Auditory neuropathy spectrum disorder: a new approach to hearing aid fitting

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Received 25 April 2016
Accepted 26 April 2016

The Egyptian Journal of Otolaryngology
2017, 33:67–77

Objective
The aim of this study was to explore the outcome of hearing aid amplification in children with auditory neuropathy spectrum disorder (ANSD) using speech P1 cortical auditory evoked potential (P1-CAEP).
Study design
Forty-five children were divided into three groups: the ANSD group (*n*=15), the sensorineural hearing loss (SNHL) group (*n*=15), and the normal hearing group (*n*=15). The ANSD group had a mean age of 48.2 (±29.4) months and included children with moderate-to-severe hearing loss, a history of bilateral hearing aid use for at least 6 months, and absence of comorbid disorders. The SNHL group was closely matched to the ANSD group. Verification of hearing aids was carried out twice with 6 months of interval and included evaluation of aided sound field and P1-CAEP, and evaluation using the Arabic version of the Infant Toddler Meaningful Auditory Integration Scale (IT-MAIS). The P1-CAEPs were elicited using the temporally modified synthetic 'ba' and 'da' syllables.
Results
In the initial evaluation, 80% of ANSD children showed P1 response to the 'ba' stimulus and 87% of children to the 'da' stimulus. Only one child from the SNHL group did not show P1-CAEP responses to the 'da' stimulus. The latency of P1 was prolonged in both groups compared with the normal hearing loss group. At 6-month evaluation, the P1-CAEP latencies improved equally in the ANSD and SNHL groups. Children with absent responses persisted to have absent responses. The mean IT-MAIS scores was initially 45.5 (±20) in the ANSD group and 79 (±9) in the SNHL group and increased after 6 months in both groups. The IT-MAIS scores negatively correlated with the P1-CAEP latency in the two evaluation sessions and positively correlated with the age of hearing aid fitting.
Conclusion
Around 50% of ANSD children demonstrated benefit from amplification. They showed evidence of normal central auditory maturation and progress in auditory skill development. Longitudinal P1 recording is recommended in the comprehensive audiological test battery in ANSD population using temporally modified speech stimuli.

Keywords:
auditory neuropathy spectrum disorder, cortical auditory evoked potential, hearing aids, temporally modified speech

Egypt J Otolaryngol 33:67–77

1012-5574

Introduction

Among children with permanent hearing loss, between 2 and 15% will have auditory neuropathy spectrum disorder (ANSD) [1–3]. Patients present with symptoms that include the presence of otoacoustic emissions, absent or grossly abnormal auditory brainstem responses (ABR) and stapedial reflexes, and speech perception and behavioral outcomes, which are disproportionate to pure-tone auditory thresholds [4].

The heterogeneity underlying this population and the lack of predictability as regards behavioral outcome make it difficult for clinicians to diagnose, understand, and treat patients with ANSD, particularly young children. There are three current forms of hearing technology that are recommended as intervention for children with ANSD: cochlear implants, hearing aids, and FM technology [5]. A number of studies examined outcomes following cochlear implantation in children with ANSD but focused mainly on children with severe-to-profound hearing loss [6–8].

Rance *et al.* [9] highlighted that the degree of hearing loss may also have an influence on the success of cochlear implants versus hearing aids for children with ANSD. Children who have less severe degrees of hearing loss and use hearing aids show better aided

 DOI: 10.4103/1012-5574.199408

speech recognition scores compared with children with cochlear implants. Furthermore, a significant number of children with ANSD may have other conditions or comorbidities that negatively impact outcomes irrespective of the treatment approach [10]. Thus, even though cochlear implantation is often cited in the literature as a successful remediation approach for ANSD, clinicians and families should be cautious when deciding on the appropriate management technique [2].

The difficulty with interpreting the results of studies on ANSD and acoustic amplification is that there is little reported evidence on how children with ANSD with hearing thresholds in the mild-to-severe range perform with appropriately fit hearing aids set to prescriptive targets [5]. Rance and Barker [11] and Ching *et al.* [12] suggested that there is additional need for research that explores the impact of hearing aid performance on children with ANSD in the mild-to-severe hearing loss range.

The American Academy of Audiology (AAA) Pediatric Amplification guidelines 2013 [13] stated that children with ANSD should have a hearing aid trial if auditory thresholds are insufficient to support speech perception at conversational levels. This trial would consist of a designated time period of experience with appropriately fit hearing aids, although the guidelines are not specific on how long a trial should last. The guidelines recommended assessment of cortical responses evoked by speech sounds to obtain the audibility of speech with and without hearing aids.

Cortical auditory evoked potentials (CAEPs) can provide information about the audibility of sounds (including speech sounds) and about the maturity of the auditory system. CAEPs in response to sounds presented in the sound field can be measured with and/or without amplification. The presence of a CAEP in response to a speech sound indicates that the sound eliciting the CAEP is evoking activity in the auditory cortex. This provides confirmation that the hearing aid settings are sufficient to achieve audibility of speech at the sound level used for testing [14].

CAEPs have been successfully recorded in children and adults with ANSD [4,9,15]. However, nearly all studies used the ba stimulus to elicit the CAEPs, which is a stop consonant with a short formant transition. Rance and Barker [11] suggested that stop consonants are particularly difficult to perceive for adult patients with Friedrich ataxia and ANSD. However, the effect of prolongation of the rapidly changing components of consonant vowel on speech perception in a group of adult ANSD was illustrated by Hassan [16], who concluded that the duration of consonant transitions could represent important clues for speech perception in this group of patients. Sharma *et al.* [4] recommended the use of temporally modified stimuli in recording CAEPs in children with ANSD.

In summary, little is known about children with ANSD who have been identified early and fit using best practice recommendations, in comparison with children with similar degrees of sensorineural hearing loss (SNHL). On the basis of the AAA [13] recommendations for pediatric amplification, this study was designed to explore the outcome of hearing aid amplification in a group of children with ANSD in the moderate-to-severe degree using P1-CAEP elicited by temporally modified speech syllables. This might provide valuable evidence to support clinical decisions about audiological management and intervention for this population.

Materials and methods

Patients

Forty-five children participated in the present study and were divided into three groups: the ANSD group (n=15), the SNHL group (n=15), and the normal hearing group (n=15). Efforts were made to include children of similar ages and sex in each group.

The ANSD group comprised 15 children (11 boys and four girls) fulfilling the criteria for ANSD in both ears (absent or abnormal ABR that is out of proportion to behavioral audiometric thresholds, with preserved otoacoustic emissions and/or cochlear microphonics). ANSD children with mild-to-severe degree of hearing loss [with unaided pure-tone average (PTA) of 500, 1000, 2000, and 4000 Hz≤80 dBHL], a history of bilateral hearing aids use of at least 6 months before study time, and absence of comorbid disorders such as blindness, neurological disorder, and mental retardation were included in the study.

At the first testing visit, their ages ranged from 16 to 120 months, with a mean of 48.2 (±29.4) months. On average, the children had a mean age of hearing aid fitting of 25.6 (±14.5) months (range=6–60 months) and had 21.2 (±21) months of experience with their devices (range=6–90 months).

The SNHL group included 15 children (seven boys and eight girls) with bilateral SNHL (unaided PTA of 500, 1000, 2000, and 4000 Hz≤80 dBHL). Both the ANSD and SNHL groups were matched as closely as

possible on chronological age, sex, better ear PTA, and better-ear aided sound field (Tables 1 and 2).

The normal hearing loss group comprised 15 age-matched and sex-matched (11 boys and four girls) normal hearing children (PTA thresholds<20 dBHL for frequencies 500–4000 Hz). Their mean age was 49 (±9.3) months (range=36–66 months). This group was included to provide a reference of typically maturing CAEPs to different speech stimuli without the influence of hearing impairment.

All children in the present study had normal middle ear functions, with at least average intelligent quotient as measured using the Arabic Hiskey Nebraska test of learning aptitude. They were recruited from clients attending the Audiology Clinic of Ain Shams University, Otorhinolaryngology Department, Cairo, Egypt, over the period from September 2013 to October 2015. Informed consent was obtained from parents with explanation of the test procedures, benefits, and risks according to the ethical rules.

Methods

The children of the three study groups were subjected to the following:

(1) Detailed history taking and age-based hearing threshold determination to ensure proper selection of children. For children older than 3 years (n=33), the method of threshold estimation for 250–8000 Hz frequencies, dependent on child cooperation, was either conditioned play audiometry or voluntary thresholds [17]. Children younger than 3 years or uncooperative children (n=12) underwent behavioral observation audiometry [17]. ABR was performed in the present study as a part of diagnosis in children with ANSD and for SNHL children who were younger than 3 years to estimate their hearing threshold levels. Speech audiometry, including speech reception/detection threshold (SDT/SRT), was performed using Arabic bisyllabic words for children [18].

The above procedures were performed in a double-walled, acoustically treated booth (I.A.C. model 1602) using the two-channel audiometer interacoustics model AC40 calibrated according to ANSI S.3.6, 1996 with headphones TDH 39 and a sound field testing facility. The middle ear functions were assessed through tympanometry, acoustic reflex threshold measurements using interacoustics model AZ26 with 220 Hz probe tone, calibrated according to ANSI S3.39–1987. Furthermore, ABR was performed during sleep, when needed, using the Auditory Evoked Potential System v7 with the Bio-logic Navigator Pro unit to collect and analyze the waveforms in a sound-attenuated room

(2) Hearing aid verification:

The hearing aid fitting process was checked for every child before contribution in the study. It was found that nine ANSD children and all SNHL children were using the same model of hearing aid. The author ensured that the fitting process of the devices were uniform and consistent with the AAA Pediatric Amplification best-practice guidelines [13]. The hearing aids were adjusted to provide the best possible match to targets at each frequency. An optimum feedback manager condition was ensured for all ears tested. The gain/advanced features were held constant throughout the test situation. Volume control, digital noise reduction, and program selector features were disabled.

Verification of hearing aids included evaluation of aided sound field, P1-CAEP, and evaluation

Table 1 Mean, SD, *F* and *P* values of age in months in the three study groups

Groups	Mean	SD	*F* value	*P* value
ANSD	48.2	29.4	0.38	0.7
SNHL	54.4	18.6		
NH	49.1	9.3		

No statistically significant difference existed in age across the three study groups. ANSD, auditory neuropathy spectrum disorder; NH, normal hearing; SNHL, sensorineural hearing loss. P>0.05, nonsignificant.

Table 2 Student's *t*-test between the auditory neuropathy spectrum disorder and sensorineural hearing loss groups

Variables	ANSD			SNHL			*t*-Value	*P* value
	Mean	SD	Range	Mean	SD	Range		
Unaided PTA	68	15.3	50–80	78	4.3	55–80	–2	0.07
SDT	68	13	45–80	68	7.3	55–80	0.1	0.9
Age of fitting	25.7	14.5	6–60	22	14.5	7–60	0.7	0.5
Duration of HA	21.2	21	6–90	33	16.8	12–77	1.7	0.1

ANSD, auditory neuropathy spectrum disorder; PTA, pure-tone average; SNHL, sensorineural hearing loss. P>0.05, statistically nonsignificant.

using the Arabic version of Infant Toddler Meaningful Auditory Integration Scale (IT-MAIS) [19]. The parents were asked to continue full time use of the hearing aids for their children with regular monthly visits to ensure the consistency of hearing aid use and to solve any problems encountered. The P1-CAEP and IT-MAIS were repeated after 6 months from the initial evaluation for the ANSD and SNHL groups. The verification procedure included the following.

(a) Aided sound field testing for frequencies 500–4000 Hz thresholds. The aided thresholds were obtained using warble tones presented through loudspeaker kept at 1-m distance and 0° azimuth. Aided SDT/SRT was performed using PBKG [18].

(b) Aided speech P1-CAEP recordings. CAEP testing was carried out using Bio-logic Auditory Evoked Potential System v7 with the Bio-logic Navigator Pro unit to collect and analyze the waveforms in a sound-attenuated room. The stimuli used were the synthetic speech stimuli 'ba' and 'da'. All stimuli were recorded by a female talker using a sound recorder Sony model ICD-PX 333/PX 333 F and were temporally modified and manipulated acoustically using the audacity software version 2.0.4. The ba stimulus had maximum energy concentration around 600 Hz and 150 ms duration with the amplitude of voicing kept constant for 140 ms. However, the da stimulus had maximum energy concentration around 4000 Hz with a duration of 200 ms and amplitude of voicing kept constant for 190 ms. The longer duration of the stimuli were selected in a trial to counteract the temporal processing deficit known in the ANSD.

The stimuli were presented at a rate of 0.5/s with ISI 1800 ms (offset to onset), in alternating polarity, and at three presentation levels 75 dBSPL. They were delivered through a single loudspeaker connected with an external amplifier to the evoked potential equipment. The loudspeaker was set at 0 azimuth facing the patient one meter apart. During CAEP recording, the children were seated comfortably watching a muted cartoon movie to distract them and to ignore the stimuli presented.

An ipsilateral recording (vertex to ipsilateral mastoid with ground Fpz) was the protocol used. The impedance at each electrode site was less than 5 kΩ and the interelectrode impedance was less than 2 kΩ. The responses were bandpass filtered between 1 and 30 Hz with an artifact rejection threshold set to ±100 μV. Response analysis window included −100 ms prestimulus to 500 ms poststimulus, total 600 ms. Two averages of 100 sweeps were obtained for each stimulus condition.

(c) *Aided speech P1-CAEP data analysis*: The replicated CAEP waveforms (P1-N1-P2-N2) were collected for all children interpreted using subjective response detection techniques. For a response to be considered present, there should be at least one peak (according to replicable data) resided within the chosen time window. The pattern of waveform morphology was determined followed by latency and amplitude measurements.

The latency values were marked taking into account the maximum amplitude points. If a single peak was present in the anticipated target window, the latency was taken at the middle of that peak. If two peaks were present, the latency was measured by taking the average values calculated from values obtained at each peak. If multiple peaks or broad response was present, latency was obtained from the intersection of the extrapolated lines from the ascending and descending slopes. The amplitude was established as the difference between the 0.0 μV point (recording baseline) and the maximum positive value, in this case the P1 and P2 components, and the negative value for the N1 and N2 components were measured in μV.

(d) The Arabic version of the IT-MAIS [19]. As a measure of auditory skill development the Arabic version of the IT-MAIS was applied by completing a structured interview with the children's parents. The IT-MAIS targets three main areas of auditory development: (a) vocalization behavior; (b) alerting to sounds; and (c) deriving meaning from sounds [20]. These areas of development were assessed in 10 open-ended questions. After listening to the parents' response to each test item, the clinician interviewer assigns a score, from 1 (lowest) to 4 (highest), to each question, for a total of 40 points.

Statistical analyses were performed using SPSS 16. The independent *t*-test was used to compare two different

(independent) groups, whereas the paired *t*-test was used to compare two paired groups. The ranked Spearman and biserial correlation test was used to study the possible association between two variables in each group. A level of *P* value less than 0.05 was considered significant and *P* value less than 0.01 was highly significant. A statistician was used for guidance in the study.

Ethics

The Research Ethics Committee approved the study.

Results

Demographic and audiological profile

The majority of ANSD (*n*=10, 67%) children had medical risk factors. Seven had a history of neonatal insult 'prematurity, low birth weight, and/or hyperbilirubinemia' and three had a family history of ANSD. In the SNHL group, six children had a family history of hearing loss, with absence of other risk factors, specifically a history of neonatal insult.

In the ANSD group, the mean better unaided ear PTA was 65 (±15.3) dBHL or less [range=50–80 dBHL and mean SDT=66 (±13) dBHL]. Six children had moderate hearing loss (between 40 and ≤55 dBHL), and the remaining were in the moderate-to-severe category (between 56 and ≤80 dBHL). Progressive nature of the disorder was seen from the serial evaluations of three children as determined by more than a 10 dBHL decline in thresholds across the child life. The other 12 children demonstrated stable thresholds.

As per selection, the SNHL group was matched to the ANSD group in nearly all variables. Table 2 shows the absence of statistical significance between the two groups in the variables tested.

Hearing aid verification

The mean aided PTA was 30 (±10) dBHL and 27 (±7) dBHL in the ANSD and SNHL groups, respectively, with no statistically significant difference between them (*t*=0.8, *P*=0. 4). Figure 1 shows the mean aided sound field thresholds in both study groups.

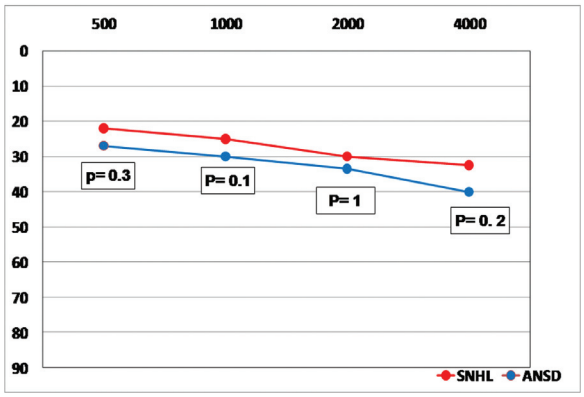
Speech P1 cortical auditory evoked potential

In all children of the control group, P1-CAEPs were recorded to both the 'ba' and 'da' stimuli (Fig. 2). The P1 latency were within the normative data for children with similar age [21,22]. In the initial evaluation, 80% of ANSD children (*n*=12) showed P1 response to the 'ba' stimulus and 87% of children (*n*=13) to the 'da' stimulus. Only one child from the SNHL could not show P1-CAEP to the 'da' stimulus, with recordable responses from all remaining children (Fig. 2). No statistically significant difference was found in the percent detection of the 'ba' (*Z* value=–1.8, *P*=0.1) and 'da' stimuli (*Z* value=–0.6, *P*=0.5) between the ANSD and SNHL groups.

The P1-N2 was the dominant waveform morphology seen across the children of the three groups. The single peaked P1 was present in 73% (*n*=11/15) of controls, in 70% (*n*=9/13) of the ANSD group, and in 60% (*n*=9/15) of the SNHL group. The double-peaked waveform pattern was detected in the remaining children.

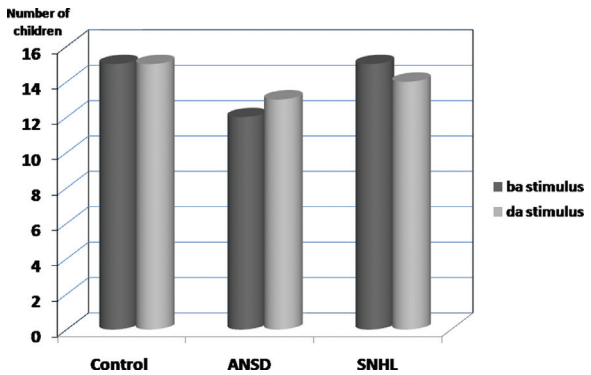
On comparing the P1 latency in both study groups with the normative values of the control group, it was found that seven ANSD children (54%) had prolonged P1-CAEP latency, beyond at least one SD, to 'da' stimulus and six children (50%) had prolonged P1-CAEP latency to 'ba' stimulus. In the SNHL group, prolonged P1-CAEP was seen in four children (28.5%) in response to 'da' stimulus and in five children (33%) to 'ba' stimulus. Normal P1 latency

Figure 1



Comparable aided sound field thresholds in auditory neuropathy spectrum disorder (ANSD) and sensorineural hearing loss (SNHL) children.

Figure 2



The percent of children in the three groups with recordable P1 cortical auditory evoked potentials (P1-CAEPs).

to both stimuli was present in the remaining children of the two groups.

Table 3 illustrates the P1 latency and amplitude measures of the test stimuli across the three study groups. One-way analysis of variance showed that, across the three groups, the mean P1 latency for the da stimulus and P1 amplitude for the ba stimulus showed a statistically significant difference (F=0.7 and P=0.04; F=0.001 and P=0.001, respectively). The post-hoc test analysis revealed that the mean difference existed between the control group and both the ANSD and SNHL groups. Meanwhile, the ANSD and SNHL groups had comparable P1 latency and amplitude except for the smaller P1 amplitude seen in ANSD to the 'ba' stimulus (Table 4).

After 6 months of continuous regular hearing aid use with the proper fitting process, all ANSD and SNHL children returned for follow-up evaluation of the P1-CAEP without dropout rate. Children with absent responses continued to have absent responses even after 6 months of stimulation. Two children from the ANSD and one child with SNHL showed improvement in P1 latency and had values that were within the normative data. The mean latencies of P1-CAEP to both stimuli were reduced with nearly same amplitude measures in the ANSD and SNHL groups. The difference in P1 latency across the evaluation sessions in the ANSD and SNHL groups was statistically significant using the paired t-test (Table 5). The change in latency and amplitude measures reduced the statistical difference across the three groups (analysis of variance, P>0.05).

Infant Toddler Meaningful Auditory Integration Scale

At the initial evaluation testing, the mean scores for IT-MAIS was 45.5 (±20) in the ANSD group. The

Table 3 One-way analysis of variance for P1 latency and amplitude across the three study groups in the initial evaluation

Variables	Stimulus	Control group			ANSD			SNHL			*F* value	*P* value
		Mean	SD	Range	Mean	SD	Range	Mean	SD	Range		
Latency	ba	113	22	78–130	145	56	70–229	143	46	81–213	0.74	0.07
	da	107	15	75.4–125	139	41	75–210	134	41	78–216	0.71	0.04*
Amplitude	ba	13.7	6.2	5.4–30	5.3	5	1.3–21	7.4	5.2	1.5–25	8	0.001*
	da	10.5	4	5.1–21	6	6.4	1.8–21	8.8	6.5	2.3–19	2.2	0.18

ANSD, auditory neuropathy spectrum disorder; SNHL, sensorineural hearing loss. P>0.05, statistically significant.

Table 4 Post-hoc test for the P1 latency and amplitude difference between the groups in the initial evaluation

Variables	Stimulus	Group		Mean difference	Significance
Latency	ba	Control	ANSD	–29.29286	0.092
		Control	SNHL	–31.18571	0.063
		ANSD	SNHL	1.89286	0.912
	da	Control	ANSD	–31.93082*	0.02
		Control	SNHL	–26.13595*	0.04
		ANSD	SNHL	–5.79487	0.657
Amplitude	ba	Control	ANSD	8.50333*	0.000
		Control	SNHL	–2.78933	0.193
		ANSD	SNHL	6.35190*	0.007
	da	Control	ANSD	–4.46667	0.040
		Control	SNHL	–2.15143	0.312
		ANSD	SNHL	–1.67733	0.431

ANSD, auditory neuropathy spectrum disorder; SNHL, sensorineural hearing loss.

Table 5 Paired *t*-test for P1 measures in the auditory neuropathy spectrum disorder and sensorineural hearing loss groups between the initial and after 6 months of evaluation

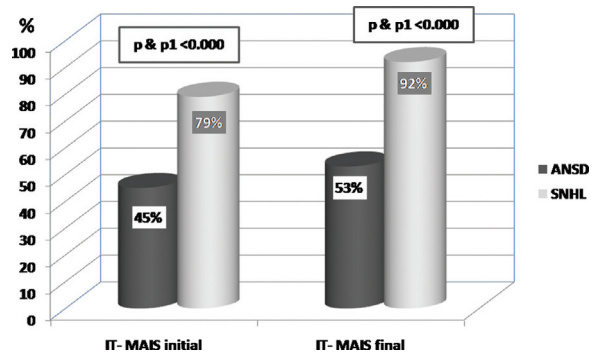
Variables	Stimulus	ANSD						SNHL					
		Initial		Final		Paired *t*-value	*P* value	Initial		Final		Paired *t*-value	*P* value
		Mean	SD	Mean	SD			Mean	SD	Mean	SD		
Latency	ba	145	60	138	56	6	0.000*	143	47	133	46	7	0.000*
	da	139	41	132	40	13	0.000*	134	42	128	40	0.4	0.7
Amplitude	ba	5.3	5	6.8	6	–1.9	0.06	7.4	5.2	9	4.5	–3.8	0.002
	da	6	6.4	7.1	4.6	–1.5	1	8.8	6.5	10	6.2	–1.9	0.07

ANSD, auditory neuropathy spectrum disorder; SNHL, sensorineural hearing loss.

SNHL group had higher mean scores of 79 (±9). This difference was statistically highly significant ($P<0.001$) (Fig. 3). The scores improved in both groups following 6 months of auditory stimulation. Although statistical significance was observed in both groups, the improvement was limited in the ANSD group.

In ANSD children of the present study, the latency of P1-CAEP in the two evaluation sessions was negatively correlated to IT-MAIS scores. The shorter the P1-CAEP, the higher was the scores of IT-MAIS (Table 6 and Fig. 4). Furthermore, the IT-MAIS was further positively correlated with the age of hearing aid fitting. The younger the age of hearing aid fitting, the higher was the IT-MAIS scores in the two evaluation sessions (Table 6).

Figure 3

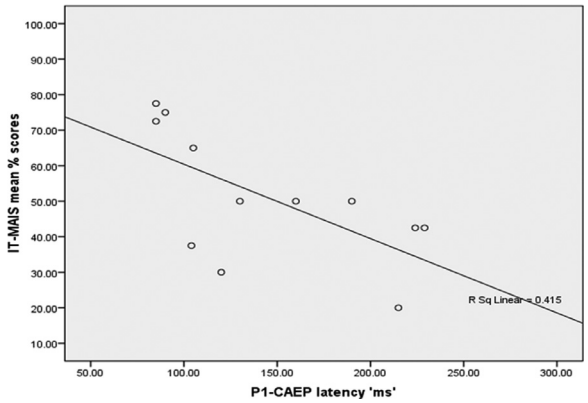


The higher mean Infant Toddler Meaningful Auditory Integration Scale (IT-MAIS) scores in the sensorineural hearing loss (SNHL) group compared with the auditory neuropathy spectrum disorder (ANSD) group across the two evaluation sessions.

Discussion

In an attempt to provide a clinical tool for guiding intervention choices and assessing their efficacy in

Figure 4



The existence of negative correlation between the Infant Toddler Meaningful Auditory Integration Scale (IT-MAIS) scores and the P1 cortical auditory evoked potential (P1–CAEP) latency in children with auditory neuropathy spectrum disorder (ANSD).

Table 6 Pearson correlation study between P1 cortical auditory evoked potential latency and Infant Toddler Meaningful Auditory Integration Scale, age of fitting in the auditory neuropathy spectrum disorder group

	Latency 'da' initial	Latency 'da' final	Latency 'ba' initial	Latency 'ba' final	IT-MAIS initial	IT-MAIS final	Age of fitting
Latency 'da' initial							
Pearson correlation		0.998**	0.836**	0.840**	–0.684**	–0.719**	
Significance (two-tailed)		0.000	0.001	0.001	0.010	0.006	
Latency 'da' final							
Pearson correlation	0.998**		0.837**	0.841**	–0.291	–0.337	
Significance (two-tailed)	0.000		0.001	0.001	0.336	0.260	
Latency 'ba' initial							
Pearson correlation	0.836**	0.837**		0.997**	–0.631*	–0.683*	
Significance (two-tailed)	0.001	0.001		0.000	0.028	0.014	
Latency 'ba' final							
Pearson correlation	0.840**	0.841**	0.997**		–0.637*	–0.689*	
Significance (two-tailed)	0.001	0.001	0.000		0.026	0.013	
IT-MAIS initial							
Pearson correlation	–0.684**	–0.291	–0.631*	–0.637*		0.964**	–0.530*
Significance (two-tailed)	0.010	0.336	0.028	0.026		0.000	0.042
IT-MAIS final							
Pearson correlation	–0.719**	–0.337	–0.683*	–0.689*	0.964**		–0.505
Significance (two-tailed)	0.006	0.260	0.014	0.013	0.000		0.04

IT-MAIS, Infant Toddler Meaningful Auditory Integration Scale.

children with ANSD, this study was carried out. This longitudinal study included a group of children with ANSD in the moderate-to severe hearing loss range with a history of regular hearing use who were assessed using P1-CAEPs and IT-MAIS. They were well-matched with a similar group of SNHL on a number of important factors, including chronological age, degree of hearing loss, age at early intervention, and duration of hearing aid use. Expectedly, the groups were not matched on birth history – the ANSD group presented with a more complicated birth history compared with the SNHL group. It is encouraging to note that all of the children with ANSD who had hearing aids fit using AAA guidelines showed aided audibility levels that were within the long-term average speech spectrum. The aided sound field thresholds were comparable between the two study groups.

In the present study, the majority of, but not all, ANSD children demonstrated recordable cortical potentials. This finding is in agreement with the reports of previous studies [4,9,23] in which P1-CAEP response have been documented for only 50–70% of children with ANSD fitted with hearing aids and 85% of children with CIs. Sharma *et al.* [4] reported that 71% of ANSD who were hearing aid users presented with the presence of CAEP responses (of whom 38% had normal P1 latencies and 33% had delayed P1 latencies) and 29% of participants had absent CAEP responses. Those figures are nearly similar to the present study, which found that P1-CAEP were recorded from around 80% of children in response to 'ba' stimulus and 87% to 'da' stimulus with normal P1 latency seen in half of them.

It is noteworthy to say that all previous studies in ANSD used only one speech syllable 'ba' to elicit P1-CAEP [4,9,11]. It is a stop consonant of 90 ms duration with a short formant transition and amplitude of voicing that is held constant for 80 ms. As designed, the present study used two different speech stimuli 'ba' and 'da' that differed in their frequency spectrum (low '600 Hz' vs. high 4000 Hz, respectively) and with longer formant transition duration. The aim for choosing two different stimuli with different frequency spectrum was to explore any variation in cortical responses related to stimulus characteristics in ANSD population, if any. The particular use of ba and da was based on previous reports emphasizing that children with auditory neuropathy could discriminate among words containing front sounds, bilabials, or labiodentals, better than those containing other sounds [24]. Similarly, Hassan [16] showed better perception for the CV that contained /t/ and /d/ as alveolar–dental compared with velar sounds /k/ and /g/. The increase in percent delectability of P1-CAEP in ANSD of this study, relative to previous studies, might be explained by the use of a longer duration of the stimulus in particular in a system with a deficit in temporal processing abilities. This processed speech provided more temporally sharp, distinguishable input that may be hypothesized to create a more robust phonetic element representation within the cortical learning machinery [25,26].

Absent or delayed P1 responses in the current study in ANSD children reflect the underlying delays and/or abnormalities in auditory cortical development, most likely resulting from highly dys-synchronous input patterns to the cortex. In contrast, typical P1-CAEP morphology, latency, and amplitudes in children with ANSD suggest a normal level of maturation of central auditory pathways, implying that the underlying neural dys-synchrony is mild enough to allow for normal cortical organization to occur [4].

In the present study, although the majority of children showed replicable CAEP responses, all children showed absent ABR. Kraus *et al.* [15] have noted that the ABR measures spike discharges, or action potentials, in the axons of the auditory nerve, whereas CAEPs are thought to measure the summation of excitatory postsynaptic potentials arising from dendritic zones in the cortex. The dys-synchronous firing in ANSD completely degrades the rapidly occurring, high-frequency ABR waveform peaks but does not have the same effect on slower, broader CAEP peaks. However, as the level of underlying jitter increases, the aggregate CAEP response will be degraded to a higher degree due to fewer time-locked peaks contributing to the averaged CAEP waveform, and/or fewer than normal active nerve fibers responding [27]. This can result in lower than normal amplitudes and delayed latencies in the aggregate waveform and absent responses.

Looking to the ANSD children in relation to the SNHL children, it was apparent that with properly fit hearing aids similar audibility in sound field situations was met. The P1 percent delectability was relatively higher to both stimuli in the SNHL. However, once P1 was recorded, both groups showed comparable P1 latencies with reduced amplitude in the ANSD. This is particularly interesting as the mean of hearing aid fitting was 25.7 (±14.5) and 22 (±14.5) years in the ANSD and SNHL groups, respectively. Sharma *et al.* [28,29] has demonstrated a sensitive period (below 3.5 years), or timeframe of optimal neuroplasticity, during which sound may be introduced to auditory cortex and promote normal, age-appropriate development.

Neuroplasticity reaches its height during a sensitive period, with reduced levels of plasticity still present as the period ends. IT-MAIS scores were obviously higher in SNHL children and continued to improve in both groups over the 6-month period. However, the percent increase in scores was limited in the ANSD group. The difference in performance between the two groups can be referred to the underlying neural dys-synchrony associated in the ANSD.

Nevertheless, the P1 latency and amplitude in the SNHL group were different compared with normal children. Cardon *et al.* [30] emphasized that, although cortical neurons may have been in place, important connections were not formed in a normal manner in congenitally deaf cats. This synaptic deficit highlights one of the consequences of sensory deprivation in which the extrinsic auditory input is not delivered to the auditory cortex normally during optimal levels of plasticity. Deficits are observed upon introduction of auditory stimulation.

Although somewhat general and not a true measure of speech perception, the IT-MAIS has proven clinically effective for several reasons [20]. For example, behavioral results can be obtained even for infants and young children who, due to developmental delay or other physical limitations, could not otherwise perform behavioral tests, which is often the case in working with a group of children with ANSD.

In the current study, there was a significant negative correlation (r=–0.6; P<0.05) between central auditory maturation (as measured by means of P1 latencies for both ba and da stimuli) and behavioral outcome (as evidenced with IT-MAIS scores). In other words, children with ANSD who had robust neural responses (i.e. CAEPs with normal morphology, latency, and amplitude) showed the highest level of behavioral auditory skill development (as reflected by IT-MAIS scores), whereas those who had abnormal or delayed CAEP responses were associated with lower levels of perceptual auditory development with a short formant transition.

These results are consistent with those of Sharma *et al.* [4], who reported that there was a strong correlation between P1 latency and IT-MAIS score (r=–0.86; P<0.01) in children with ANSD who used hearing aids. Several studies demonstrated a meaningful relationship between CAEPs and behavioral speech perception performance [9,23]. Taken together, these studies suggest that the P1-CAEP is an effective predictor of behavioral outcome in children with ANSD.

Obviously, the strong negative correlation between the IT-MAIS scores and age of early hearing aid fitting (r=–0.5, P<0.05) may indicate the existence of a sensitive period for intervention in children with ANSD. Animal studies have demonstrated the existence of sensitive periods in development for animals reared in degraded listening environments that were different from those reared in normal listening environments [31], which may have some parallels to the patients with congenital ANSD.

Thus far, there have been very few investigations examining the amount of hearing aid use in children with ANSD. Of those studies that have been conducted, some have observed poor outcomes with hearing aids, leading some researchers to argue that hearing aids may provide limited benefit because they are merely amplifying an already distorted signal [32,33]. These findings have led to general uncertainty as to whether or not children with ANSD should utilize hearing aids.

The present study found that ~50% of the ANSD children showed demonstrable benefit from amplification similar to their peers from the SNHL group, in that these children showed evidence of normal central auditory maturation and progress in auditory skill development. These results are consistent with those of Sharma and colleagues [4,9]. However, also consistent with other investigators [32] that (50%) appeared not to benefit from amplification, in that they showed delayed/abnormal P1 responses and significantly lower scores on the IT-MAIS. As suggested by Trautwein *et al.* [34], for these children cochlear implantation may be a useful alternative. In support of this, one child with ANSD who had absent P1-CAEP during this study and received an implant showed replicable P1-CAEP after implantation.

Thus, it would appear that CIs are more effective at providing the auditory stimulation needed for central auditory maturation in children with severe disruptions in neural synchrony, whereas hearing aids may only benefit children with milder cases of dys-synchrony [14].

Given that ABR and behavioral audiometric thresholds are unreliable indicators of behavioral outcome in children with ANSD, CAEPs may provide a useful alternative. P1 responses appear to be a good predictor of behavioral outcome (as measured using the IT-MAIS score) in ANSD patients, suggesting that P1-CAEP might provide a clinical tool for guiding intervention

choices and assessing their efficacy in this population. It may be considered a clinically useful biomarker of cortical development.

The current results provide support for conducting a hearing aid trial with appropriately fit amplification for children with ANSD who have behavioral thresholds in the moderate-to-severe range and do not support the provision of low-gain hearing aids for this population. Findings surrounding hearing aid fit age also seem to support the idea that timing of normal or improved input is important for typical cortical maturation.

Finally, it is recommended to use longitudinal P1 recordings in the comprehensive audiological test battery in ANSD population using temporally modified speech stimuli. The question that should be addressed in future research is whether normal cortical maturation as reflected from P1 study is sufficient for good performance outcomes and proper language development in this population.

Acknowledgements

The contribution of children in this study was highly appreciated.

The manuscript has been read and approved by the author, the requirements for authorship have been met, and the manuscript represents honest work.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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