body temperature affects both SEP latencies and SEP amplitudes. Hypothermia (35 °C) causes a noticeable prolongation of peak latencies, reflecting slowing of neural transmission with hypothermia, and a reduction in amplitudes [34, 35]. During hyperthermia (39 °C), in contrast, peak-latencies decreased significantly [36, 37]. All the changes described are reversible when normothermia is restored [35]. Therefore our patients were kept normothermic to prevent any interference of our SEP results with body temperature. Thus the validity of SEP results may be limited by febrile body temperature and hypothermia.

Interestingly, two patients lost the negative cortical N20 peak between 4 and 12 h after ROSC. In contrast, in the remaining patients with an initially detectable N20 peak the peak remained detectable and showed a partial improvement over the course of the observation period. Data analysis of the course of the CPR and the following clinical parameters revealed no striking features that would explain this delayed loss. The extremely low amplitude of the N20 peak in the initial measurement must be emphasized. One may argue that the low amplitude and the subsequent loss were related to brain edema, on the one hand, and to severe clinically undetectable microcirculatory derangements, on the other [32, 28]. Short-latency SEP are suitable for predicting poor outcome only in a subgroup of nonsurvivors with widespread cortical damage. A preserved N20 peak fails to predict outcome. Although we have previously found a statistically significant difference in the N20 peak latency between patients with good and poor outcome, the wide overlap of the N20 peak latencies in survivors and nonsurvivors counteracts the definition of a critical cutoff point for the N20 peak latency with a high sensitivity and specificity, respectively [1]. Nevertheless, as shown in previous work, the cervicomedullary conduction time is significantly longer in nonsurvivors than in survivors and healthy subjects. However, the predictive value of correct prediction of death for a cervicomedullary conduction time of less than 7 ms was only 0.67. The positive predictive value for favorable outcome at a given critical cutoff point of a cervicomedullary conduction time of 7 ms or less was 0.45 [27].

According to the present results, the reliability of outcome prediction in comatose cardiac arrest survivors based on SEP is given at 24 h after ROSC at the earliest. The specificity improved from 0.43 4 h after ROSC to 1.0 24 h after ROSC. In the present study several patients regained an cortical N70 peak within 24 h after CPR. As shown in previous work, the cortical N70 peak is highly and accurately predictive for outcome [1, 15]. The test-retest variability of SEP is very low, with a mean coefficient of variation of 1 % for the N70 peak latency [15]. The verified reproducibility of SEP results emphasizes the high reliability and thus the clinical practicability of this simple bedside technique. If the N70 peak is absent 24 h after ROSC, withdrawal of intensive care treatment may be considered, since no patient with a lost N70 peak regained the peak [1, 15]. However, the final decision to discontinue therapy should not be based solely on poor SEP results 24 h after ROSC. Additional clinical neurological findings

such as the absence of pupillary light reaction and absent motor responses to pain on day three after ROSC which are also said to be reliable predictors of unfavorable outcome should be taken into account [22]. Only in patients with poor results in all applied clinical and electrophysiological tests does the discontinuation of intensive care treatment seem to be undisputed. Nevertheless, continuous sedation or even medical paralysis is often necessary in the treatment of cardiac arrest survivors with corresponding multiorgan failure. Thus, clinical neurological functions including brainstem reflexes cannot be assessed sufficiently. In these cases the recording of SEP appears very helpful to detect those patients with bad prognosis, since this noninvasive, reproducible method is hardly affected by sedation or medical paralysis and is less susceptible to metabolic changes [1, 15, 22].

We used the Glasgow-Pittsburgh outcome categories as primary outcome measures, which have become the most widely used approach to evaluate quality of life after successful resuscitation because of its established validity and low interobserver variability [23]. We recorded the prearrest status and the status 6 months after ROSC. The best ever achieved CPC score within 6 months after ROSC was selected to identify the patients who regained complete consciousness after successful CPR, but who sustained neurological impairment or died due to a second cerebral or noncerebral event later. Therefore an exclusive final assessment at a definite time (for example, at 6 months) could substantially affect the predictive accuracy of SEP.

Based on our data, we recommend allowing a period of at least 24 h after cardiac arrest before recording SEP to ensure a reliable prognosis. The mechanism of certain metabolic, circulatory, and histopathological events during the postischemic recovery period that would explain why SEP peak latencies improved and reappeared remains speculative.

References

1. Madl C, Kramer L, Domanovits H, et al (2000) Improved outcome prediction in unconscious cardiac arrest survivors with sensory evoked potentials compared with clinical assessment. Crit Care Med 28: 721–726
2. Saltuari L, Marosi M (1994) Coma after cardiac arrest: will he recover all right? Lancet 343: 1052–1053
3. Rewers M, Tilgreen RE, Crawford ME, et al (2000) One-year survival after out-of-hospital cardiac arrest in Copenhagen according to the 'Utstein style.' Resuscitation 47: 137–146
4. Mullie A, Verstringe P, Buylaert W, et al (1988) Predictive value of Glasgow Coma Score for awakening after out-of-hospital cardiac arrest. Lancet I:137–140
5. Levy DE, Caronna JJ, Singer BH, et al (1985) Prediction outcome from hypoxic-ischemic coma. JAMA 253: 1420–1426
6. Snyder BD, Loewenson RB, Gumnit RJ, et al (1980) Neurologic prognosis after cardiopulmonary arrest. II. Level of consciousness. Neurology 30: 52–58
7. Snyder BD, Hauser WA, Loewenson RB, et al (1980) Neurologic prognosis after cardiopulmonary arrest. III Seizure activity. Neurology 30: 1292–1295
8. Delooz HH, Lewi PJ (1989) Early prognostic indices after cardiopulmonary resuscitation (CPR). The Cerebral Resuscitation Study Group. Resuscitation 17 [Suppl]:149–155
9. Rothstein TL, Thomas EM, Sumi SM (1991) Prediction outcome in hypoxic-ischemic coma. A prospective clinical and eletrophysiologic study. Electroencephalogr Clin Neurophysiol 79: 101–107
10. Schreiber P, Groger K, Wagner J (1988) Zur Prognose von Patienten mit kardiopulmonaler Reanimation. Intensivmedizin 25: 160–167
11. Roine RO, Somer H, Kaste M, et al (1989) Neurological outcome after out-of-hospital cardiac arrest. Prediction by cerebrospinal fluid enzyme analysis. Arch Neurol 46: 753–756
12. Vaagenes P, Safar P, Diven W, et al (1988) Brain enzyme levels in CSF after cardiac arrest and resuscitation and predictors outcome. J Cereb Blood Flow Metab 8: 262–275
13. Goe MR, Massey TH (1988) Assessment of neurologic damage: creatine kinase-BB assay after cardiac arrest. Heart Lung 17: 247–253
14. Madl C (1994) Prognostic evaluation of brain dysfunction after cardiopulmonary resuscitation. Intensivmedizin 31: 21–25
15. Madl C, Grimm G, Kramer L, et al (1993) Early prediction of individual outcome after cardiopulmonary resuscitation. Lancet 341: 855–858
16. Pfurtscheller G, Schwarz G, Gravenstein N (1985) Clinical relevance of long-latency SEPs and VEPs during coma and emergency from coma. Electroencephalogr Clin Neurophysiol 62: 88–98
17. Grimm G, Madl C, Katzenschlager R, et al (1992) Detailed evaluation of evoked potentials in Wilson's disease. Electroencephalogr Clin Neurophysiol 82: 119–124
18. Madl C, Grimm G, Ferenci P, et al (1994) Serial recording of sensory evoked potentials: a noninvasive prognostic indicator in fulminant liver failure. Hepatology 20: 1487–1494
19. Grimm G, Ferenci P, Madl C, et al (1988) Improvement of hepatic encephalopathy treated with flumazenil. Lancet II:1392–1394
20. Kramer L, Madl C, Stockenhuber F, et al (1996) Beneficial effect of renal transplantation on cognitive brain dysfunction. Kidney Int 49: 833–838
21. Eisenhuber E, Madl C, Kramer L, et al (1997) Detection of subclinical brain dysfunction by sensory evoked potentials in patients with severe diabetic ketoacidosis. Intensive Care Med 23: 587–589
22. Zandbergen EG, de Haan RJ, Stoutenbeek CP, et al (1998) Systematic review of early prediction of poor outcome in anoxic-ischemic coma. Lancet 352: 1808–1812
23. Cummins RO, Chamberlain DA, Abramson NS, et al (1991) Recommended guidelines for uniform reporting of data from out-of-hospital cardiac arrest: the Utstein style. Ann Emerg Med 20: 861–874

24. Emergency Cardiac Care Committee and Subcommittees. American Heart Association (1992) Guidelines for cardiopulmonary resuscitation and emergency cardiac care. JAMA 268: 2171–2391
25. Ramsay MA, Savege TM, Simpson BR, Goodwin R (1974) Controlled sedation with alphaxalone-alphadolone. BMJ 2: 656–659
26. Krieger DW (1996) Commentary: evoked potentials not just to confirm hopelessness in anoxic brain injury. Lancet 352: 1796–1797
27. Madl C, Kramer K, Yeganehfar W, et al (1987) Detection of nontraumatic comatose patients with no benefit of intensive care treatment by recording of sensory evoked potentials. Arch Neurol 53: 512–516
28. Brunko E, Zegers de Beyl D (1994) Prognostic value of early cortical somatosensory evoked potentials after resuscitation from cardiac arrest. Electroencephalogr Clin Neurophysiol 66: 15–24
29. Hossmann KA (1989) Post-ischemic resuscitation of the brain: selective vulnerability versus global resistance. In: Kogure K, Hossmann KA, Seisjö BK, Welsh FA (eds) Progress in brain research, vol 63. Elsevier, Amsterdam pp 3–17
30. Cohan SL, Mun SK, Petite J, et al (1989) Cerebral blood flow in humans following resuscitation from cardiac arrest. Stroke 20: 761–765
31. Oku K, Kuboyama K, Safar P, et al (1987) Cerebral and systemic arteriovenous oxygen monitoring after cardiac arrest. Inadequate cerebral oxygen delivery. Resuscitation 27: 141–152
32. Warner DS, Smith M, Siesjö BK (1977) Ischemia in normo- and hyperglycemic rats: effects on brain water and electrolytes. Stroke 18: 464–471
33. Nemoto EM, Bleyaert AL, Stezoski SW, et al (1984) Global brain ischemia: a reproducible monkey model. Stroke 8: 558–564
34. Coles JG, Taylor MJ, Pearce JM, et al (1997) Cerebral monitoring of somatosensory evoked potentials during profoundly hypothermic circulatory arrest. Circulation 70: 196–102
35. Porkkala T, Kaukinen S, Hakkinen V, et al (1994) Effects of hypothermia and sternal retractors an median nerve somatosensory evoked potentials. Acta Anaesthesiol Scand 41: 843–848
36. Strenge H (1991) Somatosensory evoked potentials in moderate hyperthermia. EEG EMG Z Elektroenzephalogr Elektromyogr Verwandte Geb 22: 157–163
37. Takahashi H, Tanaka R, Kameyama S, et al (1991) Somatosensory evoked potential and brain temperature in the Mongolian gerbil during whole body hyperthermia. No To Shinkei 43: 619–624