

A Developmental Study of MLAEPs (Middle-Latency Auditory Evoked Potentials) in Normal Children and Adults

Masakazu SUGAWARA*

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Abstract

As with the brainstem evoked potentials (BEPs) and the late event-related evoked potentials (ERPs), recent investigations have shown that the middle latency components are also useful for the clinical diagnosis and the developmental (maturational) evaluation of sensory information processing in the sensory pathway, even though the anatomical origin is so little well known.

The present study investigated the developmental changes of the MLAEP components (Pa, Nb, and Pb) to unattended acoustic stimuli in normal children as compared to adult subjects. Subjects, whose ages ranged from 3 to 24 years, included 63 normal children and 15 adult students. Click stimuli (100 dB SPL, 0.1 msec rise-fall time, 1 msec duration) were presented binaurally with the ISI 1 sec, during which the subjects watched silent color TV programs. MLAEPs were recorded monopolarly from midline placements over Fz, Cz and Pz with linked A1-A2 as the reference with bandpass filter of 5-300 Hz. In the MLAEP study, the amplitudes and latencies of Pa, Nb, Pb components were measured for 5 different age groups. The results showed that the MLAEP Pb latencies at Cz decreased progressively as a function of age, and the Pb amplitudes changed as an inverse U-shape function of age. However, there were no consistent statistical differences in the characteristics of Pa and Nb components among the different age groups. These findings suggested that the earlier MLAEP components (Pa and Nb) and the Pb have different developmental time-tables and generator systems. The MLAEP Pb appears obviously to be a valuable tool for developmental evaluation and the investigation of the electrophysiological characteristics of brain maturation.

Key Words : development (maturation), evoked potentials, children, MLAEP

Introduction

The evoked potentials (EPs) have been globally classified into the sensory exogenous components which are determined by the physical stimulus events, and the cognitive

* Department of Psychology, Faculty of Education, Iwate University, Morioka 020, Japan

endogenous components (Halgren, Squires, Wilson, Rohrbaugh, Babb, & Crandall, 1980) which reflect the integrity or organization of sensory pathways and the characteristics of psychological factors (Courchesne 1983, 1990 ; Hillyard & Picton, 1987). Auditory evoked potentials (AEPs) also have been generally classified into the shortest latency brainstem potentials (waves I-VII) which appear in the first 10 msec after stimulus onset, the middle latency responses (No, Po, Na, Pa, Nb and Pb), which occur in the 10 to 100 msec range, and the later event-related potentials (ERPs) (Picton, Hillyard, Krausz, & Galambos, 1974 ; Picton, Strapells & Campbell, 1981 ; Hillyard & Picton, 1987). The neural generators of MLAEP and ERP late components are not well known, while the sources of early brainstem components have been elucidated by correlative investigations between animal experiments (Jewett, 1970 ; Buchwald & Huang, 1975 ; Caird, Sontheimer, & Klinke, 1985 ; Legatt, Arezzo, & Vaughan, 1986 ; Buchwald, 1990) and clinicopathological data in human patients (Starr & Hamilton, 1976 ; Stockard & Rossiter, 1977 ; Ozdamar, Kraus, & Curry, 1982 ; Wood, Clayworth, Knight, Simpson, & Naeser, 1987). The evaluation of the brainstem function with brainstem auditory evoked potential (BAEP) technique has been commonly applied in clinical use (Galambos & Hecox, 1977 ; Picton & Duriex-Smith, 1988).

MLAEPs are recorded from the scalp at Cz between 10 and 100 msec (not between 10-50) poststimulus, although there is still the debate over the neurogenic vs myogenic origins of MLAEP components. The neural origins of major MLAEP components (Na, Pa, Nb and Pb) remain uncertain, are not as well known as the BAEPs, and continue to generate controversy. However, there are apparently functional differences in the generator systems between the earlier MLAEP components and the Pb component. The MLAEP components might arise from the medial geniculate, polysensory nuclei of the thalamus, the thalamic radiation of diencephalon, and the primary auditory cortex (Cohen, 1982 ; Kraus, Ozdamar, Hier, & Stein, 1982 ; Woods, Clayworth, & Knight, 1985 ; Deiber, Ibanez, Fischer, Perrin, & Mauguiere, 1988 ; Cacace, Satya-Murti, & Wolpaw, 1990).

The present study investigated the developmental changes of the prominent MLAEP components (Pa, Nb, and Pb) to unattended acoustic stimuli in normal children as compared to young adults. There is much developmental research on the changes of P3b latencies and amplitudes, but it is not yet known whether the MLAEP components develop at a different rate as the maturational course of P3b activity changes, because there has not been systematic developmental research of the MLAEP components. Such a neurophysiological investigation by MLAEPs may be a clue to the understanding of brain development and disorder.

Methods

Subjects

Subjects were 63 normal children whose ages ranged from 3 to 8 years, and 15 normal adult students. All subjects were screened for good health, normal development, and

absence of any symptoms suggesting middle or inner ear, ocular, or neurological pathology. One week after the preliminary training session, each subject returned for a second laboratory session. In order to make the 20-min laboratory experience as enjoyable as possible, each subject reclined in a comfortable chair with head supported to reduce muscle activity, in a sound-attenuated, electrically-shielded room, during the electroencephalographic (EEG) and MLAEP recordings. They were instructed to remain quiet while click stimuli were being presented.

Stimuli

For the MLAEP recordings, the click auditory stimuli were delivered to the right and left ear, through standard audiometric earphones applied to the subject's head. Binaural click stimuli (0.1 msec rise-fall time, 1 msec duration, 100 dB SPL, 200 trials), were presented at a rate of 1/sec, during which the subjects watched silent color TV programs.

Procedure and Recording

MLAEPs were recorded monopolarly from midline placements over Fz, Cz and Pz scalp locations according to the international 10-20 system with linked A1-A2 as the reference electrodes with bandpass filter of 5-300 Hz. The Fpz was the earth electrode. Electrode impedances were less than 10 kOM. Electrodes were also placed on the lateral canthus and above the supercilium of the left eye in order to monitor eye movements. Shortly before stimulus presentation, they were verbally reminded by the experimenter to watch the TV. EEG responses contaminated by large electro-oculographic (EOG) and electromyographic (EMG) responses were rejected from the analyzing data during computer processing. EEG was recorded using standard chlorided silver disc electrodes. Each EEG response and EP were recorded on the FM date recorder and a floppy disk for further analysis. The analysis window for the MLAEP recording was 100 msec (giving a resolution of 100 μ sec/point). The statistical significance of the MLAEP differences on the amplitude and latency values among the different age groups was evaluated by ANOVA.

Results

This research investigated the neurophysiological mechanisms of the processing of sensory acoustic input in 63 normal children and 15 adult subjects, using the technique of MLAEPs to gauge neural activity to click stimuli. A representative sample of MLAEP waveform is illustrated in Fig.1. The amplitudes and latencies of MLAEP components were calculated among different age groups at Cz. Three dominant peaks of MLAEP components were observed in all subjects at the Cz. In this study, the Pa, Nb, and Pb component of MLAEP were identified as the most prominent negative and positive peaks

Table 1. Numbers of subjects in each age group.

	Males	Females	Total
3 years	3	3	6
4 years	6	9	15
5 years	16	8	24
8 years	9	9	18
18-24 adults	6	9	15
	40	38	78

Table 2. The means and standard deviations of MLAEP Pb peak latencies and amplitudes for acoustic stimulation in different age subjects.

	Pb Latencies (msec) **	Pb Amplitudes (μ v) ns
3 years	91.7(\pm 19.2)	3.29(\pm 2.81)
4 years	81.6(\pm 17.4)	3.79(\pm 3.77)
5 years	78.0(\pm 15.9)	4.04(\pm 2.37)
8 years	68.3(\pm 14.1)	2.25(\pm 2.16)
18-24 adults	59.7(\pm 11.5)	1.65(\pm 1.39)

ANOVA (analysis of variance) **: significant P < .01 ns: not significant

Table 3. The means and standard deviations of the latencies and amplitudes of MLAEP Pa for binaural acoustic stimulation in different age children and adult subjects.

	Pa Latencies (msec) ns	Pa Amplitudes (μ v) ns
3 years	21.3(\pm 2.98)	1.55(\pm 0.75)
4 years	17.0(\pm 6.08)	1.27(\pm 1.13)
5 years	19.0(\pm 4.32)	1.12(\pm 1.03)
8 years	22.8(\pm 7.20)	0.65(\pm 0.60)
18-24 adults	23.0(\pm 5.50)	0.72(\pm 0.62)

ANOVA (analysis of variance) ns: not significant

Table 4. The means and standard deviations of the latencies and amplitudes of MLAEP Nb for binaural acoustic stimulation in different age children and adult subjects.

	Nb Latencies (msec) ns	Nb Amplitudes (μ v) ns
3 years	32.0(\pm 5.05)	-1.03(\pm 0.92)
4 years	31.5(\pm 6.71)	-1.49(\pm 1.28)
5 years	31.3(\pm 6.18)	-1.30(\pm 1.01)
8 years	35.1(\pm 9.98)	-0.80(\pm 0.59)
18-24 adults	31.7(\pm 9.16)	-0.84(\pm 0.60)

ANOVA (analysis of variance) ns: not significant

which appeared within the range of 10-100 msec after stimulus onset. The mean amplitudes and latencies of each MLAEP component are shown in Tables 2, 3 and 4. The MLAEP data were statistically analyzed using the ANOVA planned comparisons among different age groups. As can be seen in Tables 3, 4 and Figs. 2, 3, subjects did not show any statistical differences in Pa and Nb latencies and amplitudes among different age groups. The elder subjects tended to display lower amplitudes of the Pa as compared to the younger children (Fig. 4). However, this developmental difference of the MLAEP Pa amplitude did not reach statistical significance. On the other hand, there was very clear evidence for an evaluation of brain development in the MLAEP Pb component in this experiment. The result showed that the MLAEP Pb latencies at Cz decreased progressively as a function of age (Table 2, and Fig. 2). And the Pb amplitudes changed as an inverse U-shape function of age, but these amplitude differences did not reach statistical

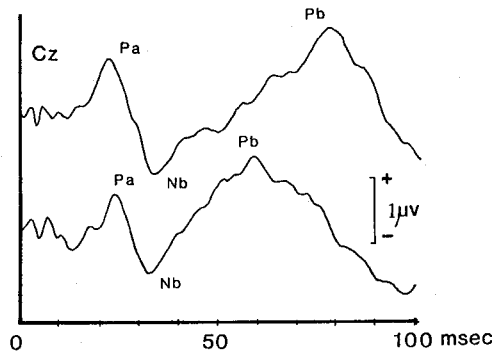


Fig. 1 Typical MLAEP wave forms obtained from two subjects (a child and adult subject) to binaural clicks at vertex (Cz).

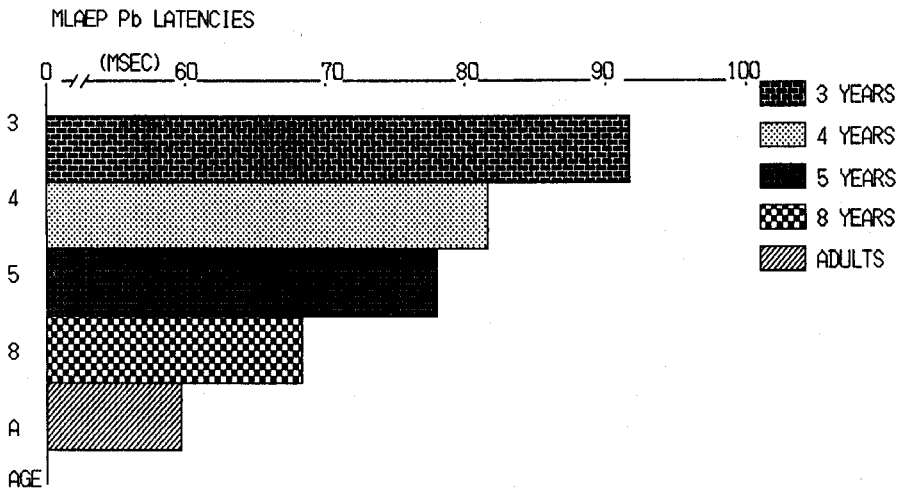


Fig. 2 Developmental changes of MLAEP Pb latencies in the different age groups.

significance. The fact that significant differences among different age groups were relatively very few in MLAEP Pa and Nb, but there were consistent differences in the Pb component among the experimental groups, suggests that MLAEP component might have different neural generators and developmental time-tables.

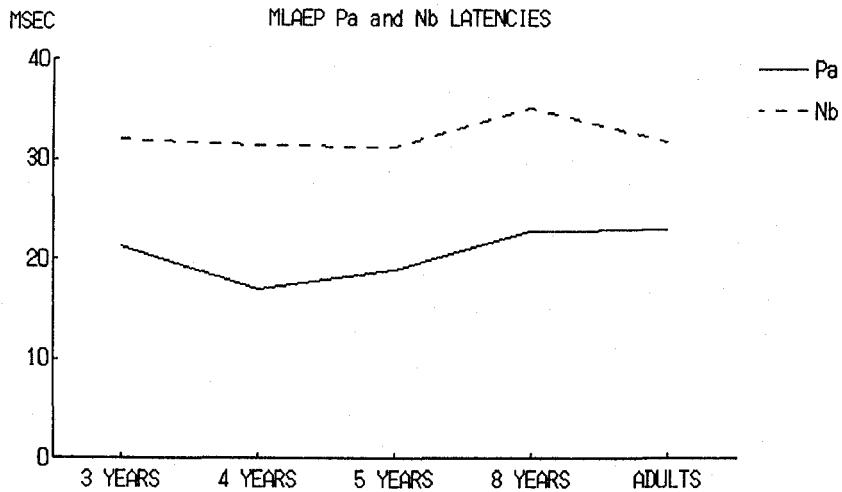


Fig. 3 Developmental changes of MLAEP Pa and Nb latencies in the different age groups.

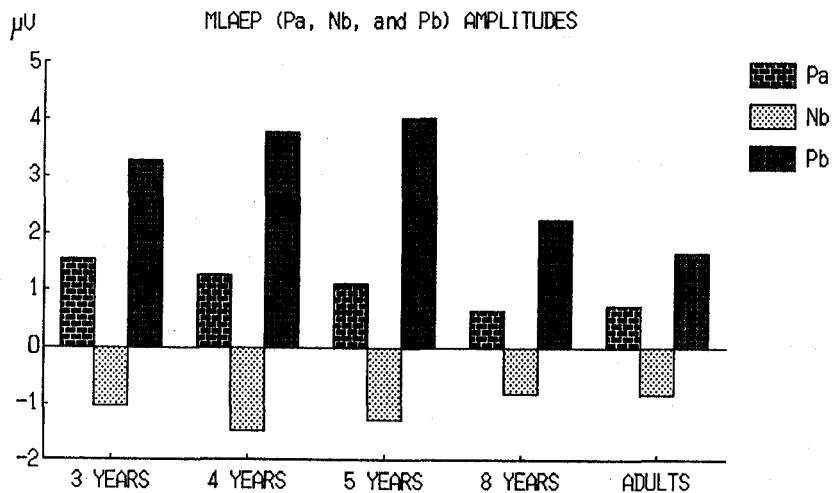


Fig. 4 Developmental changes of MLAEP amplitudes in the different age groups.

Discussion

AEPs appear to be valuable tools of physiological markers for investigating the different stages of information processing from sensory registration to cognitive levels. It has been thought that the exogenous EPs reflect the physical properties of the stimulus events, whereas the characteristics of the endogenous ERPs are determined by the integrity and organization of the sensory pathways and psychological factors (Courchesne, 1983; Hillyard & Picton, 1988). The BAEP and MLAEP abnormalities have been discussed in relationship to the orienting response, neurotransmitter deficiency and theories of arousal (Sohmer, Gafni, & Chisin, 1978; Ornitz, Mo, Olson, & Walter, 1980; Fein, Skoff, & Mirsky, 1981; Lee, Lueders, Dinner, Lesser, Hahn, & Klem, 1984; Grillon, Courchesne, & Akshoomoff, 1989). The capacity to orient to unexpected and novel information in the environment is critical to knowledge acquisition, and such functions are primarily mediated in the brainstem. Therefore, the abnormal cognitive processes might be due to abnormal sensory processing by the neural structures which generates the BAEPs and MLAEPs. Some workers interpreted the findings of abnormal BAEP latencies and amplitudes which reflect an automatic process—not under voluntary control—as perhaps showing an immaturity in the development of certain brain mechanisms (Salamy, McKean, & Buda, 1975; Rumsey, Grimes, Pikus, Duara, & Isomond, 1984). In general, early BAEP latencies reach adult values at 1-2.5 years. But attempts to establish the validity of relationships between early BAEP or MLAEP and late ERP activities have not yet been successful.

The anatomical neural origins of major MLAEP components (No, Po, Na, Pa, Nb, and Pb) have been progressively elucidated (Kileny, Dobson, & Gelfand, 1983; Kraus, Smith, & McGee, 1988; Littman, Kraus, McGee, & Nicol, 1992), but are not as well known as the BAEPs, and continue to generate controversy (Ozdamar & Kraus, 1983; Mason & Mellor, 1984; Erwin & Buchwald, 1986a, 1986b). Kraus et al. (1982, 1985) found that the MLAEP Na and Pa were normal in different patient groups including children with diagnosed communicative disorders (speech and language delays or learning disabilities), and in patients who had cortical lesions of the left and the right hemispheres. They concluded that the detectability of the Na and Pa components did not appear to be an electrical sign of language processing in the language-impaired children as compared to normal controls. Mason and Mellor (1984) also did not find any abnormality in MLAEPs recorded at the vertex site in children with mixed dysphasia or motor speech disorder due to congenital suprabulbar paresis or developmental verbal dyspraxia. However, Ozdamar et al. (1982) reported the abnormality of an absent Pa component in a subject with cortical deafness. Erwin and Buchwald (1986) reported that the Pb components disappear during NREM stages, while they reappear during REM sleep. Therefore, they suggested that such dependence on the Pb component during the arousal state might indicate origin in the ascending reticular activation system. Woods et al. (1985, 1987) suggested that the generators of Pa and Nb receive equally convergent inputs from the two ears, but the Na

generators are activated by contralateral inputs. Recent neuromagnetic study suggests that the Pa is produced by oriented dipole sources in supratemporal auditory cortex, and also exists with similarly oriented subcortical dipole sources. It may originate morphologically in Heschl's gyrus, primary auditory cortex and occur in the anterior-posterior plane (Reite, Teale, Zimmerman, Davis, & Whalen, 1988; Knight, Scabini, Woods, & Clayworth, 1988; Cacace, Satya-Murti, & Wolpaw, 1990).

MLAEP research is still in its infancy, unlike that of the BAEPs, and investigators remain uncertain about the determinants involved. However, there are some indications that the MLAEPs represent activity in the thalamus, the thalamic radiation, and the primary auditory cortex (Picton, Hillyard, Krausz, & Galambos, 1974; Cohen, 1982; Kraus, Ozdamar, Hier, & Stein, 1982; Woods, Clayworth, & Knight, 1985; Ball, Hunt, Sanford, Ross, & Morrison, 1991). Buchwald et al. (1990, 1991) suggested that the MLAEP Pb component reflects generator activities through a cholinergic brainstem-thalamus of the ascending reticular formation. Thus MLAEP records hopefully will lead to a better understanding of the arousal, orienting functions, and provide a convenient measure for clinical testing of cerebral and possibly thalamic functions.

Conclusions

There have been very few neurophysiological investigations through the analysis of MLAEP development (Kraus, Smint, Reed, Stien, & Cartee, 1985) in normal children. In the present study, MLAEP components (Pa, Nb, and Pb) elicited by loud acoustic stimuli were investigated in 63 normal children and 15 adult subjects. The goal of this work was to investigate the features of MLAEPs of humans associated with the processing of auditory information in these different age groups. Click stimuli were delivered binaurally (100 dB SPL, 0.1 msec rise-fall time) for the MLAEP records with the ISI 1 sec, during which the subjects watched silent color TV programs. The results showed that the latencies of Pb components were significantly different among different age groups. On the other hand, early MLAEP (Pa and Nb) latencies and amplitudes did not show significant differences among different age groups. The Pb is a large, positive component in MLAEPs which are usually maximum at electrode sites over the central cortex, and might be thought to reflect a cholinergic thalamic activity in diencephalic processes. This study, which focused on three potentials elicited by novel events, showed that the MLAEP Pb component would be worthwhile for objective diagnosis of early brain development associated with the diencephalic information processing, even though more sophisticated analysis will be required to further detect the generators of each MLAEP component.

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