B-ENT, 2014, **10**, 105-112

Auditory neuropathy/dyssynchrony revisited

K. Menten[1], C. Van eynde[1], C. Desloovere[1] and J. Wouters[2]

[1]Department of Otorhinolaryngology, Head and Neck surgery, University Hospitals Leuven, Belgium; [2]Department of Neurosciences, Experimental Otorhinolaryngology, University Leuven, Belgium

Key-words. Auditory neuropathy; auditory dyssynchrony; auditory synaptopathy; diagnosis; cochlear implant

Abstract. *Auditory neuropathy/dyssynchrony revisited*. Auditory neuropathy/dyssynchrony (AN/AD) is a relatively, recently described diagnostic term. It describes a disorder characterised by detectable otoacoustic emissions and/or cochlear microphonics, combined with abnormal or absent auditory brainstem responses and deficient speech understanding. Consequently, the patient's cognitive responses are inconsistent with a behavioural tone audiogram.
This review describes the epidemiology, pathogenesis, diagnosis, and treatment of AN/AD. We have focused on the diagnostic pathway, because diagnosis is sometimes difficult, and recent research has provided important insights into the aetiopathology of the disease. The diagnostic tools for AN/AD currently used in our department will be demonstrated in a clinical case.
It is very important to recognise AN/AD and provide patient counselling and support as early as possible, due to the potentially major influence of this disorder on a patient's social life and language acquisition.

Introduction

Auditory neuropathy, a heterogeneous, neurological condition that affects hearing, is characterised in the literature by three primary findings. First, patients exhibit normal otoacoustic emissions (OAE) and/or cochlear microphonics (CM). Second, the patient has a total absence of auditory brainstem responses (ABR) or abnormal ABRs. Third, the patient has poor speech understanding, inconsistent with predictions from the behavioural tone audiogram.[1-4]

The pure-tone audiograms of individuals with auditory neuropathy indicate hearing that may range from normal to severely impaired. However, the primary disorder is a disturbance in the transmission of information from the inner ear to the brain. These patients typically have enormous difficulties with speech understanding.[1]

The term "auditory neuropathy" was first coined as a diagnosis in 1996.[5] Other terms frequently used include "neural hearing loss" and "auditory dyssynchrony". Although the literature lacks consensus on a completely appropriate label, currently, the term most often used is "auditory neuropathy/dyssynchrony" (AN/AD).[1]

The purpose of this review was to survey the epidemiology, pathogenesis, and current state-of-the-art diagnosis and treatment of AN/AD. To date, no single test is available for diagnosing AN/AD. Moreover, some typical test results may be absent or even fluctuate in the same patient.[1,4] Therefore, we created a standardised test battery. This test battery was performed on every suspected AN/AD patient at our department with the aim of detecting more, and even atypical, AN/AD cases. Here, we illustrated the diagnostic pathway with a recent clinical case.

Literature review

Prevalence and aetiology

Due to the fact that AN/AD was only recently recognised, it is difficult to give scientifically accurate figures about its prevalence among children and adults. Most patients acquire symptoms in infancy, but a small group experience the first

A literature review and description of the care pathway of the Oto-Rhino-Laryngology, Head and Neck Surgery Department in Leuven University Hospitals.
Presented at the Royal Belgian Societe of Oto-Rhino-Laryngology, Head and Neck Surgery, March 24, 2012, Brussels.

complaints during adolescence or early adulthood. Only 25% of patients with AN/AD are above 10 years old at the onset of symptoms. Substantial amounts of data have become available from tests frequently used in screening and diagnostic programs in paediatric populations (ABR, CM, OAE).[6]

The prevalence of AN/AD among children with profound hearing loss ranges from 0.5 to 15%.[1,4,6-9] In addition, some children are at increased risk for AN/AD, most frequently due to hyperbilirubinaemia or hypoxia. The prevalence of AN/AD in the former group is between 0.23 and 4%, depending on the study.[1,6,8,9]

Currently, discussion continues over the aetiology of AN/AD. A few possible mechanisms have been put forward that could partly or completely explain this disorder.

First, in view of the normal OAEs and CMs, together with the aberrant ABRs, it is expected that lesions most likely exist in the inner hair cells or the auditory nerve.[6] Some research has focused on lesions in the cochlear inner hair cells. To date, no unambiguous study has explained how inner hair cells are damaged or lost. An important argument in support of a defect at this location is that it can result in the characteristically abnormal ABR, without damaging the function of outer hair cells.[6]

A second possible lesion site is at the synapse between the inner hair cells and the auditory nerve terminals.[6] To date, three potential causative factors have been identified that could affect this synapse. The first is a mutation in the *OTOF* gene, which encodes the protein otoferlin. In the inner hair cells, otoferlin is involved in synaptic vesicle-membrane fusion and membrane trafficking. A mutation might lead to a disturbance in the synaptic process. The second potential causative factor is the calcium concentration in the synapse. Some authors described a mice model, where a calcium channel deficiency in the auditory synapses resulted in a complete block of inner hair cell synaptic transmitter release and a reduced number of spiral ganglion neurons.[1,10] Nevertheless, the morphology of the outer hair cells was preserved. Those findings resulted in the total absence of ABR, but detectable OAEs.[1,10] The third potential causative factor, which may have a more important influence on synaptic transmission, was found in other mouse experiments. Those findings suggested that a decrease in the number of synapse-anchored inner hair cell ribbons may lead to dyssynchronous auditory signalling, and consequently, synaptic dysfunction.[11]

Finally, another possible lesion site could be in the auditory nerve. In that case, the auditory disorder is often part of a generalised neuropathy. The defect may be due to a myelin disorder or an axonal neuropathy.[1,6]

Furthermore, several risk factors for AN/AD have been described in the literature. The most commonly described risk factors are hyperbilirubinaemia and hypoxia. According to some authors, more than 50% of patients with early onset AN/AD had experienced one or both of these conditions in neonatal life.[7] Other potential neonatal risk factors include neural ischaemia; central nervous system immaturity; low-birth weight; the use of antibiotics, like gentamicin sulphate; the use of diuretics or another ototoxic medication; in vitro fertilisation-induced pregnancy; and consanguinity. Postnatal risk factors include measles, mumps, and meningitis.[1,6,12] However, the Sininger and Oba survey of adult and paediatric cases showed that 27% of patients were diagnosed with AN/AD without the presence or history of a risk factor.[13]

Of note, some genetic and syndromal disorders were also associated with an increased incidence of AN/AD. The two most important were Charcot-Marie-Tooth syndrome and Friedreich's ataxia.[6] Conversely, AN/AD was rarely seen in combination with Ehlers-Danlos syndrome, Stevens-Johnson syndrome, or Guillain Barré syndrome.[6]

Testing

The diagnosis of AN/AD is based on a combination of characteristic results from at least four tests (OAE, CM, ABR, speech understanding; described in detail below). Also, some additional tests can increase the diagnostic accuracy.

A. Normal otoacoustic emissions and/or cochlear microphonics

OAEs are recordable with a sensitive probe placed in the outer ear canal. The probe has a canal through which a click stimulus is presented to the ear. The click intensity is 84 dB at sound pressure level (SPL) and the click rate is 20 Hz (C. Van Eynde, UZ Leuven).[6] The normal response to the clicking is a series of detectable, transiently evoked OAEs (TEOAEs); these imply that function is preserved in the outer hair cells of the cochlea. Moreover, a normal audiogram will show thresholds < 35 dB

at hearing level (HL).[4,6,14] Nevertheless, in some cases, TEOAEs are absent in patients with AN/AD. In those circumstances, outer cochlear hair cell function is evaluated with CM.[14] CMs are potentials that originate from the polarisation and depolarisation of cochlear hair cells in response to a waveform. The waveform is evoked by tone burst stimuli (2 kHz) with intensities of 85 and 80 dB at normal HL (nHL), delivered at a rate of 15 stimuli/s (C. Van Eynde, UZ Leuven).[6] Both outer and inner hair cells contribute to the response of the cochlea. Nevertheless, this alternating current potential is dominated by the activity of the outer hair cells.[15]

OAEs may deteriorate or completely disappear during progression of AN/AD. The mechanism and time-course of this deterioration in patients with AN/AD remain unknown.[1,6]

CMs can be easily detected based on the ABRs (Figure 1). The CMs reverse polarity (180°) in response to a change in stimulus from condensation to rarefaction.[6,16] However, some studies have shown that electrocochleography, performed with a transtympanic or extratympanic approach, is a more appropriate measurement.[3,16] The disadvantage of the transtympanal technique is its invasive character. On the other hand, extratympanic electrocochleography is more comfortable for the patient. The electrodes are placed on the skull, on the earlobe, or on the eardrum in the outer ear canal, and there is no need for anaesthesia.[16] McMahon *et al*.[15] showed that frequency-specific, round-window electrocochleography may provide a means to classify auditory neuropathies into pre- and postsynaptic lesions. This proposal was based on a study that used round-window electrocochleography in 14 patients with AN/AD. Those results were compared to the results of electrically-evoked auditory brain stem responses (EABRs) immediately after cochlear implantation (CI). The summating potential (SP) is a direct current response that arises from the summed response of inner and outer hair-cell activities, but it is dominated by basal inner hair cells. The SP was evaluated in the electrocochleography, together with the dendritic potential (DP). The patients with a delayed latency SP and a reduced DP on electrocochleography showed good EABR waveforms, consistent with a presynaptic lesion. On the other hand, a normal latency SP and normal DP were observed in patients with poor or absent EABR waveforms after CIs, which suggested a postsynaptic lesion. Although those results were experimental, the authors anticipated that they held promise, because better classification of the lesion site might allow clinicians to identify the best possible management for each individual.[15]

B. Abnormal auditory brainstem responses[6]

On the basis of ABRs, it is possible to measure the conduction and the threshold of auditory nerve activation. During the click-evoked ABR, which starts at 80 db nHL, the ABR waves in individuals with AN/AD are typically totally absent, or at best, difficult to discern (Figure 1).[6,7]

The three tests discussed above provide direction to the diagnosis. Normal OAEs and CMs are signs of good cochlear function.[6,12]

C. Poor speech understanding inconsistent with behavioural tone audiogram

An initial difficulty in making an AN/AD diagnosis is the fact that the results of the pure-tone audiogram may vary from normal to profoundly impaired. Moreover, the audiogram may show fluctuations

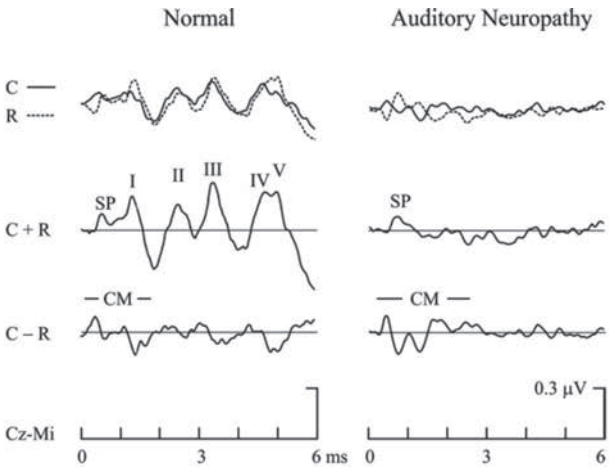

Figure 1[14]
Audio brainstem responses (ABRs). (*Left*) ABRs recorded in a normal subject, compared to (*right*) recordings in a patient with auditory neuropathy.[14] (*Top row*) Responses to condensation (solid line, C) and rarefaction (dotted line, R) clicks were recorded separately. (*C+R row*) On the left, the typical waves (I-V) are indicated on a normal ABR. On the right, the patient with AN/AD shows an absence of obvious waves. (*C-R row*) The C-R difference waveform shows that both individuals exhibited cochlear microphonics (CM); SP: Summating Potential;[14] Cz-Mi: recordings obtained between vertex and left mastoid; (*Bottom*) voltage (μV) vs. time (ms) scales.

during the course of auditory deterioration.[1,6,7] On the other hand, the audiogram sometimes indicates that further investigation is needed. For example, when the hearing levels are below a 35 dB HL, but there are detectable OAEs, these contradictory results may point to AN/AD or another neurological disorder.[17]

An analysis of speech understanding in individuals with AN/AD typically show that understanding is disproportional to the prediction based on the pure-tone audiogram.[1,6,7] Potential contributing factors include a reduced sensitivity to fast and slow temporal modulations; a reduced ability to detect gaps in continuous sound; excessive masking in noisy conditions; and reduced frequency discrimination at low frequencies.[18,19] In most individuals with AN/AD, speech understanding is worse in noisy than in quiet conditions.[1,6] Nevertheless, some reports have described cases of adults with AN/AD that did not exhibit unusually poor speech understanding. The number of patients with speech perception scores within the expected normal range varies from 25 to 30%.[5,13] A potential explanation of those findings might be that many of those adults have progressive, generalised neuropathic conditions. A longer follow-up may clarify this issue.[6]

D. Additional investigations

Additional investigations can be performed to support the diagnosis, but they are not crucial.

First, it is possible to test for abnormal acoustic reflexes in both young and old individuals with AN/AD.[1,6,14] One study showed that acoustic reflexes were absent in about 90% of patients with AN/AD, and the threshold was elevated in the remaining 10%.[20] That suggested that reflex testing may provide a means to distinguish AN/AD from mild or moderate cochlear loss, because in the latter case, the reflexes are typically preserved. The best known efferent middle ear reflex is the stapedius reflex.[14]

Other investigations that can contribute to a more complete diagnosis include tympanometry, which provides information about the state of the middle ear (C. Van Eynde, UZ Leuven); a magnetic resonance scan, to check the inner ear and the nerve structures;[1,14] genetic testing for mutations in the *OTOF* gene; and genetic testing for some other genetic syndrome, when clinically suspected; for example, the Charcot-Marie-Tooth syndrome.[1,6]

Treatments

Due to the heterogeneity of AN/AD, there is no standard treatment. Each patient requires an individual approach to attain the best possible results in hearing and language development.

A. Conservative measures

In some cases of AN/AD, the hearing may improve spontaneously; in particular, neonates most frequently improve in the first 6 months after the diagnosis. This is probably due to a maturation process.[7,21] Consequently, some authors suggest a follow up for patients with AN/AD, particularly children, with serial audiometric testing for a minimum of 6 months, before making decisions about a definitive therapy.[21]

A first potential therapeutic option is the use of conventional hearing aids, which provide sound amplification. A limited number of studies have shown some improvement in auditory test results associated with the use of conventional amplification. Those authors suggested that the provision of amplified sound may have increased the access to speech elements, and it may have improved neural synchrony by recruiting residual neurons.[6,22] Nevertheless, the majority of studies reported that conventional amplification provided very limited or no improvement.[1, 6] There are two main arguments against the use of amplification. One cautions against the risk of acoustic trauma or damage to the cochlea through overamplification. The other holds that amplification will only provide louder, but equally distorted, signals; and consequently, amplification will not lead to improvement.[1,6]

Another potential aid for some patients with AN/AD is a FM system, which improves the signal-to-noise ratio. As mentioned earlier, some patients have acceptable speech understanding in quiet conditions, but they lose speech capacities in noisy conditions. For those patients, a FM system may be beneficial in some circumstances.[1,14,21]

In addition to hearing aids, it is possible to learn visual language. For example, sign-language or lip-reading may ameliorate deficient communication skills.[1,14]

B. Cochlear implants

In AN/AD, the CI mechanism of action is related to the three most important sites of lesion. A CI directly stimulates the auditory nerve. Consequently,

the CI bypasses the cochlear inner hair cells and the synapse between the inner hair cells and type 1 auditory nerve fibres. A CI is also useful with an impaired nerve, because electric stimulation of the nerve provides much more synchronised neural firing than acoustic stimulation.[19] This latter finding was also shown in animal studies.[6]

The best outcomes of CI implantation were observed in patients with normal cognitive function and no medical comorbidity.[23] Other favourable prognostic factors included normal anatomy of the inner ear structures, brain, and the vestibulo-cochlear nerve.[23] Nevertheless, it remains difficult to determine whether a patient will be a good candidate for implantation. Some CIs in patients with AN/AD provided only minor improvements, but the majority of cases yielded fairly positive results.[1,6,14,24] In August 2012, Belgium implemented a reimbursement for CIs given to children (<18 years) with AN/AD. These reimbursements depended on the following criteria: speech understanding is inconsistent with the behavioural tone audiogram; presence of electrophysiological signs of AN/AD (ABR/CM); no improvement with conventional hearing aids or other sound systems; and 30% or less speech understanding at 70 dB SPL in a monosyllabic speech test.

Multiple studies showed positive postoperative results when CIs were performed in patients with AN/AD.[1,6,7,19] Those results included improvements in speech discrimination and speech comprehension, comparable to those observed in patients with a perceptive cochlear hearing loss that also received a CI.[1,6,7,19]

Clinical case

In our clinical department, currently, we employ a test battery that comprises three basic audiological tests. These are a tone audiogram, tympanometry, and speech understanding. In this clinical case study, we describe how these were used and additional specific investigations needed to diagnose the case. The additional investigations were the TEOAEs, the stapedius reflex, the ABR, and speech perception (in noisy conditions) (Table 1). This test battery remains in an experimental phase, but the goal was to create a standardised protocol for patients suspected of having AN/AD.

Case study

A 31-year old, French-speaking man, of African origin, was referred due to progressive hearing loss over more than 10 years. During the same period, he also developed visual problems. A recent ophthalmological examination revealed optic nerve neuropathy.

In addition to the hearing loss, the man also reported a high frequency tinnitus, which was more prominent on the right side. His other medical history was negative; he had no ear problems as a child and no history of repeated noise exposure. The family history was negative for otological disorders. He had undergone computed tomography and magnetic resonance scans of the brain and the temporal bone. However, no abnormality was found.

Table 1

Overview of the test battery for diagnosing auditory neuropathy at the University Hospitals of Leuven

TEST	EXPECTED RESULTS
Basic tests:	
Tone audiogram	Normal to impaired hearing
Tympanometry	If not an A-curve → Implications for OAE
Speech understanding: NVA (Dutch) or Fournier (French) speech list	Normal to disproportional to the tone audiogram
Additional investigations:	
Auditory brainstem responses (ABR)	Total absence or abnormal ABR
Stapedius reflex	Total absence (ipsi- as well as contralateral)
Otoacoustic emissions (TEOAEs)	Typically present, although they may be absent
Cochlear microphonics (CMs)	Present (polarity switch in response to condensation/rarefaction)
Speech understanding in noise	Usually weak

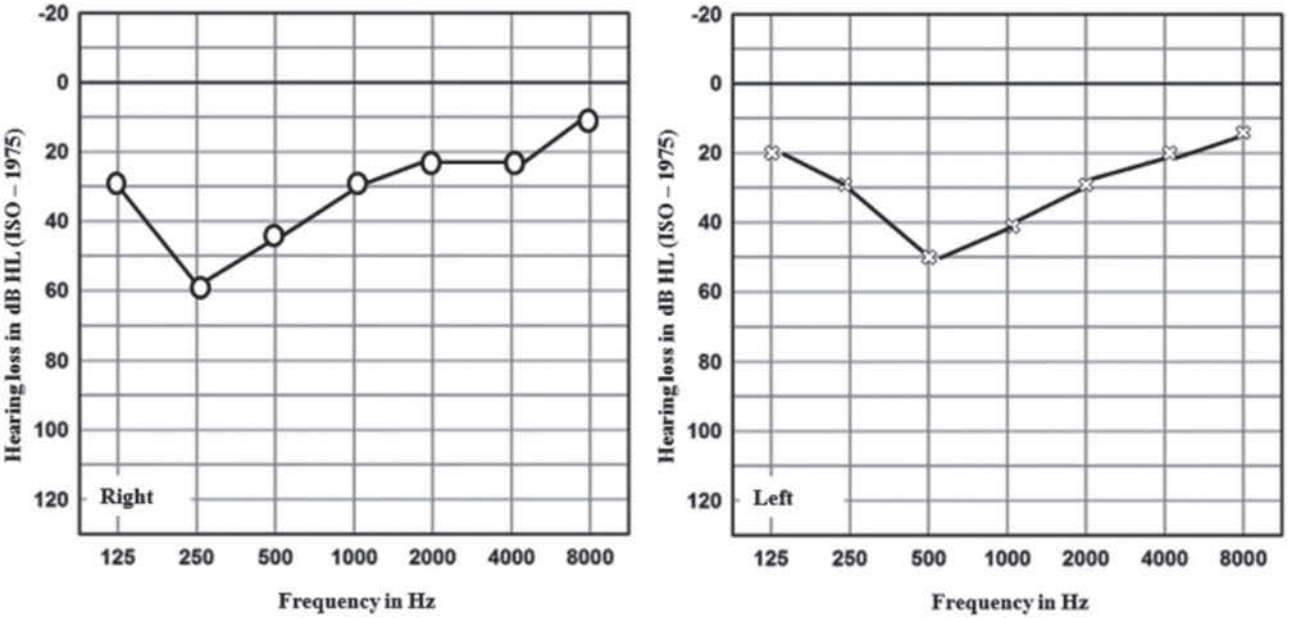

Figure 2

Pure-tone audiogram for the clinical case study (*left panel*). The audiogram for the left ear and (*right panel*) the audiogram for the right ear showed fairly symmetrical hearing loss.

A clinical examination showed a normal eardrum on both sides. The tuning-fork tests showed a positive Rinne on both sides and no lateralisation during the Weber test. The pure-tone audiogram showed fairly symmetric sensorineural hearing loss with a bilateral dip at the lower frequencies. There was a Fletcher Index of 33 dB on the right and 40 dB on the left side (Figure 2). The speech audiometry test was performed in quiet conditions. On the basis of the Fournier list (French), he reached a maximum of 60% at 90 dB SPL on the right side and 60% at 100 dB SPL on the left side. The ipsi- and contra-laterally evoked stapedius reflexes were absent on the left side and the audiologists could not measure them in the right ear, due to the form of the external auditory canal. A suspicion of auditory neuropathy prompted the need for the TEOAE, ABR, and CM tests. We found that TEOAEs, recorded in response to click stimuli (intensity of 84 dB SPL and a rate of 20 Hz), were present on both sides. However, no detectable waves were observed on the click-evoked ABR (intensity of 80 dB nHL, recorded with skull electrodes) (Figure 3). CMs were present at an intensity of 85 response to a change in the tone burst stimulus from condensation to rarefaction. The CMs were more prominent on the left side than on the right side, and they were also recorded with non-invasive skull electrodes (Figure 4).

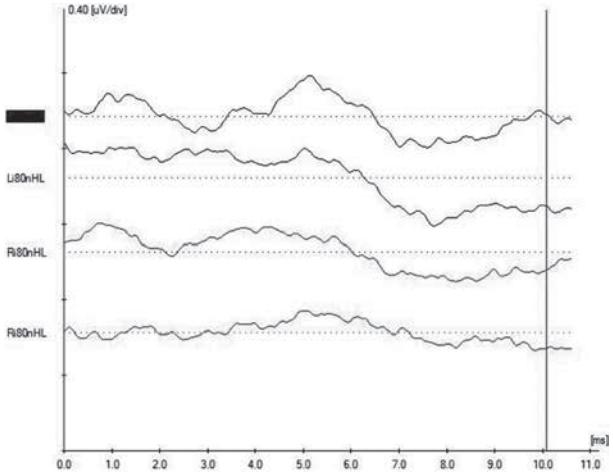

Figure 3

Auditory brainstem responses for the clinical case study. In both ears, note the absence of obvious peaks at an intensity of 80 dB nHL (2 traces at each intensity to chech the reproducibility). Li: left ear; Ri: right ear. Y-scale (0.40 mV/div): each division indicates 0.40 μV amplitude. dotted lines: baseline.

The complaint of hearing loss, combined with poor speech understanding and detectable OAEs and CMs, pointed to a diagnosis of AN/AD. This diagnosis was supported by the presumption of optic nerve neuropathy, the absence of ABRs, and the lack of stapedius reflexes.

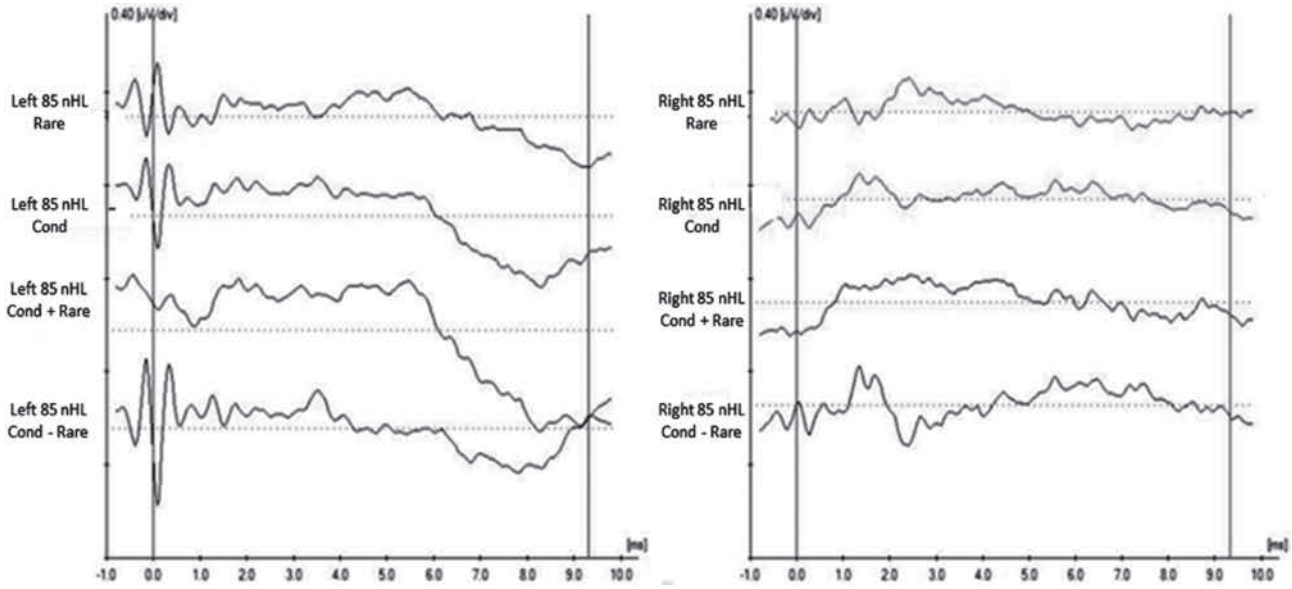

Figure 4
Cochlear microphonics for the clinical case study. Cochlear microphonics (CMs) recordings performed (*left panel*) on the left side and (*right panel*) on the right side. Clearly detectable CMs, observed at an intensity of 85 dB nHL, are more prominent on the left than on the right side. The CMs reverse polarity by 180° in response to the change in stimulus from rarefaction (Rare) to condensation (Cond).

Conclusion

AN/AD is a heterogeneous disorder that hampers the transmission of auditory signals from the inner ear to the brain, and consequently, it has a negative influence on hearing. Presumably, this disorder is caused by lesions in the cochlear inner hair cells, at the synapse between the inner hair cells and type 1 auditory nerve fibres, or at the level of the auditory nerve. To date, there is no simple diagnostic test for AN/AD. Instead, diagnosis requires the results of different tests, which must fit together, like the pieces of a puzzle.

A lot of research is going on the find the best possible therapy for AN/AD. CI has apparently become increasingly prominent as a therapeutic option for these patients. Nevertheless, one must be aware that not every patient is a good candidate for CI. Scientific research is promising, and shows that better classification of this disorder may result in better individual treatment strategies.

It is important to recognise AN/AD as early as possible, due to the influence it can have on language acquisition and social life. Increasing attention to this disorder, together with improvements in diagnostic tools, are probably responsible for the increasing prevalence of AN/AD diagnoses.

References

1. Vlastarakos P, Nikolopoulos T, Tavoulari E, Papacharalambous G, Korres S. Auditory neuropathy: endocochlear lesion or temporal processing impairment? Implications for diagnosis and management. *Int J Pediatr Otorhinolaryngol*. 2008;72(8):1135-1150.
2. Rapin I, Gravel J. "Auditory neuropathy": physiologic and pathologic evidence calls for more diagnostic specificity. *Int J Pediatr Otorhinolaryngol*. 2003;67(7):707-728.
3. Santarelli R, Starr A, Michalewski H, Arslan E. Neural and receptor cochlear potentials obtained by transtympanic electrocochleography in auditory neuropathy. *Neurophysiol Clin*. 2008;119(5):1028-1041.
4. Sanyelbhaa T, Kabel A, Samy H, Elbadry M. Prevalence of auditory neuropathy (AN) among infants and young children with severe to profound hearing loss. *Int J Pediatr Otorhinolaryngol*. 2009;73(7):937-939.
5. Starr A, Picton T, Sininger Y, Hood L, Berlin C. Auditory neuropathy. *Brain*. 1996;119(3):741-753.
6. Rance G. Auditory Neuropathy/Dys-synchrony and its Perceptual Consequences. *Trends Amplif* . 2005;9(1):1-43.
7. Madden C, Rutter M, Hilbert L, Greinwald J, Choo D. Clinical and Audiological Features in Auditory Neuropathy. *Arch Otolaryngol Head Neck Surg*. 2002;128(9):1026-1030.
8. Declau F, Boudewijns A, Van den Ende J, Peeters A, Van de Heyning P. Etiologic and audiologic evaluations after universal neonatal hearing screening: analysis of 170 referred neonates. *Pediatrics*. 2008;121(6):1119-1126.
9. Foerst A, Beutner D, Lang-Roth R, Huttenbrink K, Von Wedel H, Walger M. Prevalence of auditory neuropathy/synaptopathy in a population of children with profound

hearing loss. *Int J Pediatr Otorhinolaryngol*. 2006;70(8): 1415-1422.
10. Brandt A, Striessnig J, Moser T. Ca_v 1,3 channels are essential for development and presynaptic activity of cochlear inner hair cells. *J. Neurosci*. 2003;23(34):10832-10840.
11. Trussell L. Synaptic mechanisms for coding timing in auditory neurons. *Annu. Rev. Physiol*. 1999;61:477-496.
12. Raveh E, Buller N, Badrana O, Attias J. Auditory neuropathy: clinical characteristics and therapeutic approach. *Am J Otolaryngol*. 2007;28(5):302-308.
13. Sininger Y, Oba S. Patients with auditory neuropathy: Who are they and what can they hear? In: Sininger Y, Starr A, eds. *Auditory neuropathy*. Singular Publishing, San Diego; 2001:15-36.
14. Picton T. Auditory Neuropathy: When time is broke. In: Picton T, Ed. *Human Auditory Evoked Potentials*. Plural Publishing, San Diego, 2010:535-568.
15. McMahon C, Patuzzi R, Gibson W, Sanli H. Frequency-Specific Electrocochleography Indicates that Presynaptic and Postsynaptic Mechanisms of Auditory Neuropathy Exist. *Ear Hear*. 2008;29(3):314-325.
16. Anastasio A, Alvarenga K, Costa Filho O. Extratympanic electrocochleography in the diagnosis of auditory neuropathy/auditory dysynchrony. *Braz J Otorhinolaryngol*. 2008;74(1):132-136.
17. Hood L. Auditory Neuropathy and dys-synchrony. In: Burkard R, Don M, Eggermont J, eds. *Auditory Evoked Potentials: Basic principles and clinical application*. Williams & Wilkins, Baltimore: Lippincott, 2007:275-289.
18. Narne V, Vanaja C. Perception of speech with envelope enhancement in individuals with auditory neuropathy and simulated loss of temporal modulation processing. *Int J Audiol*. 2009;48(10):700-707.
19. Zeng F, Liu S. Speech Perception in Individuals with Auditory Neuropathy. *J Speech Lang Hear Res*. 2006;49(2): 367-380.
20. Berlin C, Hood L, Morlet T, Wilensky D, St John P, Montgomery E. Absent or elevated middle ear muscle reflexes in the presence of normal otoacoustic emissions: a universal finding in 136 cases of auditory neuropathy/dys-synchrony. *J Am Acad Audiol*. 2005;16(8):546-553.
21. Madden C, Hilbert L, Rutter M, Greinwald J, Choo D. Pediatric Cochlear Implantation in Auditory Neuropathy. *Otol Neurotol*. 2002;23(2):163-168.
22. Rance G, Cone-Wesson B, Wunderlich J, Dowell R. Speech perception and cortical event related potentials in children with auditory neuropathy. *Ear Hear*. 2002;23(3): 239-253.
23. Walton J, Gibson W, Sanli Hn Prelog K. Predicting cochlear implant outcomes in children with auditory neuropathy. *Otol Neurotol*. 2008;29(3):302-309.
24. De Leenheer E, Dhooge I, Veuillet E, Lina-Granada G, Truy E. Cochlear implantation in 3 adults with auditory neuropathy/auditory dys-synchrony. *B-ENT*. 2008;4(3): 183-191.

Kristof Mentenn, M.D., Resident
Dorpsstraat 56
3740 Bilzen
E-mail: kristofmenten@hotmail.com