Abnormal brainstem auditory evoked potentials in infants with threatened sudden infant death syndrome

James P. Orlowski, M.D.

Division of Anesthesiology
Department of Pediatrics and Adolescent Medicine
Pediatric and Surgical Intensive Care

Richard H. Nodar, Ph.D.

Department of Otolaryngology and Communicative Disorders

Derrick Lonsdale, M.D.

Department of Pediatrics and Adolescent Medicine

Sudden infant death syndrome (SIDS) is responsible for approximately 10,000 infant deaths per year in the United States and is the largest single cause of postneonatal infant mortality.[1] Several theories of causation have been suggested, one of the most popular of which is that SIDS victims have deficient central control of breathing that predisposes them to life-threatening apneas while asleep.[2] The advent of brainstem evoked potential recordings (visual, auditory, and somatosensory) provided a tool for evaluating the integrity of the brainstem in infants with threatened SIDS. Of the three approaches to brainstem evaluation (visual, auditory, and somatosensory), brainstem auditory evoked potential (BAEP) tests are the simplest to perform and most reproducible in infants. This report details our BAEP studies of infants with threatened SIDS.

Methods

The ten infants studied were referred to the Cleveland Clinic because of severe, life-threatening apneas. Each infant had had several prolonged episodes of apnea accompanied by cyanosis, which occurred during sleep. Vigorous stimulation or mouth-to-mouth resuscitation was required to revive the infant. Each of the infants was admitted to

the Pediatric Intensive Care Unit; and the heart rate, electrocardiogram, and apneic episodes were monitored continuously.

BAEP recordings were performed, analyzed, and plotted using a clinical computer of average transients (Nicolet CA 1000). The stimuli were 100-microsecond clicks presented at a rate of 11.1/sec. Stimulus presentation was at high signal levels of 90 dB HL. Analysis time was 10 msec, sensitivity was set at ± 0.625 μV, and 2000 responses were averaged. Low-pass and high-pass filters restricted the analysis to the 150- to 3000-Hz frequency range. All stimuli were presented via monaural, electrically shielded earphones (Telex). Three gold-plated, cup electrodes (Grass) were attached to the vertex (C_z) and each mastoid (A_1, A_2). The vertex served as the active electrode and was referred to the mastoid electrode of the ear tested. The contralateral electrode served as ground. Electrode resistance was always less than 5 k Ω. A minimum of two runs per ear was averaged, measured, and plotted on an X-Y recorder. The BAEP test was performed when the patient was asleep or sedated with chloral hydrate (50 mg/kg orally).

Based on published results and our clinical experience with more than 500 BAEP tests, we have compiled seven criteria for evaluating BAEP.

1. Peak latency. In normal populations, the peak latency for the seven Jewett peaks is predictable within certain tolerances (usually ± 0.2 msec). Starr and Achor's[3] latency measures have proved to be reliable for certain presentation levels. Therefore, one criterion for assessment of BAEP is the latency of the peaks, particularly Peak V, for a given sensation level (SL). In this approach, peak latencies for a given SL (usually 65 dB) for the ear under test are compared to a normal population. Latencies 0.2 msec longer than the normal are suggestive of dysfunction along the pathway of the stimulated ear.

2. Intra-ear peak latency. A measure of central conduction time is determined by evaluating peak-to-peak latencies for the stimulated ear as suggested by Starr and Achor[3] and elaborated upon by Stockard and Rossiter.[4] Central conduction time is measured by examination of the time between Jewett Peaks I to III, I to V, and III to V for the same ear. One advantage of this measure is that it is not dependent on stimulus level, allowing testing to proceed without obtaining threshold measures. Also, central conduction time measurement can be made independent of the other ear.

3. Inter-ear peak latency. This approach compares the latency differences for Jewett Peak V between ears. To make this comparison, stimulus presentations must be made at the same SL. Latency differences greater than 0.2 msec are suggestive of dysfunction along the auditory pathway with the longer latency.

4. Response stability. In normal populations and in many individuals with abnormal auditory systems, the BAEP test result is a highly stable and well-defined measure. Two successive runs usually produce results that may be superimposed on one another with few observable differences. Recently, Nodar[5] reported on results of BAEP tests that in certain patients were erratic, unstable, and poorly defined. The Jewett peak where response stability was lost suggested the level of dysfunction.

5. Amplitude. To date, little evidence exists that clearly defines the role of response amplitude in BAEP testing. As a rule of thumb, a response is considered

"suspicious" when the amplitude of a given peak is reduced by 50% when compared to the same peak obtained in the contralateral ear at the same SL.

6. Wave shape. The shape of BAEP test results is easily recognized by the seven peaks, essentially increasing in amplitude from Peak I through V, with Peak V, or the IV/V complex being the largest (*Fig. 1*). Peaks VI and VII have the amplitude of the early waves. Abnormal wave shapes include a "flattening" of the peaks, broad-based peaks, and additional peaks.

7. Peak presence. The seven Jewett peaks are thought to represent seven areas along the auditory pathway[4] (*Fig. 1*). A broad interpretation of the generators of the seven peaks is as follows: Peak I = eighth nerve, Peaks II and III = cerebellar-pons, Peaks IV and V = midbrain. The diagnostic value of waves VI and VII has not been established. The level where peaks are absent is thought to represent the level of dysfunction, i.e., if only Peak I is present, the site of lesion would be the cerebellar-pons on the stimulated side. A more specific characterization of the seven distinct peaks is as follows: Peak I is considered to be generated by the eighth nerve, Peak II by the cochlear nucleus, Peak III by the superior olivary complex, Peak IV by the nucleus of the lateral lemniscus, Peak V by the inferior colliculus, Peak VI by the medial geniculates, and Peak VII by the cortical radiations. An example of BAEP results on a normal child is shown in *Figure 1*.

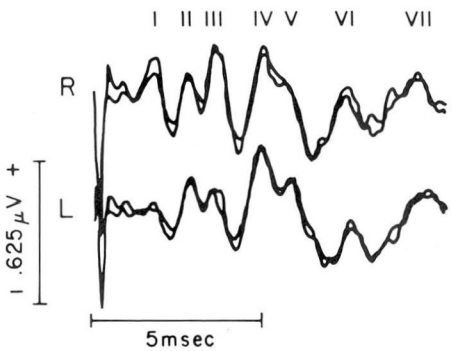

Fig. 1. BAEP results on a normal child. Wave shape, amplitude, and peak latencies are similar in both ears. Response stability is excellent, i.e., the two traces for each ear overlap one another almost perfectly.

Six normal infants hospitalized for minor surgical operations were tested with BAEP preoperatively and served as normal controls. Four infants were studied to evaluate the effects of hypoxemia on brainstem function as measured by BAEP recordings; two with apneas and cyanosis secondary to upper airway obstruction (one with laryngotracheomalacia and one with severe croup), and two infants with cyanotic congenital heart disease.

Results

Routine laboratory studies, electroencephalogram (EEG), CT of the head, and Intensive Care Unit (ICU) monitoring of the patients were normal in the ten threatened SIDS patients. The two patients with upper airway obstruction in whom apneas and cyanosis had been witnessed in the ICU had normal routine laboratory studies, normal EEG, and CT. The six control infants had normal routine laboratory studies. Each infant with threatened SIDS had BAEP recordings that were abnormal in five or more response criteria (*Table*). These abnormalities were not found in the control infants, in the two infants with documented hypoxic episodes secondary to upper airway obstruction, or in the two infants with cyanotic congenital heart disease, all of whom had normal BAEP recordings. Test results for two of the infants included in this study are shown in *Figure 2*.

Table . Abnormalities in BAEP results in ten infants with threatened SIDS

BAEP criteria	Case no. age (mo)/sex									
	1 4/M	2 3/F	3 8/F	4 4/F	5 3/M	6 2/M	7 3/F	8 6/F	9 2/M	10 3/F
Peak latency	+	+	+	+	+	0	0	0	0	+
Intra-ear peak latency	+	0	+	+	+	0	+	+	+	+
Inter-ear peak latency	+	0	+	+	+	+	+	+	+	+
Response stability	0	+	+	0	0	+	0	0	+	+
Amplitude	0	+	+	+	+	+	+	+	+	+
Wave shape	+	+	+	+	+	+	+	+	+	+
Peak presence	+	+	+	+	+	+	+	+	0	+

+ = abnormal; 0 = normal.

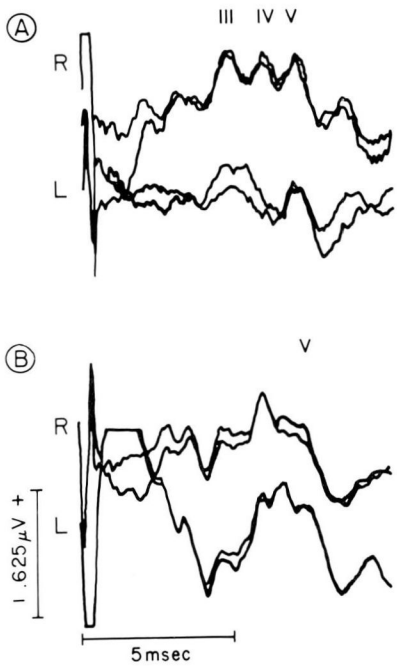

Fig. 2. BAEP test results for two infants reported in this study. The test results in **A** reflect abnormalities in wave shape, particularly for the left ear, the absence of peak presence for the left ear, and a breakdown in response stability of all waves preceding Peak V for the left ear. Responses shown in **B** reflect abnormalities in wave shape, central conduction time, and unusual high amplitudes.

Discussion

Defective central nervous system control of ventilation, possibly due to brainstem immaturity, has been implicated in the pathogenesis of SIDS.[1, 2] Evidence of chronic alveolar hypoventilation and hypoxemia prior to death has been accumulated in SIDS victims.[6] Many SIDS victims have pulmonary arterial muscle hyperplasia and hypertrophy, which is presumptive evidence of chronic underventilation of the lungs and episodes of sleep apnea prior to the final fatal episode. Naeye[7] also characterized an abnormal proliferation of astroglial fibers in the brainstems of SIDS victims, an abnormality seen in infants with known chronic hypoxemia prior to death. Recently other investigators have reported reticular dendritic spines in the brainstems of SIDS victims.[8] The neurons that exhibit these reticular dendritic spines are believed to be responsible for regulating respiratory rhythms, and these spiny protuberances are thought to indicate immaturity or maturational lag of the brainstem.

Clinical investigations in threatened SIDS infants have characterized a number of brainstem controlled abnormalities including prolonged sleep apnea,[9, 10] frequent short apneas,[11] hypoventilation and depressed ventilatory response to CO_2 breathing,[2, 12] and excessive periodic breathing.[13] Unfortunately, it has not been possible to determine which if any of these abnormalities is specific for SIDS victims as opposed to being the result of previous episodes of hypoxia.

Brainstem evoked responses provide

a rapid and reproducible method of evaluating brainstem integrity. Of the evoked potential responses available (brainstem visual, brainstem somatosensory, and brainstem auditory), the BAEP are the least invasive, simplest to perform, and easiest to interpret.[14-17]

The BAEP results obtained from ten infants with threatened SIDS showed a consistent abnormality that is not seen in normal infants or in infants with hypoxia of other origins. Because the BAEP results were normal in certain infants with hypoxia, we believe that the abnormal BAEP results reported here, suggest an abnormality in brainstem function or maturation that may be characteristic of threatened SIDS. The beneficial effect of thiamine in two of these infants is reported.[18]

Summary

Ten infants with life-threatening apneas and clinical criteria characteristic of the infant at risk for SIDS were found to have abnormal BAEP tests. These abnormalities were in contradistinction to normal BAEP results in two infants with apneas secondary to mechanical airway obstruction, in two infants with cyanotic congenital heart disease, and in six normal control infants. BAEP should prove useful in prospectively studying infants with life-threatening apnea, evaluating therapeutic modalities, and possibly as a screening tool to identify infants at risk. The abnormal BAEP implicates the respiratory center and brainstem as the area of dysfunction in SIDS.

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