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Auditory brainstem responses after out-of-hospital cardiac arrest: are they useful for outcome prediction?

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Abstract: We evaluated whether we could predict the neurologic outcome in 55 out-of-hospital cardiac arrest patients using auditory brainstem responses (ABR). ABR patterns were classified into one of 3 types by evaluation of 5 components: type 1, with all 5 components; type 2, lack of at least one response between the 2nd and 5th components; type 3, with only the first component or no response. The relation between the ABR patterns on the 3rd day following resuscitation and the neurologic outcome on hospital discharge was evaluated. The specificity that the 5 awake patients had type-1 ABR was 38%. The sensitivity that the 10 brain dead patients had type-3 ABR was 60%. In the type-1 ABR patients, the negative predictive value that the patients were awake was 100%. In the type-3 ABR patients, the negative predictive value that the patients became brain dead was 90.9%. These results suggest that ABR on the 3rd post-resuscitation day may not be useful for predicting if patients are awake or become brain dead, although the loss of components may be a sign of morbidity, and the presence of the 2nd or later components indicates possible future prevention of brain death.

Key words: Brain, Resuscitation, Out-of-hospital cardiac arrest, Auditory brainstem responses (ABR), Neurologic outcome, Brain death

Introduction

The neurologic outcome of patients who survive an out-of-hospital cardiac arrest varies from complete recovery without any neurologic dysfunction to brain death. Many investigators have tried to predict the prognosis of these patients by analyzing a variety of factors, including those of the Glasgow coma scale [1], neurological findings [2], factors related to cardiopulmonary resuscitation (CPR) in the peri-resuscitation period [3,4], and the duration of cardiac arrest, CPR, and coma [5–7]. From an electrophysiologic viewpoint, it has been reported that the initial electroencephalogram is correlated with the clinical outcome in patients with post-anoxic coma [8].

Auditory brainstem response (ABR) is an evoked response that can be used to estimate brainstem function. In patients with head trauma or cerebral vascular disease, ABR has been reported to be useful for predicting neurologic outcome [9,10]. Fisher et al. reported that ABR testing was a useful aid in the assessment of neurologic outcome following submersion-induced cardiac arrest in children [11]. In their study, changes in amplitude or latency were adopted to assess ABR changes. Amplitude and latency of ABR are also affected by several other factors including age and body temperature. Accordingly, they concluded that standardization of ABR testing was difficult if change in amplitude or latency was used for the assessment. In this retrospective study, we examined changes in ABR patterns following out-of-hospital cardiac arrests by simply observing whether each ABR component was present or absent and evaluated their usefulness in predicting neurologic outcome.

Patients and methods

The study protocol was approved by the Ethical Committee of Sapporo City General Hospital, and informed consent was obtained from the patients' families. We evaluated 86 patients who, during the last 5 years, had an out-of-hospital cardiac arrest and survived for more than 7 days and who underwent ABR tests on at least the 3rd day (between 30 and 60 h following resuscitation) and the 7th day. We included the patients whose spontaneous circulation persisted until the 7th day although brain death had been diagnosed before the 7th

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day. Among these 86 patients, 31 were excluded from this study because they met one of the following conditions: (1) cardiac arrest due to trauma or massive gastrointestinal bleeding (to exclude the influence of the changes in circulating blood volume on neurologic outcome [12]); (2) cardiac arrest due to brain disorders such as cerebral vascular diseases or carbon monoxide intoxication, or patients who had secondary cerebral hemorrhage in the post-resuscitation period; and (3) patients with a history of hearing impairment or suffering from middle ear infection. We studied the remaining 55 patients (36 men and 19 women) with an average age of 50.7 ± 22.7 years. The etiology of cardiac arrest is shown in Table 1.

ABRs were recorded using a Neuropack 2 (Nihon Kohden, Tokyo, Japan). An active electrode was placed on the cranial vault, reference electrodes on both mastoids, and the ground electrode was placed on the forehead. We used stainless steel needle electrodes (length; 1 cm; diameter, 0.3 mm). The skin was carefully cleaned and the impedance of the electrode was below 5 kW in all cases. A total of 2048 stimuli (0.1-ms duration) was delivered on both sides simultaneously at a rate of 10/s and an intensity of 90 dB. Averaging was performed over a 10-ms period. All recordings were repeated to assure reproducibility.

All the ABR measurements were reexamined for this study by a neurosurgeon and two staff physicians in the emergency department, both of whom had significant experience in interpreting ABR. The examiners were blinded to patients' outcomes. ABR patterns were classified into one of 3 types: ABR with all 5 components belong to type 1; type 2 is defined as the lack of at least one response between the 2nd and 5th components; type 3 shows only the first component or no response (Fig. 1). Because the first component of ABR is thought to originate from the cochlear nerve, we regarded this response as one outside the brainstem. Accordingly, the ABR patterns with only the first component or no response were included in the same group.

Table 1. Etiology of cardiac arrest

Cardiogenic	8
Acute myocardial infarction	5
Arrhythmia	1
Electric shock	1
Pulmonary embolism	1
Respiratory	31
Asphyxia	12
Bronchial asthma	8
Hanging	6
Respiratory Failure	5
Unknown	16
Total	55

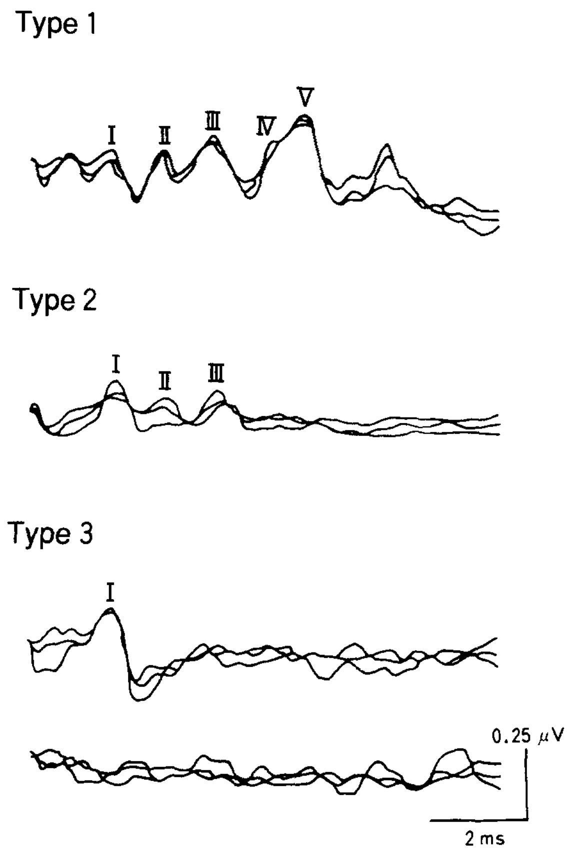

Fig. 1. Classification of auditory brainstem response (*ABR*) types. Type 1, existence of five components; type 2, lack of at least one response between the second and fifth components; type 3, existence of only the first component or no response

First, we evaluated the change in ABR patterns from the 3rd day to the 7th day. As an index of the brainstem reflex, the direct pupillary light reflex was routinely examined every day. Second, the changes in ABR patterns and the pupillary light reflex were compared. Neurologic outcome was assessed on hospital discharge using the Glasgow-Pittsburgh cerebral and overall performance categories (OPC) [13]. OPC1 is normal, OPC2 is moderate disability, and OPC3 is severe disability but conscious. We regarded the patients with OPC1, 2 and 3 as conscious. OPC4 is coma and OPC5 is brain death. Third, the relation between the ABR pattern on the 3rd day and the neurologic outcome on discharge were evaluated using the sensitivity, specificity, positive predictive value, and negative predictive value. Sensitivity was defined as the number of patients who both showed a type-1 ABR pattern on the 3rd day and were awake on the 7th day, divided by all the awake patients on the 7th day; or as the number of the patients who both showed type-2 or -3 ABR patterns on the 3rd day and were not on the 7th day, divided by all the patients who were not awake on the 7th day; or as the number of patients who both showed type-1 or -2 ABR patterns on the 3rd day and were not brain dead on the 7th day, divided by all the patients who were not brain dead on the 7th day. The positive predictive value was determined as the number of patients who both showed type-1 ABR on the 3rd day and were awake on the 7th day, divided by all the patients who showed type-1 ABR; or as the number of the patients who both showed type-3 ABR on the 3rd day and were brain dead on the 7th day, divided by all the patients who showed type-3 ABR on the 3rd day. The negative predictive value was determined as the number of patients who both showed type-2 or -3 ABR and were not awake on the 7th day, divided by all the patients who showed type-2 or -3 ABR on the 3rd day; or as the number of the patients who both showed type-1 or -2 ABR and were not brain dead on the 7th day, divided by all the patients who showed type-1 or -2 ABR on the 3rd day. All values are expressed with 95% confidence intervals.

Results

Changes in ABR over time

At the initial ABR measurement on the 3rd day, 36 patients showed type 1, 8 patients type 2, and 11 patients type 3. At the subsequent measurement on the 7th day, the ABR pattern was unchanged in 32 of 36 type-1 patients. The ABR pattern changed to type 3 in the 4 remaining type-1 patients. In all 8 type-2 patients, the pattern changed to another type on the 7th day: One to type 1 and 7 to type 3. In the 11 patients who showed type-3 ABR pattern at the initial measurement, the pattern was unchanged on the 7th day. Consequently, 33 patients showed type 1, 22 patients showed type 3, and no patients were type 2 on the 7th day.

In the 31 patients whose etiology was respiratory, 13 patients showed type 1, 7 patients type 2, and 11 patients type 3 on the 3rd day. The ABR pattern in 4 out of 13 type-1 patients and in 7 type-2 patients changed to type 3 on the 7th day. As a result, 22 of 31 respiratory patients belonged to type 3 on the 7th day. On the contrary, the ABR pattern in all 8 cardiogenic patients remained type 1.

Relation between ABR changes and light reflex

In all 55 patients, the pupillary light reflex was absent on arrival at the hospital. On the 7th day, the light reflex had been restored in all patients who showed type 1. In contrast, no patients with type 3 had the pupillary light reflex on the 7th day. Of the 22 type-3 patients, 8 of 11 patients whose ABR patterns changed from type 1 or 2 showed transient recovery of the light reflex with time. On the contrary, 9 of 11 patients whose ABR patterns

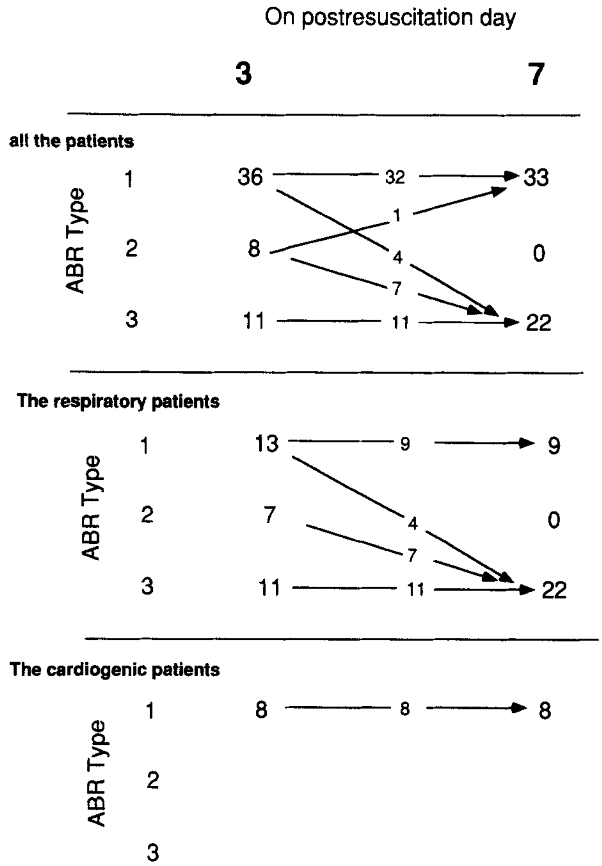

Fig. 2. Changes in ABR types over time. The numbers represent the patients belonging to each type of ABR

remained type 3 had no transient recovery of the light reflex and the pupils remained dilated since their arrival.

Neurologic outcome

As shown in Table 2, on hospital discharge, 5 patients were conscious, all of whom had type 1 ABR on the 3rd day, which had a sensitivity of 100.0% (95% confidence intervals; 100.0%), a specificity of 38.0% (95% confidence intervals; 24.5%–51.5%), in detecting recovery of consciousness. Thirty-six patients had type-1 ABR on the 3rd day, 5 of whom regained consciousness before hospital discharge, which had a positive predictive

Table 2. Relation between auditory brainstem response (*ABR*) type on post-resuscitation day 3 and neurologic outcome on discharge (conscious patients)

ABR type	Conscious	
	+	–
1	50	31
2 or 3	0	19

Table 3. Relation between ABR type on post-resuscitation day 3 and neurologic outcome on discharge (brain-dead patients)

ABR type	Brain dead	
	+	–
3	6	5
1 or 2	4	40

value of 13.9% (95% confidence intervals; 2.6%–25.3%) and a negative predictive value of 100% (95% confidence intervals; 100%) in predicting recovery of consciousness.

As shown in Table 3, on hospital discharge, 10 patients were brain dead, 6 of whom had type-3 ABR on the 3rd day, which had a sensitivity of 60.0% (95% confidence intervals; 25.0%–95.0%) and a specificity of 88.9% (95% confidence intervals; 79.7%–98.1%) in detecting brain death. On the 3rd day, 11 patients had type-3 ABR, 6 of whom became brain dead before hospital discharge, which had a positive predictive value of 54.5% (95% confidence intervals; 21.0%–88.0%) and a negative predictive value of 90.9% (95% confidence intervals; 82.4%–99.4%) in predicting brain death.

Discussion

This study revealed that the changes in ABR after resuscitation following out-of-hospital cardiac arrest followed four patterns: Perseverance of the five components, gradual appearance or disappearance of the components over time, and no response of the brainstem from the initial stage. Eight of the 11 patients who had gradual disappearance of ABR components experienced transient recovery of the light reflex. These results support the idea that cerebral disturbances (especially brainstem disturbances) continue to deteriorate even after a few days following the resuscitation in some patients who suffer out-of-hospital cardiac arrests.

All the patients who had brainstem disturbances experienced cardiac arrests due to respiratory distress. The reason why the ABR patterns in the respiratory patients were worse was not elucidated and is beyond the scope of this study. However, a previous report indicated that gradual development of brain swelling was more often seen in the respiratory patients of out-of-hospital cardiac arrests [14]. Accordingly, the acidosis accompanied by respiratory distress in the peri-ischemic period and the subsequent production of brain swelling may be related to this worse outcome.

Because of the low specificity, ABR on the 3rd day was not useful to predict whether patients regained consciousness. However, the high positive predictive value shows that loss of ABR components at the initial stage may predict that consciousness will not be regained. Snyder et al. studied the neurologic outcome following cardiopulmonary arrest using the brainstem reflexes [15]. Their study suggests that reflex abnormalities were significant predictors of a poor outcome but that normal reflexes did not assure a good outcome. Steen-Hansen et al. examined the relationship between neurologic outcome and the pupil size and pupillary light reflex after resuscitation [16]. In their study, absent pupillary light reflexes 6–24 h after resuscitation were ominous signs. These studies and ours suggest that these indices reflecting brainstem function may be useful for predicting morbidity.

Middle latency response (MLR) and/or slow vertex response (SVR), which are components of the auditory evoked potentials that occur after ABR, have been reported to be useful for predicting whether consciousness will be restored in comatose patients [17–20]. A technique that reflects cortical function, such as MLR and SVR, may be necessary to determine whether a patient will regain consciousness following out-of-hospital cardiac arrest.

The results of the present study suggested that ABR on the 3rd day was not useful in predicting whether the patients will become brain dead because of the low sensitivity. However, the high negative predictive value indicates that there is a great possibility of escaping brain death in the patients who showed a type-1 or -2 ABR pattern on the 3rd day.

In summary, the changes in ABR after resuscitation following out-of-hospital cardiac arrest showed four patterns. ABR on the 3rd day may not be useful for predicting if patients will be awake or become brain dead. However, loss of components at the early stage of post-resuscitation period may be the sign of morbidity, and the preservation of the 2nd or later components until the 3rd day after resuscitation indicates the possible future prevention of brain death.

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