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A positive wave at 8 ms (P8) and modified auditory brainstem responses measurement in auditory neuropathy spectrum disorder

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ABSTRACT

Objective: Auditory neuropathy spectrum disorder (ANSD) is characterized by absent or atypical auditory brainstem responses (ABR), recordable otoacoustic emissions and/or cochlear microphonics. Modification of ABR stimuli is discussed to improve wave V synchronization in ANSD patients.
Design: Ten ANSD children (seven unilateral) underwent ABR measurement with an alternating stimulus (40.5 s^{-1}), constant rarefaction and condensation stimuli, a reduced click-rate (11.1 s^{-1}) and a chirp-stimulus.
Results: The results showed no remarkably better synchronization with modified stimuli. Whereas higher levels showed no synchronization, reproducible positive waves at 8 ms (P8) at intensities of 65–85 dB were found in six patients with all stimuli.
Conclusions: We suggest an ipsilateral auditory origin of the positive potentials at 8 ms. They could be characteristic of synchronization abnormalities in some cases of ANSD.

1. Introduction

Auditory neuropathy spectrum disorder (ANSD) describes a hearing impairment with at least initially intact function of the outer hair cells and impaired synaptic transfer or neural transmission of acoustic signals, characterized by absent or atypical auditory brain stem responses (ABR) and recordable otoacoustic emissions (OAE) and/or cochlear microphonics (CM) [1–3], clinically appearing as sensorineural hearing loss (SNHL) with speech perception disproportionate to pure tone audiogram. ANSD patients' pure tone audiometry ranges between normal hearing and profound hearing loss. Language comprehension is poor, especially in noise. Language acquisition cannot be predicted from pure tone hearing and may be seriously impaired. The prevalence is reported to vary from 5 to 11% in children and adults with SNHL [3–5]. Risk factors for acquired ANSD in children are prematurity requiring intensive care, extremely low birth weight, perinatal hypoxia, mechanical ventilation, postpartal hyperbilirubinemia, and ototoxic drugs such as diuretics and aminoglycosides. Hereditary ANSD can be syndromic as in sensorimotor neuropathy, Charcot–Marie-Tooth disease, Refsum disease or Friedreich ataxia. Non-syndromic ANSD can be related to mutations in the otoferlin, GJB2 and GJB3 genes, and to mitochondrial rRNA mutations [6].

The audiological profile can be explained by impaired or interrupted excitation of the spiral ganglion neurons, caused by inner hair cell lesions, impaired transmitter release of the inner hair cells, dysfunction of the synapses between the inner hair cells and terminal dendrites or dysfunction of the spiral ganglion neurons and the auditory nerve. Reduction or desynchronization of activated neurons leads to pathological ABR results. When ABR stimuli are presented through headphones, an alternating click is recommended to minimize electromagnetic artifacts. A reduced rate (11.1 s^{-1}) of the alternating click stimulus is discussed as a means of enhancing ABR waveform morphology [7]. Collecting ABR in response to single polarity pulses (condensation and rarefaction) in ANSD can lead to robust waveform responses between 4 and 6 ms, with changing polarity when the stimulus is inverted [8]. These responses can be mistaken for ABR, they disappear with an alternating stimulus and are supposed to be of cochlear origin. Their presence when a single polarity stimulus is used and their absence with an alternating stimulus could point to ANSD.

Rising frequency chirp stimuli were initially thought to improve synchronization of ABR compensating basilar membrane dispersion [9]. Subsequent studies reported that wave V amplitude can increase with the chirp (depending on signal characteristics), while

Abbreviations: ANSD, auditory neuropathy spectrum disorder; ABR, auditory brainstem responses; OAE, otoacoustic emissions; CM, cochlear microphonics; SNHL, sensorineural hearing loss; TEOAE, transient evoked otoacoustic emissions; MRI, magnetic resonance imaging; ECochG, electrocochleography.

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early ABR components (Jewett waves I–III) disappear and latency is delayed compared to the click stimulus [10,11]. Petoe et al. [11] concluded that the chirp does not increase synchronization. Cebulla and Elberling [12] suggested that the largest advantage of the chirp is found at lower levels.

Better synchronization and increased wave V amplitudes could enable threshold identification at lower levels and possibly improve ANSD diagnosis. The objective of this work is to investigate whether different ABR thresholds can be detected in ANSD patients when ABR stimuli are modified.

2. Patients and methods

Ten children (seven males, three females; mean age 6.6 ± 2.7 years) fulfilled the inclusion criteria of normal or elevated pure tone or behavioral audiometry thresholds, recordable otoacoustic emissions and elevated or absent ABR. They underwent pure tone audiometry, speech audiometry in silence and noise, transient otoacoustic emission (TEOAE) measurement, tympanometry, ipsi- and contralateral acoustic reflex measurement and ABR recording.

Pure tone and speech audiometry were performed with an Auritec® AT900 audiometer (Auritec, Hamburg, Germany). Depending on age, either the Göttingen Audiometric Speech Test for Children (<9 years) or the Freiburger Speech Intelligibility Test (monosyllabic; ≥9 years) was used. Tympanometry and stapedial reflex measurements were performed with a GSI 33 Middle Ear Analyzer (Grason Stadler Inc., Eden Prairie, USA). TEOAE were recorded with an ILO 292 (Otodynamics, Hatfield, England). TEOAE were collected with the standard ILO 292 settings (260 sweeps of a non-linear click stimulus of 83 (±1) dB peak, noise rejection level of 55.9 dB). Responses were regarded as significant when the SNR was >5 dB in at least three of five frequency bands (1.0, 1.4, 2.0, 2.8 and 4.0 kHz).

ABR stimuli were presented via supraaural headphones (DT 48) and with contralateral masking (−30 dB). ABR were recorded with a Pilot Evoselect ABR system (Pilot, Blankenfelde, Germany) and standard electrode montage. Preamp sensitivity of the ABR system was 100 μV peak to peak. Hardware filter settings were 30 Hz high-pass and 2500 Hz low-pass. Analysis of result waveforms was first performed without software filters, and additionally with software filters (150 Hz high-pass, 1500 or 2000 Hz low-pass). The time window used was 20 ms, the number of sweeps was at least 2000, with the opportunity of splitting the result waveforms for reproducibility assessment.

For ABR recording, we used click stimuli of 150 μs duration and flat chirps with a frequency bandwith of 100–10,000 Hz and 10.5 ms duration. Five different stimuli were applied: an alternating click stimulus with a stimulus rate of 40.5 s^{-1} (used as a standard stimulus in our clinical practice), a rarefaction and a condensation click stimulus with the same duration and sampling rate, an alternating click stimulus with a rate of 11.1 s^{-1} and a broad band chirp stimulus with a rate of 18.7 s^{-1}. Intensities were applied in 10 dB steps, starting with moderate levels (45–55 dB HL), and increasing to a maximum of 100 dB when no response was found at lower levels. Depending on the result waveforms, assessment was repeated at some levels. Visual threshold estimation was performed by two experienced investigators. Additional diagnostic tests were vestibular assessment including caloric testing and magnetic resonance imaging (MRI) of the head.

This work has been approved by the Committee of Ethics of the University of Muenster and the "Ärztekammer Westfalen-Lippe". All patients and parents gave informed consent.

3. Results

Seven out of ten children (five males, two females) presented single-sided hearing loss with the characteristics of ANSD, three on the right and five on the left ear, three children presented with bilateral ANSD. Subjective audiometry results and clinical characteristics are shown in Table 1. Mean pure tone hearing loss on the affected ears was 72.2 ± 33.6 dB. Eight affected ears showed poor or no speech discrimination. All affected ears presented TEOAE, elevated or absent ipsi- and contralateral acoustic reflexes and pathologically elevated or absent click ABR thresholds (Tables 1 and 2) and met the criteria for ANSD diagnosis. Vestibular assessment and MRI scans showed normal results in all cases. In two children, ipsilateral acoustic reflexes were present, while contralateral reflexes were absent.

Modification of ABR-stimuli did not lead to remarkable threshold changes. Compared to the standard 40.5 Hz alternating

Table 1
Clinical characteristics and results from subjective audiometry.

	Age	Gender	Ear	PTA	Speech	AR ipsi	AR contra	Suspected Etiology	Therapy
1	4.5	m	R	100	–/–/0	[a]	[a]	Unknown	HA
2	5.1	m	R	103	–/–/0	90	NR	Fetal alcohol syndrome suggested	CROS
3	9.8	f	R	64	0/0/10	NR	NR	Preterm, Epilepsy, Learning Disability, Consanguinity of parents	HA
			L	75	0/0/30	NR	NR		HA
4	9.6	m	L	101	–/0/0	NR	[b]	Consanguinity of parents	CROS
5	5.3	f	L	90	0/0/–		NR	No risk factor	CROS
6	10.7	m	R	11	45/80/–	NR	NR	Familial ANSD	HA
			L	11	65/100/–	NR	NR		NT
7	3.5	m	L	91	0/0/70	NR	NR	No risk factor	CROS
8	6.3	m	L	>100	–/0/0	NR	NR	Preterm 32nd week, postpartal resuscitation, ototoxic antibiotics	HA
9	4.3	f	R	>100	0/0/50	NR	NR	Unknown	NT
10	13.3	m	R	43	35/45/90	90	NR	Familial ANSD Consanguinity of parents	HA
			L	50	20/30/45	90	NR		HA

Patient; age; gender; ear side; PTA (mean hearing loss in pure tone audiometry (500, 1000, 2000 Hz) [dB HL]); Speech recognition (% at 65, 80 and 95 dB HL); ispsi- and contralateral acoustic reflex thresholds (in dB HL)

[a] Tympanostomy tube.

[b] Eardrum perforation.

NR = no reflex answer; suspected etiology and therapy (HA = Hearing aid, CROS = Hearing aid with contralateral routing of signals, NT = No therapy).