ARTICLE

Hearing impairment in patients with myotonic dystrophy type 2

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Abstract

Objective

To systematically assess auditory characteristics of a large cohort of patients with genetically confirmed myotonic dystrophy type 2 (DM2).

Methods

Patients with DM2 were included prospectively in an international cross-sectional study. A structured interview about hearing symptoms was held. Thereafter, standardized otologic examination, pure tone audiometry (PTA; 0.25, 0.5, 1, 2, 4, and 8 kHz), speech audiometry, tympanometry, acoustic middle ear muscle reflexes, and brainstem auditory evoked potentials (BAEP) were performed. The ISO 7029 standard was used to compare the PTA results with established hearing thresholds of the general population according to sex and age.

Results

Thirty-one Dutch and 25 French patients with DM2 (61% female) were included with a mean age of 57 years (range 31–78). The median hearing threshold of the DM2 cohort was higher for all measured frequencies, compared to the 50th percentile of normal ($p < 0.001$). Hearing impairment was mild in 39%, moderate in 21%, and severe in 2% of patients with DM2. The absence of an air–bone gap with PTA, concordant results of speech audiometry with PTA, and normal findings of BAEP suggest that the sensorineural hearing impairment is located in the cochlea. A significant correlation was found between hearing impairment and age, even when corrected for presbycusis.

Conclusions

Cochlear sensorineural hearing impairment is a frequent symptom in patients with DM2, suggesting an early presbycusis. Therefore, we recommend informing about hearing impairment and readily performing audiometry when hearing impairment is suspected in order to propose early hearing rehabilitation with hearing aids when indicated.

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Glossary

BAEP = brainstem auditory evoked potentials; **dB HL** = decibels hearing level; **DM1** = myotonic dystrophy type 1; **DM2** = myotonic dystrophy type 2; **mRS** = modified Rankin Scale; **PROMM** = proximal myotonic myopathy; **PTA** = pure tone audiometry.

Myotonic dystrophy type 2 (DM2), formerly known as proximal myotonic myopathy (PROMM), is a dominantly inherited multisystem disorder with a heterogeneous phenotype, caused by a CCTG expansion in intron 1 of the *CNBP* gene on chromosome 3q21.3.1 The mean age at onset of symptoms is 34 years.[2] Important neuromuscular symptoms are proximal weakness, myotonia, and pain. Other organs are prominently involved, with frequent early-onset cataract, cardiac conduction abnormalities, gastrointestinal symptoms, endocrine changes, and CNS symptoms.[2–5]

There are many similarities between DM2 and myotonic dystrophy type 1 (DM1).[6] In DM1, hearing impairment is a well-known feature.[7–11] In clinical practice, we observed several patients with DM2 complaining of hearing impairment, sometimes wearing or requiring hearing aids after evaluation. Although hearing impairment has been reported in some cases of DM2, it has never been systematically evaluated.[12–18] To date, hearing impairment does not belong to the classical description of DM2. However, to optimize guidance and treatment of patients with DM2 and to learn more about its pathophysiology, it is important to explore auditory function in a larger DM2 cohort than family reports.

We hypothesized that there is a high prevalence of hearing impairment in patients with DM2.

The aim of the present international study was to systematically assess the presence and characteristics of hearing impairment in a large population of patients with genetically confirmed DM2 and to establish whether hearing impairment is part of the DM2 clinical phenotype.

Methods

Patients

All patients with DM2 in the Netherlands (n = 54) and the Myology Institute in Paris (n = 26) were invited to participate. Inclusion criteria were genetically confirmed DM2 and age >17 years. The CCTG expansion in the *CNBP* gene had been detected using standard methods.[19] No repeat size was measured, as no clear correlation has been established between repeat size and clinical symptoms.[1,2,20] In case of a history of otologic surgery, the concerning ear was excluded.

Standard protocol approvals, registrations, and patient consents

The study was carried out according to the Helsinki Declaration and all patients provided written informed consent. Both the Dutch and French local ethics committee approved the study (CMO Arnhem-Nijmegen, 2013/109; ERB Paris VI, A01741-44).

Methods

Medical history and general features were recorded during the visit, including the presence of cataract, diabetes mellitus, and cardiac abnormalities. Age at onset was documented and the 6-point modified Rankin Scale (mRS) was used to indicate the severity of the disease.[21] An otorhinolaryngologic structured interview and examination was conducted by an otologist, including questions about subjective hearing impairment and its onset, associated symptoms, otologic history, previous noise exposure, and the use of ototoxic drugs (figure e-1, http://links.lww.com/WNL/A137). To finish, pure tone audiometry (PTA), speech audiometry, tympanometry, acoustic middle ear muscle reflexes, and brainstem auditory evoked potentials (BAEP) were performed systematically to objectively qualify and quantify hearing impairment (figure 1).

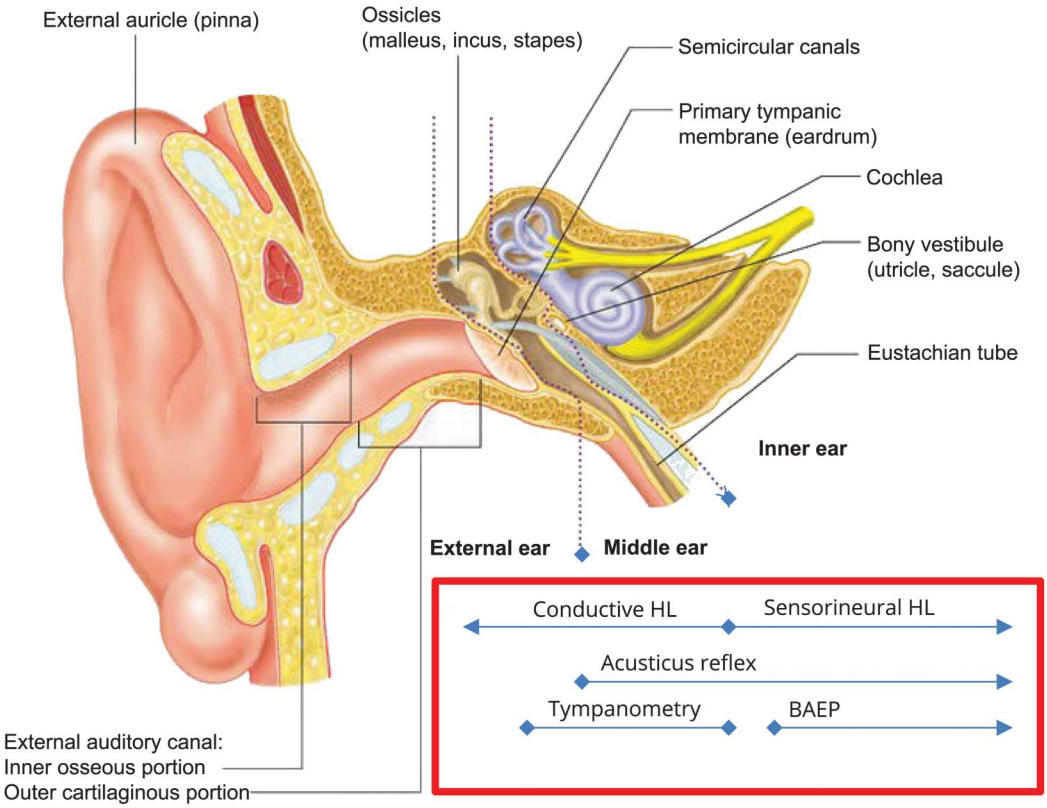
Pure tone audiometry

With PTA, both air and bone conduction hearing thresholds in decibels hearing level (dB HL) were determined at 0.25, 0.5, 1, 2, 4, and 8 kHz. It was carried out in a sound-treated room, calibrated according to ISO 389, and measured according to the ISO 8253-1 standard.[23,24] Hearing impairment was defined as asymmetric when a difference of more than 10 dB HL was found in at least 2 frequencies.[25] The difference between air and bone conduction (air–bone gap) was calculated for the mean of 0.5, 1, and 2 kHz to differentiate between conductive and sensorineural hearing impairment.[25] The mean of the hearing thresholds of 0.5, 1, 2, and 4 kHz of the best ear was used to define the severity of hearing impairment (none 0–20 dB, mild 21–40 dB, moderate 41–70 dB, and severe >70 dB).[25]

Speech audiometry

Speech audiometry was performed to determine speech intelligibility and discrimination and word recognition abilities. It was performed in a sound-treated room, using a standard monosyllabic (consonant-vowel-consonant) Dutch or French word list, respectively. The maximum monaural phoneme recognition scores (percentage correct recognition) were evaluated for each ear from a performance-intensity plot constructed for monaurally presented words.

Figure 1 Hearing tests in relation to the ear anatomy



Pure tone audiometry (PTA) measures the hearing thresholds for 6 frequencies (0.25, 0.5, 1, 2, 4, and 8 kHz). The difference between air and bone conduction, according to the PTA, and the results of the speech audiometry differentiate between conductive and sensorineural hearing impairment. Tympanometry assesses the function of the tympanic membrane and middle ear. The acoustic middle ear reflex measures the function of the stapedius muscle, stapes, and retrocochlear function. Brainstem auditory evoked potential (BAEP) evaluates retrocochlear function. Reprinted with permission from Wenig[22] by permission of Elsevier (c) 2016.

Tympanometry and acoustic middle ear muscle reflexes

Tympanograms and acoustic middle ear muscle reflexes were recorded with an impedance audiometer AT235. The results of the tympanometry were categorized according to the modified classification of Jerger as type A (normal middle ear), B (decreased mobility tympanic membrane, consistent with middle ear pathology), C1 (moderate negative middle ear pressure), or C2 (negative middle ear pressure with retracted tympanic membrane).[26]

The acoustic middle ear muscle reflex is the involuntary muscle contraction of the stapedius muscle in response to a high-intensity sound stimulus, and is normally present bilaterally. This reflex was elicited at 1 kHz, measured at the peak tympanometric pressure. A broadband noise and a reflex-activating stimulus were provided ipsilaterally, starting at 85 dB HL with a maximum of 110 dB HL.

Brainstem auditory evoked potentials

BAEPs were obtained with a Keypoint (Medtronic, Langhorne, PA) and measured to assess retrocochlear function (acoustic nerve and brainstem). Monoaural click stimuli with a duration of 50 μs were delivered through shielded earphones with a frequency of 10 Hz and intensity of 70–90 dB HL. Both ears were stimulated separately. Masking of the contralateral ear was accomplished by noise with an intensity of 20 dB below click intensity. The bandpass filters were set at 100–3,000 Hz. At least 2 trials of 1,000 clicks were recorded to assess reproducibility. The BAEP I-V interpeak latency was recorded and considered abnormal above the upper limit of normal based on the 95% sex- and age-related confidence limits. All BAEPs were assessed for reproducibility and analyzed by 2 or 3 trained neurophysiologists or otologists. The opinion of the majority was taken as the definite conclusion.

Statistics

SPSS version 21 (SPSS Inc., Chicago, IL) was used for statistical analysis. All included ears were used for analysis. Normality of variables was evaluated by histograms and the Shapiro-Wilk test. $p < 0.05$ Was considered statistically significant. Considering the observational study design, we did not correct for multiple testing.

The ISO 7029 standard contains normal values for hearing thresholds by air conduction (PTA) as a function of sex and

age for otologically normal persons, with exclusion of participants with undue noise exposure.[27] It was used to determine the individual 50th and 95th percentile threshold values (P50 and P95) in relation to sex and age for all measured frequencies.[7,28] Thresholds beyond the P95 value were considered abnormal. Participants with noise exposure—the definition based on the expert opinion of the otolaryngologist—were excluded for comparison with the ISO 7029 standard. The excess in hearing impairment was calculated for each participant by subtracting the P50 threshold for the same sex and age from the established hearing threshold at a given frequency.[7,28] The sign test was used to calculate the difference between the excess in hearing impairment and the P50, both for all included ears and for the best ear of each participant only, to correct for the possible influences of exogenous and endogenous factors. The best ear was defined as the ear with the lowest hearing threshold of the mean of the frequencies 0.5, 1, 2, and 4 kHz.[25] Missing data in tympanometry, acoustic middle ear reflexes, and BAEP due to planning difficulties are addressed.

Results

Patients

Between September 2013 and March 2016, 56 patients with DM2 were enrolled in this study, respectively; 31 Dutch patients from 18 different families and 25 unrelated French patients (75% unrelated). Two ears were excluded: 1 from a patient with a history of a vestibular schwannoma and another from a patient who was Barany deaf unilaterally due to several ear infections and had had a meatoplasty. Two included patients were diagnosed with cerebellar benign tumors (meningioma and hemangioblastoma).

Demographic features and symptoms of hearing impairment are shown in table 1. Only 2 patients received an ototoxic drug (respectively, quinine for a few weeks and cyclosporine). Two patients had meningitis in their childhood, with no hearing damage observed afterwards. Sixteen patients were exposed to noise (14 work-related, 1 orchestra member, and 1 frequently visited discotheques). Three patients reported hearing impairment as one of the first symptoms (5%). Otologic examination was normal in all patients, except unilateral retraction of the tympanic membrane in 1 patient and unilateral fluid behind the tympanic membrane in another patient.

Table 1 Demographic characteristics and symptoms of hearing impairment

Characteristics	Myotonic dystrophy type 2 (n = 56)
Female sex	34 (61)
Age, y	
Mean (SD)	57 (11.8)
Range	31–78
Age at disease onset, y	
Mean (SD)	39 (13.4)
Range	12–71
mRS, median (P25–P75)	2 (2–3)
Cataract	36 (64)
Surgery	22 (39)
Diabetes mellitus	8 (14)
Arrhythmia	13 (25)
Hearing impairment[a]	42 (75)
Slowly progressive	39 (93)
Sudden[b]	3 (7)
Age at onset hearing impairment, y[c]	
Mean (SD)	51 (10.6)
Range	26–73
Hearing aid[d]	12 (21)
Noise exposure	16 (29)
Otitis in history	11 (20)
Tinnitus	18 (32)
Vertigo	13 (23)
PTA: Hearing impairment[e]	
None (0–20 dB)	21 (38)
Mild (21–40 dB)	22 (39)
Moderate (41–70 dB)	12 (21)
Severe (<71 dB)	1 (2)

Abbreviations: mRS = modified Rankin Scale; PTA = pure tone audiometry.
Data are n (%) unless otherwise specified.
[a] Hearing impairment: none in 2, mild in 3, moderate in 2, and severe in 1 patient.
[b] Both patients with acoustic schwannoma and meatoplasty had acute hearing impairment unilaterally; one other patient had unilateral sudden deafness, which recovered completely.
[c] 32 Patients; 2 did not know the age at onset of hearing impairment; in 8 patients, it is unknown.
[d] Median age 65 years (range 37–76), in 10 (83%) patients bilaterally.
[e] Mean 0.5, 1, 2, and 4 kHz in the best ear.

Pure tone audiometry (n = 56, 110 ears)

The threshold values were symmetrical (≤10 dB HL) between right and left in 39 patients (72%). An asymmetry was observed for 2 frequencies in 10 patients (maximum difference 25 dB HL), for 3 frequencies in 1 patient, for 4 frequencies in 3 patients (maximum difference 35 dB HL), and, in 1 patient, all frequencies differed more than 10 dB HL.

Bone conduction audiometry was performed in 33 patients (62 ears; in 4 patients bone conduction was only measured unilaterally given the symmetrical air conduction results and absent air–bone gap) in addition to air conduction. Ninety-eight percent (61 ears) had no air–bone gap. One patient had an

air–bone gap of 25 dB HL on the right. He also had asymmetric air conduction thresholds, and fluid behind the right tympanic membrane, and thus had mixed hearing impairment.

Mean hearing threshold level (average of 0.5, 1, 2, and 4 kHz) was more than 30 dB in at least one ear in 25 patients (44.6%), indicative for the use of hearings aids.[29]

Sixteen patients had a history of noise exposure. Patients with and without noise exposure were compared by calculating the excess in hearing impairment for each frequency. A difference was found for 2 kHz only ($p = 0.02$, Mann-Whitney U test) in favor of patients without noise exposure, but not for the frequencies 0.25, 0.5, 1, 4, and 8 kHz ($p = 0.71$, 0.90, 0.31, 0.17, and 0.73, respectively).

Pure tone audiometry compared to ISO 7029 (n = 40, 78 ears)

In 87% of all included ears (n = 40, 78 ears, 16 patients with noise exposure excluded) at least 1 of the frequencies was outside the P95 of normal (1 frequency in 22%, 2 frequencies in 24%, 3 frequencies in 10%, 4 frequencies in 20%, 5 frequencies in 16%, and all frequencies in 9%; figure e-2, http://links.lww.com/WNL/A137). All 8 patients younger than 40 years (median 32, range 31–35) had at least 1 hearing threshold outside the P95 of normal. Median hearing impairment for each frequency is presented in table 2 and figure 2. For both all included ears and the best ear only, median hearing impairment was higher than the corresponding P50 for all frequencies ($p < 0.001$, sign test).

Figure e-3 (http://links.lww.com/WNL/A137) demonstrates the correlation between excess in hearing impairment and age (Spearman ρ 0.514, $p < 0.001$). Also, a correlation was found between excess in hearing impairment and mRS (Spearman ρ 0.271, $p = 0.016$).

Speech audiometry (n = 56, 110 ears)

Speech recognition was normal in 90% (104 ears). In 5 patients (6 ears), speech recognition was below 90%, and all these cases showed severe hearing impairment (unilateral loss of speech recognition of 88%, 85%, 85%, and 55%, and bilateral 75% and 30%, respectively).

Tympanometry and acoustic middle ear muscle reflexes (n = 51, 101 ears)

Tympanometry was normal in 94% of cases. One patient with frequent otitis in the past and a labyrinthitis had a unilateral type B tympanogram. Two patients had a bilateral type C tympanogram, 1 patient had a retracted tympanic membrane on the left, the other patient had fluid behind the right tympanic membrane and had severe hearing impairment. Acoustic reflexes were absent in 8 patients (4 bilateral, 4 unilateral), probably due to the severe hearing impairment in all but 2 cases.

BAEP (n = 51, 102 ears)

All BAEPs were normal, except for one, showing a prolonged latency of the I-V complex on the left. In 14%, no reproducible response was found.

Discussion

We present the results of a comprehensive study on audiologic characteristics in a large international cohort of patients with genetically confirmed DM2 from multiple families. Hearing impairment was reported by 75% of the patients, and PTA results clearly established that hearing impairment is a common symptom in patients with DM2. Furthermore, the absence of an air–bone gap in PTA, concordant speech audiometry to PTA, normal tympanometry, and normal BAEPs strongly suggest that the origin of the sensorineural hearing impairment is located in the cochlea.

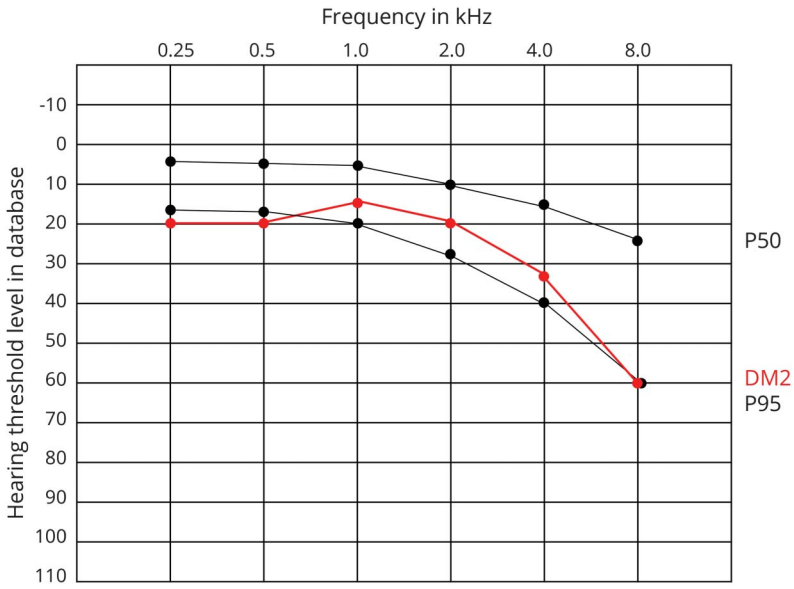
Hearing impairment has been reported in several case reports of PROMM, proximal myotonic dystrophy, and DM2, including in different familial cases.[13,15–18,30] Sensorineural deafness was described in 40% of 60 patients with DM2, although the severity was not otherwise specified.[14] Also, 6 out of 22 patients with DM2 were reported with hearing

Table 2 Results of pure tone audiometry

Frequency, kHz	Hearing threshold (dB), all ears (n = 78)	Hearing threshold (dB), best ear (n = 40)	P50 (ISO 7029 values)	*p* Value[a]
0.25	20 (15–30)	20 (10–25)	4.5 (3–6)	<0.001
0.5	20 (15–30)	20 (10–30)	5 (4–7)	<0.001
1	15 (10–35)	15 (10–32.5)	5.5 (4–8)	<0.001
2	20 (10–40)	17.5 (10–37.5)	10 (6–14)	<0.001
4	32.5 (20–50)	27.5 (15–50)	15.5 (9–24)	<0.001
8	60 (40–80)	55 (32.5–77.5)	24.5 (15–36)	<0.001

Median (P25–P75) hearing impairment for each frequency, for all included ears and best ears. The P50 was calculated according to the ISO 7029 for each participant of the same sex and age; the median of all participants is shown. The signed-rank test was used to calculate the difference between the median of the myotonic dystrophy type 2 population and the corresponding P50, according to the ISO 7029 standard.
[a] For both all ears and best ears.

Figure 2 Pure tone audiometry with median hearing threshold of each frequency for both ears



The median hearing threshold in decibels is shown for each frequency in patients with myotonic dystrophy type 2 (DM2) (red line), as well as the P50 and P95 for healthy controls with the same age and sex (black lines), according to the ISO 7029.

impairment before age 60 years.[12] The results of the PTA of the present study confirm and extend these reports, and establish the high prevalence of hearing impairment in patients with DM2, while the additional investigations indicate the origin in the cochlea.

Sensorineural hearing impairment is also an established feature of DM1, a disorder that shares many clinical similarities to DM2.[12] In DM1, a prominent hearing impairment of the higher frequencies has been found, implicating a precocious auditory dysfunction similar to an early presbycusis.[7–11] Interestingly, in the present study, more patients had abnormal hearing thresholds (>P95) on the lower frequencies (0.25 and 0.5 kHz) compared to the higher frequencies. However, hearing impairment was more severe at the higher frequencies (4 and 8 kHz). Moreover, a significant correlation was found between hearing impairment and age, even when corrected for presbycusis. Hearing impairment in DM2 is present in all frequencies and suggests early presbycusis like in DM1. It would be of interest to repeat the present study in a large group of patients with DM1 to compare the results. Moreover, an interesting additional objective test is otoacoustic emission, to screen for the presence of hearing impairment and to confirm the localization in the cochlea.[9]

The finding of early presbycusis is of interest for the hypothesis that many symptoms of myotonic dystrophies can be viewed as a result of premature aging, such as muscular weakness, cataract, baldness, and cognitive decline.[31] Both DM2 and DM1 are considered spliceopathies, meaning that the repeat expansion leads to an alteration of alternative splicing.[20] The current investigations locate the origin of hearing impairment in DM2 in the cochlea, as in DM1.[8,9] Particularly vulnerable for injury in the cochlea are the stria vascularis and inner and outer hair cells; these sites are probably also involved in presbycusis.[32] Malfunctioning of the outer hair cells may play a role in DM1, due to somatic electromotility alteration that affects voltage-dependent shape changes in DM1.[9] Accordingly, cochlear dysfunction may be linked to a misregulation of an alternative splicing of ionic channels or cytoskeletal myosin proteins able to interact with membrane channels in outer hair cells.[33] The same mechanism may be applied to DM2, and could explain why patients with DM1 and DM2 show sensorineural hearing impairment.

Another interesting possible explanation is the finding of a locus for hearing impairment (*DFNA-18*) immediately adjacent to the DM2 locus.[34] A family was described with autosomal dominant nonsyndromal progressive hearing impairment with an onset in the first decade of life, affecting the higher frequencies first and the middle and lower frequencies in the following decades. The *DFNA18* locus has also been linked to age-related hearing impairment.[35] In both DM1 and DM2, the repeat expansion influences the expression of neighboring genes.[32,36] Perhaps this locus for hearing impairment is influenced by the repeat expansion of the *CNBP* gene. An autosomal dominant locus for hearing impairment has been found close to the DM1 locus as well (*DFNA4*).[37]

Acoustic middle ear reflexes were absent in 8 patients. Perhaps this is caused by the severe hearing impairment in these patients. However, this could also be explained by weakness of the stapedius muscle as part of DM2.

In DM1, the symptoms may worsen with from one generation to the next, a well-known mechanism called anticipation that also concerns hearing impairment.[7] Anticipation does not seem to play a role in DM2, or at least is very rare.[2,38] In this study, no evidence of anticipation for hearing impairment was found. Indeed, the excess in hearing impairment was worse in the older generation than the younger generation in 3 of 4 related family members.

While there is no causal treatment for DM2, the finding of hearing impairment is important for daily clinical practice to treat patients symptomatically. Patients with DM2 should be asked about hearing impairment and be informed about the risk of early presbycusis. Audiometry should be performed readily. Furthermore, DM2 may be added to the differential diagnosis of the combination of proximal muscle weakness and hearing impairment, also associated with mitochondrial myopathies (both adult-onset slowly progressive mild to moderate sensorineural hearing impairment as well as sudden-onset hearing impairment),[39,40] facioscapulohumeral dystrophy (adult-onset sensorineural hearing impairment as well as child-onset progressive high-frequency hearing impairment in patients with a genetic small EcoRI/bInI fragment)[e1,e2] (http://links.lww.com/WNL/A138), and occasionally, limb-girdle muscle dystrophies (mild to moderate hearing impairment in patients with LGMD2D).[e3]

Strengths of the present international study are the large cohort of patients with DM2 and the extensive hearing tests. Nonrespondent bias of the Dutch patients may have affected the results as the participants may not be representative for the whole Dutch cohort, although almost all of the invited French patients participated. A limitation is the cross-sectional study design; it would be of interest to investigate whether hearing impairment is already present when DM2 is diagnosed. All ears were included to enlarge statistical power. However, PTA was also calculated for only the best ear of each participant as 2 ears are not entirely independent. The same significant differences were found when compared to the P50.

The present study distinctly established that hearing impairment is a frequent symptom in patients with DM2. Hearing impairment was mild in 39%, moderate in 21%, and severe in 2% of patients. All hearing tests performed suggest a sensorineural hearing impairment due to cochlear damage evoking a possible early presbycusis. Clinicians should inform all patients with DM2 about the risk of hearing impairment, and readily perform audiometry and prescribe hearing aids when indicated.

Author contributions

Judith van Vliet: study concept and design, acquisition of data, analysis of data, statistical analysis, drafting the manuscript. Alide Tieleman: study design, study supervision, revision of manuscript. Baziel van Engelen: study design, study supervision, revision of manuscript. Guillaume Bassez: acquisition of data, revision of manuscript. Laurent Servais: acquisition of data, revision of manuscript. Anthony Béhin: acquisition of data, revision of manuscript. Tanya Stojkovic: acquisition of data, revision of manuscript. Jan Meulstee: analysis of data, revision of manuscript. Joost Engel: study design, acquisition of data, analysis of data, revision of manuscript. George Lamas: acquisition of data, analysis of data, revision of manuscript. Bruno Eymard: study concept and design, study supervision, revision of manuscript. Wim Verhagen: study design, analysis of data, study supervision, revision of manuscript. Elisabeth Mamelle: study concept and design, acquisition of data, analysis of data, study supervision, revision of manuscript.

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Hearing impairment in patients with myotonic dystrophy type 2

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Study question

What are the characteristics of auditory function in patients with genetically confirmed myotonic dystrophy type 2 (DM2)?

Summary answer

Cochlear sensorineural hearing impairment was common among patients with DM2 and it correlated with the patient's age.

What is known and what this article adds

Hearing impairment is a well-characterized feature of DM1, yet no study to date has systemically evaluated this symptom in patients with DM2. The present study provides evidence to challenge the designation of hearing impairment as a non-classical feature of DM2.

Participants and setting

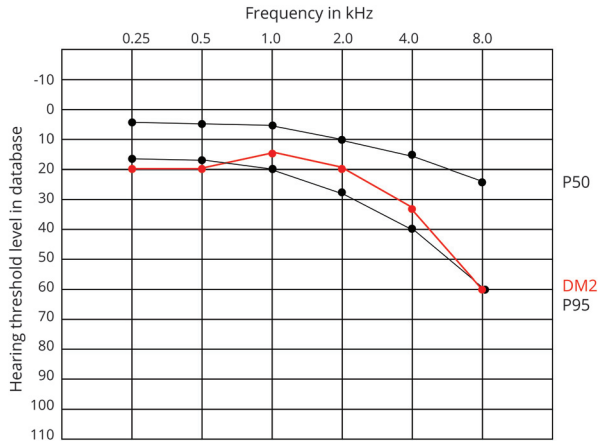
The study included 31 patients enrolled from the known DM2 population in the Netherlands and 25 patients from the Myology Institute in France (61% women). All patients had genetically confirmed DM2.

Design, size, and duration

The study was a cross-sectional analysis of patients with DM2, prospectively enrolled between September 2013 and March 2015. Patients completed a structured interview about hearing symptoms, a standardized otologic examination, and specialized testing to determine characteristics of auditory function.

Primary outcomes

Primary outcomes included findings from pure tone audiometry, speech audiometry, tympanometry and acoustic middle ear muscle reflexes, and brainstem auditory evoked potentials (BAEPs). Impairment was assessed by comparison with the ISO 7029 standard.



Main results and the role of chance

The median hearing threshold of patients in the DM2 cohort was higher compared to the 50th percentile of normal individuals for all measured frequencies ($p < 0.001$). Hearing impairment was mild in 39% of patients, moderate in 21% of patients, and severe in 2% of patients with DM2. The absence of an air–bone gap combined with normal speech audiometry and BAEP findings indicated cochlear sensorineural hearing impairment. A correlation analysis revealed an association between hearing impairment and age, even after correcting for age-related hearing loss.

Bias, confounding, and other reasons for caution

The study was limited by a small sample size and cross-sectional design, which did not permit the assessment of hearing impairment at the time of diagnosis.

Generalizability to other populations

The results are applicable to other populations with DM2.

A draft of the short-form article was written by A. Symons, a writer with Editage, a division of Cactus Communications. The authors of the full-length article and the journal editors edited and approved the final version.

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