Cortical Auditory Evoked Potentials in Children with Auditory Neuropathy/Dys-Synchrony

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Abstract Auditory neuropathy/spectrum disorder (ANSD), also referred to as auditory neuropathy/dys-synchrony (AN/AD) is a recently described form of hearing impairment. Many studies have shown that changing the pattern of afferent input to the cortex significantly affects cortical organization and there is little studies about cortical neuromaturation and plasticity in children with ANSD. Study of P1 component of cortical auditory evoked potentials (CAEPs) in children with ANSD. This survey was descriptive cross-sectional. During that 97 hearing impairment children were under hearing screening tests. Of these, 14 selected subjects (ear = 28) diagnosed with ANSD (an average age of 8.5 years) and evaluated by P1 component of CAEPs. Based on latency results of p1 wave, the ears of the subjects fell into two separate groups: Control (normal: n = 10) and case {total: n = 18 (delayed: n = 12) + (absent: n = 6)}. The averages of mean latency of P1 components of the case group in the right and the left ears compared to the control group had significant differences ($p < 0.05$). Abnormal latency of p1 component in ANSD children shows the possibility of different scales of disturbances in cortical auditory maturation and grow.

Keywords Auditory neuropathy/spectrum disorder · Cortical auditory evoked potentials · Auditory neuropathy/dys-synchrony

Introduction

Auditory neuropathy/spectrum disorder (ANSD) refers to damage of the peripheral nerves and not associated with loss of the myelin tissues or the death of the axons in the central nervous system [1]. The site of lesion in ANSD includes damage to the internal hair cells, lesion of the auditory nerve fibers, synaptic involvements between the internal hair cells and the type-1 of the auditory nerves [2].

ANSD is a type of the problem in the synchronization of the neural fibers and in terms of the location of the pre-synaptic lesions can have side effects on the dimensions of one's life [1]. Children who do not show expected progress in hearing rehabilitation programs, despite the appropriate treatment protocol, can be suspected to ANSD. In these children, there is the probability of normal hearing thresholds, but in most cases, hearing loss is in limits of mild to severe [3]. Patients with ANSD are likely to be either better or worse and or to be unchanged. As the age increases, it may be possible to improve the hearing thresholds and the ability to recognize speech in the silence [2]. Therefore, it is expected that peoples with abnormal cortical and subcortical potentials have neurological problems. Diagnosis of ANSD is not done correctly and this group of the children may have learning disabilities, central hearing impairments, behavioral disorders, which can cause irreversible consequences [4].

One of the most trusted adjudicative tests for ANSD is CAEPs. They measure the developmental status and limits of plasticity of the auditory cortical pathways and use to

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characterize the neural detection and/or discrimination of sounds. It helps in the evaluation and rehabilitation of people with auditory-based communication disorders [5]. Therefore, in light of the above, the aim of the current survey was the study of P1 component of the CAEPs in children with ANSD.

Materials and Methods

This survey was a descriptive case- control study, which done from June 2015 to April 2017. It was funded by Hamadan university of medical sciences on November 2015. Its number was 9410015544.

The participants consisted of 97 children with hearing impairment with a minimum of 8 months and a maximum of 18 years. The subjects were volunteers and all their parents received detailed information about the study and testing that would be involved.

The exclusion criteria consisted of the cases, who had cochlear implantation, abnormalities in the outer ears, the tympanic membranes and tympanograms [6]. The inclusion criteria were the lack of middle and the external ear diseases and being afflicted to ANSD [7].

Assessments

The subjects evaluated on air and bone conduction hearing thresholds, impedancemetric tests, distortion product otoacoustic emissions (DPOAEs) and auditory brainstem response to the click stimulation (ABR). These measures are part of the standard clinical audiological battery and therefore are not described here. In addition, children with normal results in DPOAEs and abnormal click ABR, who were diagnosed as being ANSD. Then, all them were under evaluation of p1 component of CAEPs with their hearing aids on.

The children were seated comfortably in a reclining chair or on their parent's lap in a sound attenuating booth during CAEPs testing. Stimuli were presented to this group at suprathreshold levels via loudspeakers placed in a sound attenuating booth. The state of the subjects were awaked and alerted. Eyes were open during passive recording and individuals were asked to watch a closed-captioned video during the test to reduce drowsiness. The audio levels of the movie were muted during recording of the CAEPs.

Detection of responses were onset and monaural stimulation applied (interonset interval: 0.2 ms, frequency: 1-kHz, stimulus duration: 150 ms, time window: 400 ms, intensity: 80 dB spl, rise/fall times: 60 ms). Silver/chloride cup electrodes were used for the recordings. Test conditions consisted of the active electrode was placed at Cz.

The reference electrode was placed on either one of the mastoids of the subject. The ground electrode was placed on the subject's forehead. With recording of vertical and horizontal EOG for eyeblink artifacts. Measurements and visual detection was based on baseline-to-peak amplitude. Sweeps greater than $\pm 100 \mu\text{V}$ were rejected offline, after that the remaining sweeps were averaged to compute an averaged waveform. Individual subjects had at least two averaged CAEP waveforms of 300 sweeps each. If the waveforms were judged replicable based on visual inspection, then the waveforms were averaged together to create a grand average waveform for individual subjects. The P1 peak was defined as the first robust positivity in the waveform. Peak latencies were measured in milliseconds (ms). For subjects in whom P1 latencies were computed, the latencies were compared to the 95% confidence intervals for normal P1 latency development [7].

Also, for norming process of the CAEPs, fourteen healthy persons selected of normal hearing students (7 females and 7 males; ears = 28, mean age = 8, min = 6 and max = 10 years). All had not neurological disorders (autism, attention deficiency, learning disability ...). They had normal results in standard clinical audiological battery tests and their mean latency of P1 component (right ear: mean = 110, min = 78, max = 115 and left ear: mean = 109, min = 77, max = 120). The P1 waveform was independently rated by 2 experienced clinicians as normal or abnormal across two runs.

Methodological considerations/limitations: In this research, privacy and personal information were reserved and respected. There was no action that was in conflict with their safety, health and well being. The participants were excluded from the survey at any stage that the individuals concerned were reluctant to continue to cooperate.

Data Analyses: All analysis was done by means of the statistics software SPSS₁₇. Kolmogorov–smirnov test was used for evaluation of normal test distribution. Independent *t* test used to compare findings among the groups.

Findings

Of the 97 children who were under auditory screening, 14 cases (28 ears) had ANSD (Table 1), with the average age of 8.5 years (min = 6 and max = 10 years).

Based on latency of p1 component of CAEPs, the subjects (ears) fell into two separate groups: 1- the case, who had normal latencies of P1 components ($n = 10$, 35.7%) and 2- the control with abnormal P1 latencies (18, 64.3%) which consisted of delayed waves ($n = 12$, 42.8%) and absent responses ($n = 6$, 21.5%), (Table 2).

Referring to Table 2, it is interesting to note that every ten children (right ear = 9 and left ear = 1) with normal

Table 1 Result of the case history information of children with auditory neuropathy/dys-synchrony (ANSD)

Subject	Etiology	Auditory brainstem response to the click stimulation (ABR)	Distortion product otoacoustic emissions (DPOAEs)	Unaided hearing thresholds mean right ear (dB HL)	Unaided hearing thresholds mean left ear (dB HL)	Hearing aids fitting age (year. month)
1.	No risk factors	Absent	Present	65	70	2.03
2.	Hypoxia	Absent	Present	95	100	0.90
3.	Premature, low birth weight, jaundiced, ototoxic medication	Absent	Present	80	75	0.20
4.	Premature, mechanical ventilation, ototoxic medication	Absent	Present	85	85	0.11
5.	Premature, jaundiced, blood transfusion, mechanical ventilation	Absent	Present	65	75	1.20
6.	Mechanical ventilation	Absent	Present	90	85	2.10
7.	No risk factors	Absent	Present	95	95	0.09
8.	Premature, low birth weight, jaundiced, blood transfusion	Absent	Present	75	85	1.10
9.	Premature, ototoxic medication, mechanical ventilation	Absent	Present	80	75	2.01
10.	No risk factors	Absent	Present	80	85	2.04
11.	No risk factors	Absent	Present	95	90	1.10
12.	Jaundiced	Absent	Present	100	90	2.0
13.	Premature, blood transfusion, ototoxic medication	Absent	Present	95	90	0.19
14.	Family history of hearing loss	Absent	Present	70	65	0.11

Table 2 The mean latency of P1 component of the cortical auditory evoked potentials (CAEPs) in children with auditory neuropathy/dys-synchrony (ANSD): case group (ears = 18) and control group (ears = 10)

SD	Maximum (ms)	Minimum (ms)	Mean (ms)	Number	Latency of P1 component of CAEPs	
1.44	120	87	113	9	Right ear	Normal (control group)
3.43	127	85	115	1	Left ear	
3.41	196	128	174	5	Right ear	Abnormal (case group)
8.14	199	122	178	13	Left ear	

latency of P1 components had time interval between use of hearing aids in the ears (mean = 14, min = 11 and max = 22 months). Also, four children with bilateral abnormal P1 components were fit with hearing aids at a significantly later age of language learning {case-1 = 2.10, case-2 = 2.04, case-3 = 2.03, case-4 = 2.0 (years. months)}.

The averages of mean latency of P1 components of the case group in the right and the left ears compared to the

control group had significant differences ($p < 0.05$). Therefore, the probability of observing the abnormalities in the latency of p1 component of CAEPs was one of the signs of our ANSD.

Discussion

The aim of the current survey was the study of P1 wave of CAEPs in children with ANSD. Our findings confirmed that all our ANSD children had abnormal ABR. Whereas, some of them had normal P1 responses (35.7%) and the rest showed abnormal patterns (64.3%).

Since, ABR has been used to examine synaptic events related to more peripheral sensory functions and CAEPs have been used to examine more central processes related to how the brain makes use of the sound. So, we conclude that our children with ANSD had malformations in synaptic events and cortical contributions of the processing the sound. In other hand, abnormal results of the ABR shows reduced neural synchronization, which can be a sign of decreased speech comprehension [7–9]. As a result, this abnormality, which is expected to occur in neuronal transmission, can be including cortical events [10, 11]. Therefore, people with ANSD may have defects at the entire of the ascending and the descending auditory pathways. However, observable cortical potentials was found in some of our participants, which is consistent with previous studies [12–14].

Since, CAEPs are to result from stimulus-locked post-synaptic potentials within apical dendrites of pyramidal neurons in the cerebral cortex. So, typical P1 component of CAEPs in our ANSD children suggested normal maturation of central auditory system. They are regularly used in research to determine how physical acoustic energy translates into patterns of brain activity and contributes to perception in normal and hearing-impaired listeners [5, 15]. Therefore, the abnormal responses of some of our cases with ANSD indicated an impairment in growth and maturity of the neural structures in the cerebral cortex. The studies by other researchers in this area are matched by our research findings. They also reported abnormal responses in their study samples of their ANSD children [13, 15, 16].

Indeed, abnormal latencies of P1 components in our ANSD children, showed decreasing of temporal processing related to the neural encoding [7]. Because that the P1 component of CAEPs does not approximate a person's ability to perceive these sounds, but, it is the change response that corresponds well to a person's behavioral ability to discriminate the stimuli. It is the change in acoustic information, from one auditory signal to another. In other words, the change from silence to sound is so robust that all age groups can detect it [5, 17, 18]. However, we found that the majority of our subjects (64.3%) appeared not to benefit from amplification or their hearing aids, in that they showed delayed/abnormal P1 responses and since P1 latency is considered a biomarker for maturation of the auditory cortical areas [5, 11]. So, our results

demonstrated that children exhibit different levels of central auditory maturation. For this group, instead of using hearing aids, it seems that cochlear implant is beneficial. However, we refer them for the exact evaluations of the cochlear implantation candidate at Beasat hospital's cochlear implantation center (Hamadan, Iran).

Conclusion

We believe that in children with ANSD, there is the possibility of the abnormal cortical auditory evoked potentials and as the latency of the P1 component reflects the sum of synaptic delays throughout the peripheral and central auditory pathways [12, 13]. So, the findings of our survey showed that children with ANSD had different patterns of central auditory grow. In fact, ANSD can be a widespread lesion in the entire auditory system, not be separated from central auditory processing disorder and is one of its sub-categories. The children with ANSD, according to the degree of insufficient growth and immaturity of the central auditory system, show different levels of the lesions in the performing of hearing functions.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

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