Brain-Stem Auditory Evoked Potentials (BAEPs)
in Normal and Autistic Children

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Abstract

Currently, there are two main hypotheses explaining the autistic syndrome, concerning the sensory and cognitive information processing levels in the central nervous system (CNS). One possibility is that the autistic patients have a disturbance of the subcortical brain-stem sensory processing, and the other is that information processing at the higher cortical cognitive level is impaired. Brain-stem evoked potential (BEP), middle latency evoked potential (MLEP) and event related potential (ERP) techniques could be clinically useful for the evaluation of the subcortical brain-stem function, and the cortical function.

This research investigated the neurophysiological mechanisms of the processing of sensory input in 9 normal (control) and 9 autistic children, using the technique of brain-stem auditory evoked potentials (BAEPs) to gauge neural activity to click auditory stimuli. In the earliest components which occur in the 10 msec range, the wave I represents activity in the auditory nerve, and the remaining waves represent synaptic transmission upwards through the ipsilateral and contralateral lemniscal pathways. In this experiment, only 2 of 9 autistic subjects showed BAEP abnormalities, but the other autistic subjects did not show any difference as compared to the controls. If BAEP abnormalities were found, they might be related to organic neurological disorders. It is known that the P3b component is small in autistic children. But, some autistic subjects have deviant BAEPs, and they also have deviant middle latency auditory evoked potentials (MLAEPS). Such a neurophysiological investigation by evoked potentials (EPs) may be a clue to the understanding of a subtype of the autistic syndrome.

Key Words: Evoked potentials (EPs), Brain-stem auditory evoked potentials (BAEPs), neurophysiological auditory pathway, autistic children.

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In 1943, L. Kanner reported the earliest detailed description of a unique behavioral syndrome of autistic children who had failed to develop normal interpersonal and object relationships (Kanner, 1943). Children with this syndrome could be differentiated from children with other neurophysiological and psychological disorders. He also referred (Kanner, 1949) to the relationship between parental personality characteristics and early infantile autism, and described their parents as cold, formal, intelligent perfectionists, obsessive, and humorless mechanists. Unfortunately, Kanner’s description on parental personality characteristics has been elicited as evidence for a psychological cause in the etiology of the autistic syndrome (e.g. Eisenberg & Kanner, 1956; Eisenberg, 1957). The features which seem to be characteristic of autistic children include a delay in speech acquisition, the noncommunicative use of speech after it develops, delayed echolalia (Simon, 1975), pronominal reversal, repetitive and stereotyped activities, an obsessive sameness, a lack of abstract imagination, and a good rote memory, but poor metamemory. Similar symptomatic patients have been reported in detail throughout the world (Ritvo, 1976; Ornitz & Ritvo, 1976; Rutter, 1978; Freeman & Ritvo, 1984; Howlin & Rutter, 1987). However, no physiological or biological (not behavioral) objective marker could be found in autistic syndrome during the past two decades after Kanner’s first investigation. Most researchers on autistic syndrome had referred to it as basically a deficiency in ego-developmental disorder in the 1940s and 1950s (This continued until the beginning of 1980s in Japan and Europe. See e.g. N. Tinbergen: Ethology and stress diseases, 1974. This is the article of the Nobel Lecture in Stockholm when N. Tinbergen received the Nobel Prize in 1973 for Physiology or Medicine. It was translated into Japanese, but there was a delay in the acceptance a new physiological hypothesis of brain function on the etiology of autism in Japan.; Tinbergen & Tinbergen, 1983).

In 1964, B. Rimland presented a new etiological hypothesis that a malfunction of the reticular formation within the central nervous system (CNS) might be the direct cause of the syndrome of infantile autism, and he completely rejected Kanner’s hypothesis that autism is primarily an affective disturbance (Rimland, 1964). A neurophysiological marker of autistic syndrome during REM sleep was initially reported by E. M. Ornitz and his colleagues. They found abnormalities of auditory evoked potentials (AEPs), significantly reduced number of single eye movements and percent of time of eye movement burst activity, and a greater amount of 10.5–15 Hz EEG activity during REM sleep in the autistic children as compared with the normal controls (Ornitz, Ritvo, Panmann, Lee, Carr, & Walter, 1968; Ornitz, Ritvo, Brown, La Franchi, Parmelee, & Walter, 1969). Thus, they hypothesized that there are maturational or fundamental disturbances of phasic excitatory and inhibitory CNS mechanisms involved with the modulation of sensory input, perception and motility (Ornitz & Ritvo, 1968a; Ornitz & Ritvo, 1968b, Ornitz, 1969). The distorted modulation of sensory input may become the basis of the deviant object and interpersonal relationships.

H. Sohmer and M. Student (1978) were the first reporters on the abnormalities (transmission times) of brain-stem auditory evoked potentials (BAEPs) in autistic children. They
mentioned that these abnormal and deviant responses seem to present electrophysiological evidence for the presence of functional (or structural) brain damage such as microcrania, perinatal encephalopathy, at least in the region of the brain-stem, in these autistic children.

Three global classifications of auditory exogenous (sensory) and endogenous (cognitive) evoked potentials are the shortest latency brain-stem components (waves I - VII) which appear in the first 10 msec after stimulus onset, the middle latency responses, and the later event-related components (Fig. 1). The BAEPs have been clinically useful for evaluation and investigation of acoustic responses in the auditory periphery pathway and the brain-stem (Galambos & Hecox, 1977; Sohmer, Gafni, & Chisin, 1978; Sohmer 1985), and have been

![Fig. 1](image)

A: Schematic illustration of auditory evoked potentials and the main ascending and decending pathways of the auditory nervous system. (a) Exogenous and endogenous auditory evoked potentials are composed of three global classifications which are early brain-stem components (wave I - VII), middle latency potentials (No, Po, Na, Pa, Nb, and Pb), and late event-related potentials (P1, N1, P2, Nd, N2a, N2b, P3a, P3b, and SW). (b), (c) ML: medial lemniscus, RF: reticular formation, *; corticocortical tract, 5; motor trigeminal nucleus, 7; motor facial nucleus, 8; spiral ganglion (Reproduced from (a) Hillyard & Picton (1987) and Picton & Hillyard (1988), (b) Morest (1975), (c) Bossy (1970)).
suggested to be generating from the wave I—the acoustic nerve, II—the cochlear nuclei, III—the superior olives, IV—the lateral lemniscus, V—the inferior colliculi, VI—medial geniculate and VII—auditory radiations on clinicopathological correlation in human patients (Starr & Hamilton, 1976; Stockard & Rossiter, 1977; Picton, Strapelles, & Campbell, 1981; Picton, &Durieux-Smith, 1988) and animal experiments (Jewett, 1970; Buchwald & Huang, 1975; Caird, Sontheimer, & Klinke, 1985; Legatt, Arezzo, & Vaughan, 1986). Middle latency auditory evoked potentials (MLAEPS) are recorded from the scalp between 10 and 50 msec post stimulus. The neural origins of major MLAEP components (No, Po, Na, Pa, Nb, and Pb) have been progressively elucidated, but are not as clear as the BAEPs. The obtained MLAEP data in this experiment will be published elsewhere (in preparation).

While specific behavioral disturbances consisting of interpersonal and object relationships and language are predominant features of the autistic syndrome, there are other important deficiencies of the modulation of sensory input in autistic children. This distorted sensory input becomes distorted information-processing when transmitted to higher-centers, and that becomes the basis of the deviant language and social relationships. The distorted modulation of sensory input may become the basis of the deviant object and interpersonal relationships (Ornitz & Ritvo, 1976).

The disturbed neurophysiological or anatomical positions in CNS are not clear in autistic syndrome even now. However, there are two main hypothesized possibilities involving with the sensory and information processing levels: the brain-stem subcortical sensory processing, and cognitive cortical processing. This research investigated the neurophysiological mechanisms of the processing of sensory input in 18 children (9 control and 9 autistic), using the technique of BAEPs to gauge neural activity to click auditory stimuli.

**Methods**

**Subjects**

(1) Control group

Nine normal children (8 males and 1 female) of ages 8–12 years constituted the control group. The normal subjects were screened for good health, normal development, and the absence of any symptoms suggesting middle or inner ear, ocular, or neurological pathology. They were matched to autistic group for age and gender.

(2) Autistic group

Nine autistic subjects, whose ages were from 8 years 3 months to 12 years 6 months (mean age: 10 years 2 month, 8 males and 1 female), had the full diagnostic criteria for autism described in DSM-III or DSM-III-R (American Psychiatric Association, 1980, 1987). They had been screened for normal hearing. There was no evidence of hearing impairment in any subject, within the normal range.

**Stimulus**
Eighty dB SPL click auditory stimuli with a duration of 0.1 msec, at a rate of 10/sec were binaurally presented through circumaural standard audiometric earphones applied to the subject's head, to the right and left ear for the BAEP recording. The BAEP was the average of 1,000 stimuli and the second 1,000 stimuli were presented.

Procedure and Recording

The subjects were seated comfortably in a reclining chair with their heads supported to reduce muscle activity in a half darkened, sound-attenuated, and electrically-shielded room during the BAEP, electroencephalographic (EEG), electrooculographic (EOG), and electromyographic (EMG) recordings. After becoming fully adapted to the experimental room, several practice click trials were carried out to familiarize the subjects with the experimental situation. One week after the preliminary training session, each subject returned for a second laboratory session. The subjects were instructed to close their eyes to and remain quiet throughout the period of click stimulus presentation. The scalp locations of chlorided silver disc electrodes were central (Cz, T3, T4) and parietal (Pz) according to the international 10-20 system. Electrodes were also placed on the lateral canthus and above the supercilium of the left eye in order to monitor eye movements. EEG potentials were recorded monopolarly from Pz, T3 and T4 with linked mastoides (A1-A2) or ear lobes as reference electrodes. The BAEPs were simultaneously recorded from the Cz region of the scalp. The Fpz was the earth electrode. Electrode impedances were less than 5 k Ohm. BAEPs and EEG responses were recorded on a floppy disk or the FM data recorder for further analysis. The responses contaminated by large EOG and EMG artifacts were rejected from the analyzing data. The BAEP recording window (analysis time) was 10 msec with a resolution of 10 μsec/point. Bandpass settings were the lowcut 100 and highcut 3000 Hz at BAEP recording, and the bandwidth 1~100 Hz at EEG recording.

Results

The BAEP components were identified as prominent peaks which appeared within the range of 10 msec after click stimulus onset. The amplitudes of waves I-VII of the BAEPs were defined as the amplitude from their peaks to the immediately negative peak following each wave (peak-to-peak). The transmission time (TMT) and latencies were also calculated. The wave I, II, III, and V components were identifiable in all the subjects. The statistical significance of the BAEP differences on the amplitude and latency values between the control and autistic subjects was evaluated by the multivariate analysis of variance (MANOVA) and the Mann-Whitney U test for between-groups planned comparisons. The means and standard deviations of the amplitude and latency measures (mean ± SD) for each BAEP component (wave I-V) are presented in Table 1. The samples of BAEP wave-forms for each experimental group are displayed in Fig. 2. As is seen in Table 1, autistic children tended to display
Fig. 2

Table 1  
Means (± SD) of BAEP latencies and amplitudes in normal and autistic children

<table>
<thead>
<tr>
<th>Wave</th>
<th>I</th>
<th>II</th>
<th>III (IV)</th>
<th>V</th>
<th>VI</th>
<th>VII</th>
<th><strong>TMT (I-V)</strong></th>
</tr>
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<tr>
<td>Latencies (msec)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Normal</td>
<td>1.54 (±0.15)</td>
<td>2.63 (±0.26)</td>
<td>3.62 (±0.16)</td>
<td>5.68 (±0.25)</td>
<td>4.14 (0.23)</td>
<td></td>
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<tr>
<td>Autism</td>
<td>1.57 (±0.21)</td>
<td>2.67 (±0.34)</td>
<td>3.84 (±0.23)</td>
<td>5.89 (±0.36)</td>
<td>4.32 (0.37)</td>
<td></td>
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<tr>
<td>*significance</td>
<td>ns</td>
<td>ns</td>
<td>ns (p&lt;0.1)</td>
<td>ns (p&lt;0.1)</td>
<td>ns (p&lt;0.1)</td>
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| Amplitudes (µV) |        |        |          |        |    |     |              |
| Normal | 0.47 (±0.18) | 0.38 (±0.17) | 0.54 (±0.19) | 0.63 (±0.20) |    |     |              |
| Autism | 0.45 (±0.21) | 0.34 (±0.18) | 0.46 (±0.25) | 0.51 (±0.27) |    |     |              |
| *significance | ns     | ns     | ns (p<0.1) | ns (p<0.1) |    |     |              |

*significance (ns: not significant)
MANOVA-multivariate analysis of variance
** TMT: transmission times
lower amplitudes of the BAEP components as compared to the normal controls, however, these differences did not reach statistical significance. On the other hand, the TMTs for autistic patients tended to show prolonged values as compared to the TMTs of normal children. This difference also did not reach statistical significance.

Only two autistic subjects displayed decreased BAEP amplitudes and prolonged transmission times. However, there were also no significant differences in the latencies of the BAEP components elicited by click stimuli as compared to the latencies of the normal control group.

**Discussion**

The purpose of the present research was to provide data on the BAEP values in normal and autistic children. The BAEP for binaural stimulation was measured in normal and autistic children. Clinically, it has been observed that autistic children show inconsistent responses to sensory stimuli, with occurrences of hypoactivity and hyperactivity. Damasio and Maurer (1978) hypothesized that the autistic syndrome is a direct result of neurological dysfunction in a system of bilateral neural structures, but there is no clear evidence for the presence of structural brain damage in autistic syndrome. Several researchers reported that the BAEP amplitudes decreased, competent latencies and TMT increased in autism (Fein, Skoff, & Mirsky, 1981; Gillberg, Rosenhall, & Johansson, 1983; Runsey, Grimes, Pikus, Duara, & Ismond, 1984). The decrease in TMT or BAEP conduction time may be related to increased myelination or increased synaptic efficiency in the brain-stem nuclei. The TMT is also affected by maturation (Salamy, McKean, & Buba, 1975; Thivierge & Cote, 1990; Jiang, Wu, Zheng, Sun, Feng, & Liu, 1991). The TMT is longer in infants and reach adult values at 1–2.5 years (Hecox & Galambos, 1974). The increased variabilities of BAEP latencies and amplitudes, and increased brain-stem TMT may be accounted for by a defect in synaptic efficiency (Novick, Vaughan, Kurtzburg, & Simson, 1980; Rosenblum, Arick, Krug, Stubbs, Young, & Pelson, 1980; Taylor, Rosenblatt, & Linschoten, 1982). This experiment did not show that autistic subjects have statistically deviant brain-stem electrophysiological responses. The BAEP differences were relatively very few between autistic and control groups.

Recently, it is known that several children with autistic traits have evidence for a neural profound hearing loss. Auditory threshold abnormalities might have influenced the decreased amplitudes and increased TMTs and latencies. Unfortunately, earlier BAEP investigations on autistic syndrome did not take account of the neural hearing loss. Currently, more sophisticated researches have presented that the BAEPs are found to be normal in the majority (about 75%, in personal communication with Prof. E. Ornitz and Dr. E. Courchesne) of subjects with autism, if subjects with neurological disorders other than autism are excluded and most of these factors are controlled (Courchesne, Elmasian, & Yeung-Courchesne, 1987).

On the other hand, autism has come to be regarded as a cognitive process disorder with a
common underlying basis of brain dysfunction. Some authors have reported the differences of P3b component in autistic children with the main dysfunction in relation to cognitive abnormalities and memory processing disorder (Novick, Kurzberg, & Vaughan, 1979; Novick, Vaughan, Kurzberg, & Simson, 1980). Courchesne et al. asserted smaller P3b components in autism than in normal subjects in auditory classification tasks requiring subjects to press a key at the occurrence of target stimuli randomly interposed within sequences of other stimuli (Courchesne, Kilman, Galambos, & Lincoln, 1984; Courchesne, Lincoln, Kilman, & Galambos, 1985; Courchesne, Elmasian, & Yeung-Courchesne, 1987). Under the key-press condition, the performance level of those with autistic syndrome is poor, while the performance level among normal controls is generally good in both the counting and key-press conditions (Niwa, Ohta, & Yamazaki, 1983).

Courchesne's hypothesis is noteworthy, but there are two drawbacks to be surmounted in the experimental method (oddball paradigm) and data. Some autistic subjects are unable to perform the required task, and frequently lose count halfway through the session under the oddball paradigm (counting or key-press condition). This may be because they are not motivated, and are not eager to perform the required task, even though it is possible for them.

It has been suggested that P3b recordings may provide an appropriate investigation for the cognitive processes. It is well known that the P3b component of event related potentials (ERPs) is an endogenous potential which is reflected in the cognitive process, specifically the updating process (Donchin, 1981; Hillyard & Picton, 1987; Picton & Hillyard, 1988). However, the P3b component is strongly effected by motivational state. The amplitude diminution of P3b in the autistic syndrome might be caused by the subject's motivation to perform the required task, more than the cognitive process.

The another drawback is that the amplitude diminutions are shown not only at the P3b component but also at the other ERP components in autistic subjects.

Because objective biomedical markers common to all cases have not yet been identified, autism is a behaviorally defined syndrome which is assumed to be composed of many subtypes, each with different etiologies, pathologies, and possible treatments. Autism begins before 30 months of age, however, and has two distinct types of clinical onset. The first type is patients who display developmental delays and their symptoms are observable during the first few weeks and months of life. The second type is patients who display normal development until 12 to 24 months of age, and after that, they display the first regressions with the specific symptoms and plateaus in development. It is not yet known if an association exists between type of onset and course of illness. The attempts to establish the validity of these relationships and to differentiate the subtypes have not been yet successful in autistic syndrome. But the BAEP, MLAEP, and ERP recordings may be able to contribute the early diagnosis of brain lesions and for the differentiation of nosological autistic subgroups. In the next paper (in preparation), the author intends to present and discuss the MLAEP (No, Po, Na, Pa, Nb, and Pb components) and ERP (especially N2 and P3a components) features of autistic syndrome, comparing it with other neuropathological disorders.
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References


