No auditory conduction abnormality in children with attention deficit hyperactivity disorder

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Summary

Attention deficit hyperactivity disorder (ADHD) is a neurobehavioral developmental disorder characterized by lack of sustained attention and hyperactivity. It has been suggested that asymmetrical conduction of the auditory stimulus in the brainstem plays a role in the pathophysiological process of ADHD. In the present study, the functional integrity of the central auditory pathway was assessed using the auditory brainstem response (ABR), mid-latency response (MLR) and slow vertex response (SVR). Twenty ADHD children and twenty controls were recruited for the study and recordings were done on a computerized evoked potential recorder using the 10-20 system of electrode placement. There emerged no significant difference in absolute peak latencies, interpeak latencies and amplitude of ABR or latency of MLR in the ADHD children as compared with the controls. Prolongation of the SVR latency was found in the children with ADHD versus the controls, but the difference was statistically insignificant. The present study does not suggest any auditory conduction abnormality as a contributory factor in ADHD.

KEY WORDS: attention deficit hyperactivity disorder, auditory brainstem response, mid-latency response, slow vertex response

Introduction

Attention deficit hyperactivity disorder (ADHD) is a neurobehavioral developmental disorder characterized primarily by the co-existence of attentional problems and hyperactivity (1,2). These symptoms appear early in a child's life; many children may have these symptoms but at a low level (3-5). It is important that children receive a thorough examination and appropriate diagnosis by a well qualified professional. Children with ADHD usually have functional impairments across multiple settings including home, school and play and these are especially evident at school. These children are at risk for learning difficulties and often demonstrate academic failure and underachievement, especially during elementary schooling. It has been suggested that asymmetrical conduction of the auditory stimulus in the brainstem plays a role in the pathophysiological process of ADHD (6). Many studies have used electrophysiological techniques to objectively assess neurodevelopmental disorders or central nervous system pathologies. We have previously studied the cognitive status of children with ADHD using auditory event-related potentials (7). Nowadays, various non-invasive methods are used to study and understand neuronal functions and neuronal connectivity in the brain and to help in evaluating quantitatively the neurophysiological functions in different disease states (8,9).

Stimulus-related potentials are obligate neuronal responses to given stimuli and they are independent of whether the subject is attentive to or interested in the stimulus. They reflect the functional integrity of the anatomical sensory/motor pathways in the brain and spinal cord and at the periphery. The response to an auditory stimulus has been divided into three sequential time periods:

i) early latency or auditory brainstem response (ABR) (0-8 msec)
ii) middle latency or mid-latency response (MLR) (8-50 msec)
iii) long latency or slow vertex response (SVR) (50-300 msec) (10).

The auditory brainstem response (ABR), or brainstem auditory evoked potentials (BAEPs), is a series of potentials arising from the acoustic nerve and brainstem that are volume conducted to surface recording electrodes at the scalp (11). The ABR serves as a non-invasive clinical tool in characterizing the electrophysiological phenomenon of neural excitation, conduction and transmission across the auditory pathway in the brainstem.

The ABR waveforms are labeled from I-V. Wave I is believed to reflect activity in the auditory nerve; waves II and III, activity in the cochlea and superior olivary nuclei, and waves IV and V, activity in the lateral leminiscus and inferior colliculus (11). The latency of the waveforms denotes the conduction time along the auditory pathway. The amplitude of the ABR waveforms depends on the number of neural elements activated by the sound stimulus and the degree of synchronized activity of these neural elements (12).

The interpeak latencies (IPLs) reflect neural conduction in the corresponding segments of the central auditory pathway: IPL I-V is a measure of total conduction time, IPL I-III is a measure of conduction from the acoustic nerve to the pontomedullary portion, and IPL III-V is a measure of pontomesencephalic conduction time (11).

BAEPs have achieved widespread clinical application in the assessment of neurological and audiological problems. Several technical and subject-related factors affect the amplitude and latencies of BAEP components

besides lesions and dysfunctions involving the peripheral auditory structures and brainstem auditory pathways. Abnormally prolonged IPLs reflect dysfunction of central auditory conduction (13).
The MLR and SVR represent conduction in the central auditory cortex. Thus, integrity of the thalamocortical projections, the primary auditory cortex and association cortex can be assessed by using the MLR and SVR.
ABR abnormalities have been reported in children with learning problems (14,15), speech and learning disorders (16), and auditory processing deficits (17). MLR abnormalities have been found in children with learning or speech/language disabilities (16,18).
The literature available on the status of these auditory projections to the cortex in ADHD children is very scant. Hence the present study plan to use electrophysiological measures, namely auditory evoked responses (ABR,MLR,SVR), as a means of investigating, objectively, the auditory sensory process in the brainstem, thalamocortical and cortical areas in ADHD children and in controls.

Materials and methods

The study was conducted on 20 male ADHD children with a mean age of 10.29±2.29 years and 20 normal male children with mean age of 10.44±2.3 years in the Electrophysiology Laboratory of the Department of Physiology, University College of Medical Sciences, Delhi.
The ADHD subjects were selected from a school for special children (i.e. children with ADHD, dyslexia, or mental retardation, slow learners, etc.) in Delhi. The subjects recruited for the study were among those identified by their respective class teachers as having behavioral or academic problems and subsequently referred to the school's clinical psychologist. Only those subjects diagnosed with ADHD of the combined type, according to the DSM IV criteria, were recruited for the study. Conners' Teacher Rating Scales (CTRS) and Conners' Parent Rating Scales (CPRS) were used to assess the subjects (19). Children born preterm and with a history of perinatal asphyxia, CNS infection, convulsive disorders, mental retardation or psychiatric or neurological abnormalities were excluded from the study.
The 20 controls (age- and IQ-matched) were recruited from an elementary school in the vicinity of our institution. No member of the control group showed any indication of symptoms of ADHD, as evaluated using the CTRS and CPRS; no control subject had a history of neurological disorder or substance abuse. All the children included in the study underwent a standard IQ test (MISIC, Malin's Intelligence Scale for Indian Children, which is an Indian adaptation of the Wechsler Intelligence Scale for Children, WISC). This was administered by a clinical psychologist. Only children with an IQ of over 85 were included in the study. All the children had been medication-free for at least 24 hours before the electrophysiological recording.
Ethics committee clearance was obtained and informed written consent was given by all the parents of the children after the recording procedure had been explained to them. All subjects and controls were tested under similar laboratory conditions. They were familiarized with the experimental procedure and environmental (laboratory) conditions. The recording was done in the presence of either a parent or a teacher.

Recording procedure

The evoked potentials (EPs) were recorded from each subject's scalp using a computerized EP recorder (Nihon Kohden Neuropack μMEB 9100, Japan) with silver-silver chloride disk electrodes placed in standard scalp locations according to the international 10-20 system. The electrodes were thus placed at Cz (active electrode), FPz (ground electrode), A1 and A2 (reference electrodes) after cleaning the scalp or skin site with alcohol followed by Skinpure™ skin preparation gel and Elefix™ EEG paste. A1 was the reference electrode when the auditory stimulus was presented to the left ear and A2 when it was presented to the right ear. The skin electrode contact impedance was kept below 5 KΩ. The subjects were instructed to close their eyes to avoid blink artifacts.
For recording the ABR, 1000 click stimuli at the rate of 10Hz and with a duration of 0.1 msec were delivered at 60 dB above hearing threshold through shielded headphones with -40 dB white noise masking the contralateral ear. Signals were filtered with a 100 Hz to 3 KHz bandpass and averaged over 1000 stimuli. Peak latencies of all the waves, IPLs I-III, III-V and I-V, and amplitudes of wave I and V were determined for each ear separately with the help of digital cursors. The amplitude was measured as the maximum height of the peak from the subsequent trough.
For recording the MLR, 500 click stimuli at the rate of 5 Hz with a duration of 0.1 msec and a stimulus interval of 100 msec were delivered at 60 dB above hearing threshold through shielded headphones with -40 dB white noise masking the contralateral ear. Signals were filtered with a 20 Hz to 1 KHz bandpass and averaged over 500 stimuli. The peak latencies of the No, Po, Na, Pa, Nb, and Pb waves were recorded.
For recording the SVR, 100 click stimuli at the rate of 0.5 Hz with a duration of 0.1 msec and stimulus interval of 100 msec were delivered at 60 dB above hearing threshold through shielded headphones with -40 dB white noise masking the contralateral ear. Signals were filtered with a 1 Hz to 50 Hz bandpass and averaged over 100 stimuli. The peak latencies of P1, N1, P2 and N2 were recorded.

Statistical analysis

The data obtained were analyzed using SPSS software (Version 13.0). The averages for the left and right ear were taken and analyzed. The statistical analysis for the comparison between controls and ADHD children was done using the unpaired t test. All tests were two-tailed. The results are expressed as mean values ± SD.

Results

The ADHD children had a mean IQ of 95±3.97, which was comparable to that of the controls (92±8.83).
There were no statistically significant differences in the absolute peak latencies (Table I), IPLs (Table I) and amplitude (Table II) of the ABR waves in the ADHD children as compared with the controls.

The mean latencies of the MLR waves Na, Pa and Nb are shown in Table III. The remaining waves, No, Po, Pb, were not prominent in any of the recordings.
The mean latencies of the SVR waves are shown in Table III. The latency of the SVR waves was found to be prolonged in the ADHD children, although the difference was not statistically significant.
Waveforms representative of those recorded in the control and ADHD children are shown in the figures: ABR waveforms in figures 1 and 2, MLR waveforms in figures 3 and 4 (over), and SVR waveforms in figures 5 and 6 (over).

Table I - Mean absolute peak latencies (msec) and inter-peak latencies (msec) of ABR waves (mean values ± SD)

	Controls	ADHD	p value
I	1.49±0.14	1.55±0.39	0.691
II	2.58±0.17	2.7±0.40	0.459
III	3.69±0.21	3.86±0.5	0.359
V	5.44±0.24	5.8±0.73	0.257
I-III	2.2±0.22	2.31±0.17	0.272
III-V	1.75±0.14	1.94±0.57	0.331
I-V	3.95±0.21	4.25±0.51	0.114

Table II - Mean amplitudes (μV) of ABR waves (mean values ± SD)

	Controls	ADHD	p value
I	0.34±0.18	0.32±0.18	0.898
V	0.8±0.28	0.62±0.23	0.189

Discussion

In our study, there was no statistically significant difference in the absolute peak latencies, IPLs (Table I) and amplitude (Table II) of the ABR in ADHD children as compared to the corresponding recordings in the controls. Our findings are consistent with those of Schochat et al. who recorded the ABR using the oddball paradigm and found that all ADHD subjects had normal ABR (20). On the contrary, Puente et al. (21) found prolonged latencies of waves III and V in children with attention deficit disorder (ADD) and significant difference between mean interwave intervals I-III and I-V in ADD subjects as compared with controls. These findings seem to suggest an abnormal brainstem transmission and a

Table III - Mean latencies (msec) of MLR and SVR components (mean values ± SD)

		Controls	ADHD	p value
MLR	Na	19.8±5.48	19.38±4.67	0.869
	Pa	28.84±4.84	27.83±5.45	0.695
	Nb	36.23±5.35	34.17±2.61	0.412
SVR	P1	67.63±16.89	77.12±27.35	0.437
	N1	116.38±22.42	130.75±33.78	0.306
	P2	183.53±23.42	201.5±20.21	0.121
	N2	262.88±38.06	271.04±36.74	0.665

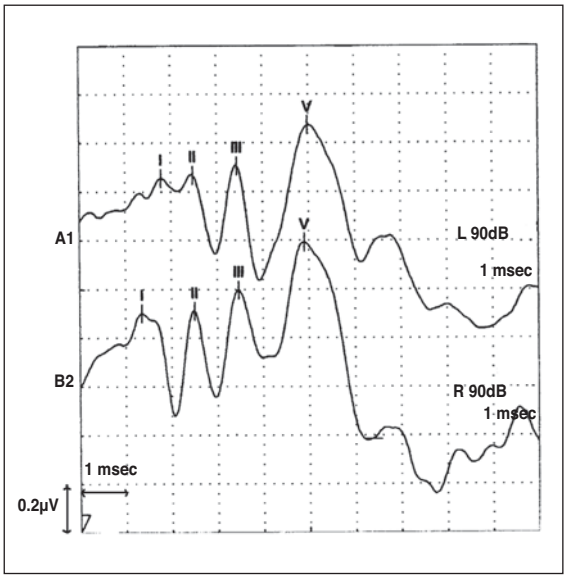

Figure 1 - Representative ABR waveforms in a control. (L: left-ear recording, R: right-ear recording)

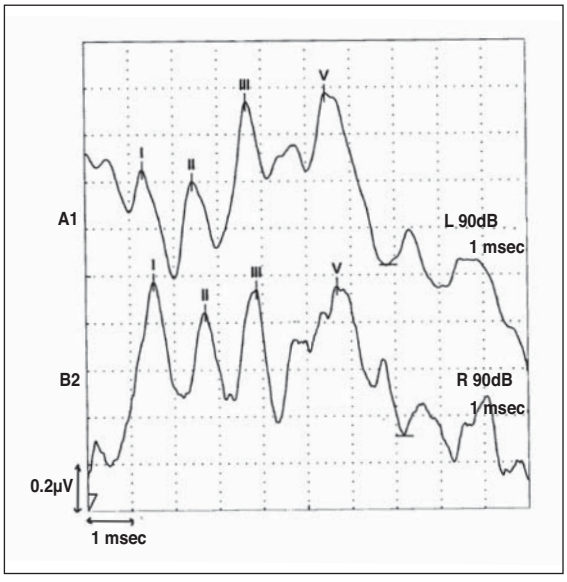

Figure 2 - Representative ABR waveforms in a child with ADHD. (L: left-ear recording, R: right-ear recording)

deficit in the activation of the central auditory process. In their study, males and females were equally distributed in the control group whose average age was 22 years, whereas 17 of the 18 children with ADD were males and the average age of this group was 9 years. The explanation for the statistically significant prolongation of ABR latencies in the ADD group may be related to gender and age. This gender and age discrepancy was eliminated in our study which included only male ADHD children and age-, sex-matched controls (21).

Another study, by Lahat et al., found prolonged latencies of wave III in females and of wave V in both males and females of the study group (6). The brainstem transmission time of waves I-III in the female subgroup and of I-V in both the male and female subgroups of the study group were significantly longer than those of the control group. Thus the results demonstrating prolonged latencies of waves III and V suggest diffuse disturbance of stimuli conduction in the brainstem. The latency of wave I in the two groups was almost identical which suggests that the disturbances in auditory stimulus conduction in children with ADD are not due to abnormalities in the inner ear. These results suggest that asymmetrical conduction of the auditory stimulus in the brainstem plays a role in the pathophysiological process of ADD/ADHD (6).

The mean latencies of the MLR waves (Na, Pa, Nb) and SVR waves (P1, N1, P2, N2) recorded in our study are shown in Table III. The MLR is thought to reflect a combination of muscle reflex activity and neural activity pos-

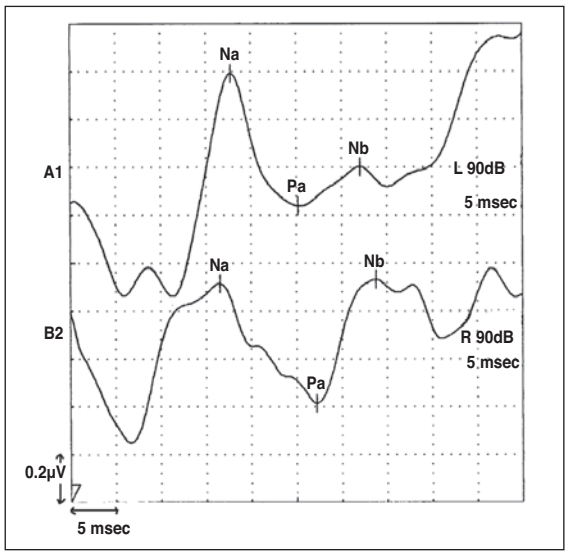

Figure 3 - Representative MLR waveforms in a control. (L: left-ear recording, R: right-ear recording)

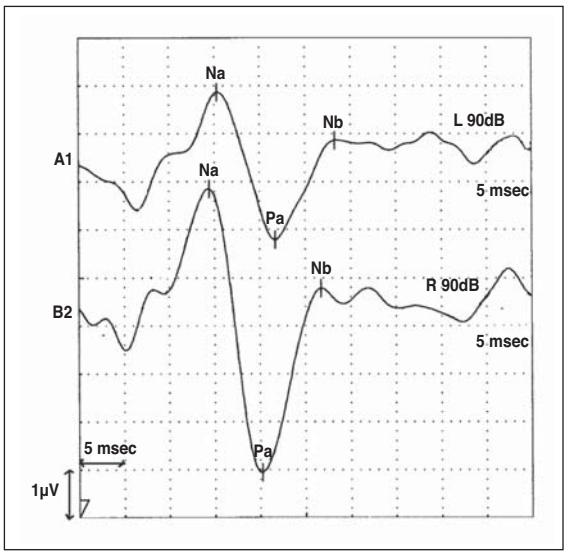

Figure 4 - Representative MLR waveforms in a child with ADHD. (L: left-ear recording, R: right-ear recording)

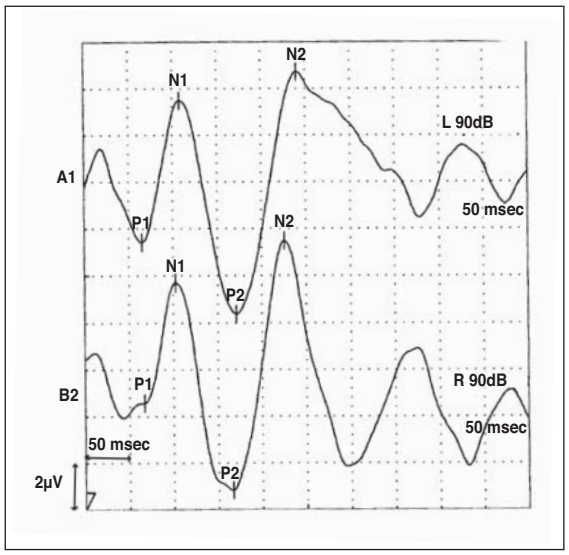

Figure 5 - Representative SVR waveforms in a control. (L: left-ear recording, R: right-ear recording)

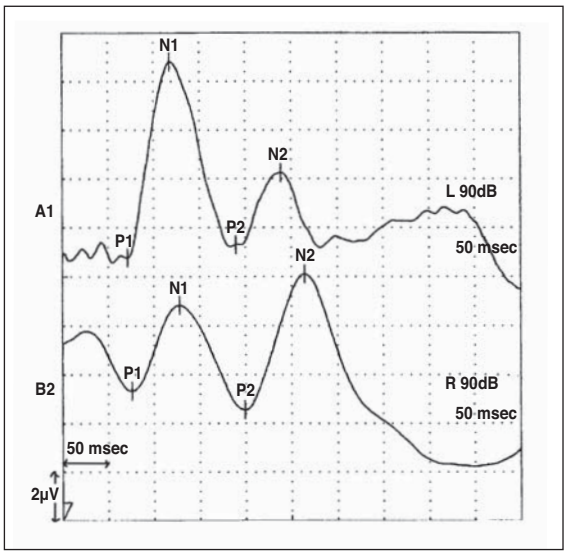

Figure 6 - Representative SVR waveforms in a child with ADHD. (L: left-ear recording, R: right-ear recording)

sibly arising in the thalamocortical radiations, the primary auditory cortex and early association cortex (10). The long latency response or SVR consists of the P1, N1, P2 and N2 waves which are widely distributed over the frontocentral scalp area. Vaughan and Ritter suggested that these potentials arise from the primary auditory cortex and temporoparietal association area and have a latency of 50-300 msec (22).The primary auditory cortex exerts a control over association cortex responses through corticocortical and corticothalamocortical connections. The SVRs are of relatively large amplitude and probably originate in the cortex (23). There emerged no significant group differences in the MLR waves between the two groups though there was prolongation of the latency of SVR waves in the ADHD children, but the difference was not statistically significant. There have been very few studies in which the ABR, MLR, SVR have been recorded, and these have given various contradictory findings. Consequently, more extensive studies are needed to comment on the electrophysiological findings in ADHD subjects. Although the present study does not suggest any auditory conduction abnormality as a contributory factor in ADHD, further studies with larger numbers of subjects are required to validate this observation.

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